46th CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP) 2014

TORONTO, CANADA 22nd–25th OCTOBER, 2014 SIOP ABSTRACTS

ABSTRACT CONTENTS:

DOI 10.1002/pbc.25314
Published online in Wiley Online Library (wileyonlinelibrary.com).

46th CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP) 2014

TORONTO, CANADA 22nd–25th OCTOBER, 2014 SIOP ABSTRACTS

ORAL PRESENTATIONS

NEUROBLATSOMA 1

O-001

RESULTS OF AN INTENSIVE INDUCTION PROTOCOL FOR HIGH-RISK NEUROBLASTOMA IN MOROCCO (HR-NBL-MA-10)

M. Khattab[1], M. Elkababri[1], S. Cherkaoui[2], S. Benmiloud[3], J. ElHoudzi[4], L. Hessissen[1], C. Lam[5], N. Parikh[6], S. Howard[5], K. Matthay[7]

[1]Pediatrics, University Mohammed V-Souissi, Rabat, Morocco; [2]Hematology, Hospital 20 Août 1953, Casablanca, Morocco; [3]Pediatrics, University Hospital Hassan II, Fez, Morocco; [4]Oncology, University Hospital Mohammed VI, Marrakech, Morocco; [5]Oncology and International Outreach Program, St. Jude Children's Research Hospital, Memphis Tennessee, USA; [6]Hematology/Oncology, Connecticut Children's Medical Center, Hartford Connecticut, USA; [7]Pediatrics, UCSF Benioff Children's Hospital, San Francisco, USA

Objectives: The Survival for high-risk neuroblastoma in Morocco has been <10%, despite recent improvements in high-income countries to 50%. In 2012, we activated the first multi-center treatment protocol for high-risk neuroblastoma in Morocco, and report here the early results of our first aim, to test the feasibility, toxicity and response to an intensive induction therapy.
Methods: Eligible patients with newly diagnosed high-risk neuroblastoma from Rabat (n = 23), Casablanca (n = 15), Fez (n = 9), and Marrakech (n = 10) were treated with five cycles of rotating pairs of combination chemotherapy without G-CSF (*Pediatr Blood Cancer*2012; 59:902-7). Disease evaluations were performed at diagnosis and end of induction.
Results: Fifty seven patients were entered on study, including 53 with stage 4 disease and 4 with stage 3. The median age was 2.5 years. Initial evaluation showed metastases in bone (52%), bone marrow (75%), liver (14%) and 74% had adrenal primary. MIBG scans were performed in 17 patients, and MYCN copy number was determined in only 1 patient. As of February 1, 2014, 37 patients completed 5 cycles of induction, 9 progressed during induction and are off study, and 11 are still on induction therapy. The regimen was tolerable, without any toxic deaths. There were 17 hospitalizations for complications, consisting of 13 fever/neutropenia and 3 sepsis. At completion of induction therapy, 37 evaluable patients had 10 complete responses, 6 partial responses, 3 stable disease, 2 progressive disease. Surgery on the primary tumor was performed on 14 patients, with 9 complete resections.
Conclusions: An intensive induction therapy for high-risk neuroblastoma in a multi-center setting is feasible in Morocco without unusual toxicity and with response in 43%, which would allow proceeding with myeloablative therapy and ASCT, with improved chance of survival. Future efforts are underway to improve access to *MYCN* testing, MIBG scans, PBSC harvest and to ASCT.

O-002

LATE RECURRENCES, MORTALITY AND SECOND CANCERS IN FIVE-YEAR SURVIVORS OF HIGH RISK NEUROBLASTOMA

R. Mody[1], C. Van Ryn[2], W.B. London[3], J.R. Park[4], M.D. Hogarty[5], L. Diller[3]

[1]Pediatrics, University of Michigan, Ann Arbor, USA; [2]Biostatistics, University of Florida, Gainesville, USA; [3]Pediatrics, Dana-Farber Cancer Institute, Boston, USA; [4]Hematology/Oncology, Seattle Children's Hospital, Seattle, USA; [5]Oncology, Children's Hospital of Philadelphia, Philadelphia, USA

Objectives: To investigate late outcomes in 5-year survivors of high-risk neuroblastoma (HR-NB) treated between 2001 and 2009.
Methods: We identified a cohort of 708 HR-NB patients enrolled on the COG Neuroblastoma Biology Study ANBL00B1 who survived at least five years from diagnosis. The 5-year timepoint was chosen to be comparable to other survivor cohorts. Clinical, demographic and biologic features of this group were examined, including cause of death (COD) in those who subsequently died after 5 years. Event-free survival (EFS) and overall survival (OS) (± standard error) were calculated using the Kaplan-Meier method. Cumulative incidence of secondary malignant neoplasm (SMN) was calculated, and second tumors are described.
Results: Median follow-up time from diagnosis for the 5-year survivor cohort was 7.7 years (range: 5 to 12.1 years). Eleven SMNs were reported after 5 years from diagnosis: osteosarcoma (5), soft-tissue sarcoma (2), meningioma (1), thyroid cancer (1), AML (1), unknown (1). Cumulative incidence of SMN at 10 years from diagnosis was 3% ± 1%. 459 patients reached the 5-year timepoint without an event; for these survivors the 10-year EFS was 87% ± 6%. Seventy-nine patients died after the five-year time-point. COD included progressive disease (n = 73), treatment related toxicity (n = 3), SMN (n = 1) and other (n = 2). The OS at 10 years from diagnosis was 81% ± 3% (n = 708).
Conclusions: Within HR-NB patients who survive at least 5-years from original diagnosis, progressive NB remains a major cause of mortality; however, patients without a relapse before 5 years appear to have a favorable outcome. Further investigation of this newly established cohort will probe the incidence and impact of treatment-related illness and identify genetic factors associated with late toxicities including second cancer.

O-003

RELAPSES AFTER HDC AND ASCT IN HIGH RISK NEUROBLASTOMA PATIENTS: CLINICAL PRESENTATION, TREATMENT AND PROGNOSIS FACTORS

C. Dupraz[1], C. Pascalini[2], C. Dufour[2], B. Geoerger[2], V. Minard Colin[2], D. Valteau Couanet[3]

[1]Pédiatrie, CHU Poitiers, Poitiers, France; [2]Pédiatrie, Gustave Roussy, Villejuif, France; [3]Pédiatrie, Institut Gustave Roussy, Villejuif, France

Objectives: This study aimed analysing high-risk neuroblastoma recurrence after high dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT). To this purpose, we focused on clinical presentation, treatments performed, and prognosis factors.
Methods: Between 2000 and 2010, at Gustave Roussy Cancerology Institut, 67 out of 134 children affected with high-risk neuroblastoma, who had received HDC and ASCT, presented tumour recurrence.
Results: Out of 67 patients, 40 had a progression and 27 a relapse. There were 35 males and 32 females. Median age at diagnosis was 39.5 mos (3% <1 year; 74.6% between 1-5 years; 15 >5 years). 65 patients had a stage 4 neuroblastoma and 2 had a stage 3 with *MYCN* amplification. 17 patients (26%) presented *MYCN* amplification. HDC consisted of busulfan and melphalan in 62 patients (92%). Median time from transplantation to first relapse was 13 months (1-48). Median survival after recurrence was 9 months (0-28 months). All patients died but 3 (5.5%) who are alive (11 months+, 14 months+ and 50 months+). Patients (N = 35) treated with temozolomide alone or in combination with topotecan had the longest time to progression, median 122 days (4-632+). Oral etoposide (40 patients), even if administered late, increased survival with a good quality of life, median 65 days (9-393). Prognosis factors, influencing life

expectancy after recurrence, were: age at diagnosis <18 months, *MYCN* amplification, and time <1 year between diagnosis or transplantation and recurrence.
Conclusions: Outcome after recurrence post HDC and ASCT is poor. However, factors involved in life expectancy duration can be identified. These factors should be taken into account in trials evaluating new treatment strategies as well as stratification criteria in randomized studies to avoid bias and wrong conclusions.

O-004

VIROTHERAPY DELIVERED BY AUTOLOGOUS MESENCHYMAL STEM CELLS FOR CHILDREN WITH METASTATIC AND REFRACTORY NEUROBLASTOMA: RESULTS OF A TRIAL OF COMPASSIONATE USE

M. Ramírez[1], J. García-Castro[2], R. Alemany[3], G.J. Melen[1], L. Franco[1], A. González-Murillo[1], I. Mirones[2], M. Bazán-Peregrino[3], D. Ruano[1], L. Madero[1]

[1]Hematology & Oncology, Hospital Niño Jesús, Madrid, Spain; [2]Cellular Biotechnology Unit, Instituto de Salud Carlos III, Madrid, Spain; [3]Cancer Virotherapy, Instituto Català d'Oncología IDIBELL, Barcelona, Spain

Objectives: We have developed a new strategy for the systemic delivery of oncolytic viruses: Celyvir. Celyvir consists of autologous marrow-derived mesenchymal stem cells (MSCs) carrying an oncolytic adenovirus. We previously reported a pilot study on the use of Celyvir in 4 children with metastatic neuroblastoma (NB) (Cancer Gene Therapy, 2010, 17: 476) and now present the extended clinical experience of this program of compassionate use of Celyvir in 14 new patients.
Methods: The Spanish Medicine Agency and the hospital internal review board approved the trial. All patients had failed to at least 3 lines of therapy, and presented a metastatic disease. The children received multidosis of Celyvir in a weekly basis (minimum 4, maximum 70, total 218) with no concomitant treatments. Total cells (min. 70×10^6, max. 2640×10^6) and viral particles (min. $1{,}8 \times 10^{12}$, max. $5{,}28 \times 10^{13}$) varied among patients. Hematological and biochemical test were done in blood samples at the time of each infusion. Clinical outcome was evaluated after 8 doses.
Results: The tolerance was excellent, with very mild and autolimited viral-related toxicities. Peripheral blood lymphocytes raised and the profile of tumor infiltrating lymphocytes (whenever a biopsy was available) changed after Celyvir therapy. Clinical outcomes were progression (10), stable disease (1), partial remission (3) and complete remission (1). The patient with a complete response relapsed after 6 months and received a second round of Celyvir, achieving a partial remission. MSC cultures presented differences in the expression levels of adhesion molecules and immune-related molecules, suggesting interpatient differences in the homing and immune modulation capacities of the therapy administered.
Conclusions: Celyvir has an excellent safety profile in children with metastatic NB. Further uses of this strategy are needed in order to find out factors related with efficacy.

EPIDEMIOLOGY 1

O-005

A STATEWIDE ASSESSMENT OF CHILDHOOD CENTRAL NERVOUS SYSTEM TUMORS AND TRAFFIC-RELATED AIR POLLUTION

H. Danysh[1], L. Mitchell[2], K. Zhang[2], M. Scheurer[1], P. Lupo[1]

[1]Department of Pediatrics Hematology-Oncology Section, Baylor College of Medicine, Houston, USA; [2]Division of Epidemiology Human Genetics and Environmental Sciences, University of Texas School of Public Health, Houston, USA

Objectives: Few risk factors have been identified for childhood central nervous system (CNS) tumors. Due to increasing concerns regarding air pollution and childhood cancer risk, we conducted a population-based assessment evaluating the association between selected traffic-related air pollutants (benzene, 1,3-butadiene, or diesel particulate matter [DPM]) and the incidence of childhood CNS tumors.
Methods: All CNS tumors diagnosed at <15 years of age in Texas for the period of 2001-2009 (n = 2,014) were identified from the Texas Cancer Registry. Information on the corresponding at-risk population was obtained from the 2000 United States' (US) Census. Annual census tract-level pollutant concentrations, estimated by the US Environmental Protection Agency's 2005 National-Scale Air Toxics Assessment, were categorized (low, medium, medium-high, and high) using cutpoints based on quartiles of the statewide distribution of each pollutant. Poisson regression was used to estimate relative risk (RR) and 95% confidence intervals (CI) adjusted for age at diagnosis, sex, race/ethnicity, and area-level poverty. Tumor phenotypes were independently evaluated and included astrocytomas (n = 386), medulloblastomas (n = 243), ependymomas (n = 145), and primitive neuroectodermal tumors (PNET) (n = 49). The affiliated institutions' Institutional Review Boards approved this study and waived informed consent.
Results: Medium DPM levels were associated with increased incidence of all CNS tumors (RR = 1.20, 95% CI: 1.06-1.37) and astrocytomas (RR = 1.42, 95% CI: 1.05-1.94) compared to low DPM levels. Medium and medium-high 1,3-butadiene levels were associated with increased incidence of astrocytomas (RR = 1.46, 95% CI: 1.05-2.01 and RR = 1.69, 95% CI: 1.22-2.33, respectively) and were suggestive of an increased incidence of PNET (RR = 2.60, 95% CI: 0.94-7.24 and RR = 2.76, 95% CI: 0.98-7.72, respectively) compared to low levels. No statistically significant associations were found with medulloblastoma or ependymoma incidence.
Conclusions: This large population-based assessment indicates a positive association between traffic-related air pollution and childhood CNS tumors, particularly among astrocytomas. Additionally, our results suggest a strong positive association with PNET, although, not statistically significant.

O-006

TEMPORAL CLUSTERING OF NEUROBLASTOMA IN CHILDREN AND YOUNG PEOPLE FROM NORTHERN ENGLAND

C.R. Muirhead[1], D.A. Tweddle[2], R. McNally[1]

[1]Institute of Health & Society, Newcastle University, Newcastle Upon Tyne, United Kingdom; [2]Northern Institute of Cancer Research, Newcastle University, Newcastle Upon Tyne, United Kingdom

Objectives: The aetiology of neuroblastoma (NB) is unclear. Hereditary NB with germline mutations accounts for < 1% of all NB with single nucleotide polymorphisms predisposing to NB in other cases. Environmental factors have also been implicated with the possibility that an infectious agent may be involved. 'Temporal clustering' occurs if cases display an irregular temporal distribution and may provide evidence for the aetiological involvement of an agent that exhibits epidemicity. We tested for the presence and nature of temporal clustering of date of diagnosis.
Methods: We extracted all cases of NB diagnosed in children and young people aged 0-24 years during 1968-2003 from the Northern Region Young Persons' Malignant Disease Registry. This population-based registry includes all cases of cancer in children and young people who were resident in northern England at the time of diagnosis. Tests for temporal clustering were applied using a modified version of the Potthoff-Whittinghill method. Estimates of extra-Poisson variation (beta), together with standard errors (SEs), were obtained.
Results: There were 193 cases of NB diagnosed during the study period. All the analyses between fortnights and between months found significant extra-Poisson variation, with estimates of beta of 0.440 (SE 0.179, $P = 0.009$) for the analysis between months within quarters, and 0.609 (SE 0.334, $P = 0.036$) for the analysis between fortnights within months. Restricting the analyses to the 49 cases diagnosed at age < 1 year did not show significant evidence of extra-Poisson variation, although there was borderline evidence from the analysis between fortnights within months (estimated beta = 2.006, SE 1.155, $P = 0.057$).
Conclusions: This study suggests that transient environmental agents may be involved in NB aetiology in children and young people. In particular, our findings indicate that the initiating factor might be an agent such as an infection that occurs in 'mini-epidemics'.

O-007

CONSTITUTIVE MISMATCH REPAIR DEFICIENCY SYNDROME: CLINICAL DESCRIPTION IN A FRENCH COHORT

C. Colas[1], G. Sebille[2], O. Cabaret[3], C. Charpy[4], T. Frebourg[5], N. Entz Werle[6], Q. Wang[7], S. Lejeune[8], D. Leroux[9], G. Couillault[10], G. Leverger[11], F. Bourdeaut[12], M. Muleris[13], O. Caron[14], L. Brugieres[15]

[1]Genetic, Pitié Salpétriére University Hospital, Paris, France; [2]Dermatology, Gustave Roussy, Villejuif, France; [3]Biology and Medical Pathology, Gustave Roussy, Villejuif, France; [4]Pathology, Gustave Roussy, Villejuif, France; [5]Genetic, CHU Rouen, Rouen, France; [6]Pédiatrie, Strasbourg University Hospital, Strasbourg, France; [7]Genetic, Centre Léon Bérard, Lyon, France; [8]Clinical Genetic, Jeanne de Flandre University Hospital, Lille, France; [9]Genetic, Grenoble University Hospital, Grenoble, France; [10]Pediatry, Dijon University Hospital, Dijon, France; [11]Pediatry, Armand Trousseau University Hospital, Paris, France; [12]Pediatry, Institut Curie, Paris, France; [13]Cancer, INSERM UMR S938, Paris, France; [14]Medical Oncology, Gustave Roussy, Villejuif, France; [15]Pédiatrie, Institute Gustave Roussy, Villejuif, France

Objectives: Constitutive mismatch repair deficiency syndrome (CMMR-D) is a recently described childhood cancer predisposition syndrome involving biallelic mutation of MMR genes (*MLH1, MSH2, MSH6* and *PMS2*). More than 140 cases have been previously reported but only as case reports. We present here the first series of unselected patients.
Methods: We performed a retrospective review of all 28 cases of CMMR-D diagnosed in French genetics laboratories in order to describe clinical characteristics, treatment and outcome of malignancies, and biological diagnosis data of an unselected series of patients.
Results: Overall, 60 tumors were diagnosed in these 28 patients, 17 (28%) hematologic malignancies, 19 (32%) brain tumors, 21 (35%) Lynch syndrome-associated malignancies, and 3 (5%) other tumors. Median age of onset of first tumor was 6.98 years [1.23-22]. 21 (75%) patients had NF1-unrelated CALMs or hypopigmented macules and 4 (14%) had brain malformative features. Overall, 18 patients died, 7 (39%) due to the primary tumor. Median survival after diagnosis of the primary tumor was 23.3 months [0.26-213.2]. Among the patients who survived after their first malignancy, 19 (68%) developed a second malignancy. No obvious excess of toxicity to treatment was reported. A familial history of LS-associated cancer was found in only 5 families, and consanguinity in 35% of cases. *PMS2* mutations (15 patients) were more frequent than mutations of *MLH1 (4 pts), MSH2* (3 pts) and *MSH6 (6 pts)*.

Conclusions: CMMR-D is a severe condition associated with multiple malignancies in childhood. Its rarity warrants international collaboration to define diagnosis criteria and guidelines for surveillance and prevention in order to decrease tumor-related mortality.

O-008

MOLECULAR CHANGES IN SAUDI PATIENTS WITH FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

A. Al-Ahmari[1], A. Sheereen[2], T. Elamin[2], A. Jabr[2], M. Al- Awwami[3], O. Alsmadi[2], L. Eibaik[2], S. Al-Shambri[1], I. Al-Fawaz[1], M. Ayas[1], B. Al Saud[4], M. Viqaruddin[1], K. Siddiqui[1], A. Hawwari[1]

[1]PHO, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [2]Genetics Research Center, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [3]Pathology and Laboratory Medicine, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [4]Pediatric Allergy/Immunology, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

Objectives: Familial Hemophagocytic lymphohistiocytosis (FHL) in different ethnicities has been described in the literature, but this is the first report from Saudi Arabia. Here we describe the mutations present in FHL genes in Saudi patients diagonsed with FHL.
Methods: DNA from 87 patients diagnosed with FHL were used for mutation detection in various FHL-causing genes by PCR- sequencing method.
Results: In a total of 15 patients with STX11 gene, a novel mutation (c.173 C > T) were identified in 14 patients of the same tribe. Another one (Q140Pfs*46) was identified in one patient. Among 7 patients with PRF1 gene mutations one patient was found to have a nonsense novel mutation (W374*). For 12 patients with UNC13D gene, Y673 STOP, E1017R, V495Gand A1018D; C > A were identified in one, five, one and two patients respectively. The previously reported mutation (c.766 C > T; R256X) were identified in 3 patients. Although, STXBP2 was found to be the most common defective gene of FHL in Saudis, only one novel mutation (W288R) was found in one patient, the remaining 24 patients were found to have the previously reported P477L mutation. Four patients were found to have 3 novel mutations (Splice site c. 9044+1G > T EX39, Splice site c.7503+1G > C EX43 and A1546V) in LYST gene. Another two novel mutation (I397Nfs*405 and K134Q) were identified in one and two patients with XIAP and Rab27A respectively. All patients with STX11 mutations were from one tribe and majority of patients with STXBP2 mutations were from another tribe. No molecular defects were identified in the remaining 21 (24%) patients.
Conclusions: Almost half of the mutations in our FHL cohort were novel. This data shows the high consanguinity rate in Saudi population. There are still more genetic aberrations to be discovered in this subset of patients as no molecular defects were identified in a quarter of our patients.

SUPPORTIVE CARE

O-009

ANALYSIS OF PALONOSETRON VS ONDANSETRON IN PREVENTING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV) IN PEDIATRIC PATIENTS RECEIVING MODERATELY OR HIGHLY EMETOGENIC CHEMOTHERAPY (MEC/HEC)

G. Kovacs[1], A.E. Wachtel[2], E.V. Basharova[3], T. Spinelli[4], P. Nicolas[4], E. Kabickova[5]

[1]Second Department of Pediatrics, Semmelweis University, Budapest, Hungary; [2]Department of Pediatrics, Institutoi Nacional de Enfermedades Neoplasicas, Lima, Peru; [3]Oncohematology Center, Chelyabinsk Pediatric Regional Clinical Hospital, Chelyabinsk, Russia; [4]Research and Development, Helsinn Healthcare SA, Lugano/Pazzallo, Switzerland; [5]Department of Pediatric Hematology and Oncology, Charles University 2nd Medical School, Prague, Czech Republic

Objectives: Evaluate efficacy/safety of two palonosetron (PALO) dose-levels, compared with ondansetron (standard comparator) in preventing CINV in pediatric patients receiving MEC or HEC in a multicenter, multinational, randomized, double-blind, non-inferiority study.
Methods: Patients with malignant disease scheduled for treatment with MEC or HEC were randomized to receive PALO 10 mcg/kg, PALO 20 mcg/kg, or ondansetron (three 150 mcg/kg doses) and stratified by emetogenicity (HEC/MEC, day 1) and age.
Results: A total of 502 patients were randomized and 493 included in the full analysis set (166 PALO 10 mcg/kg, 165 PALO 20 mcg/kg, 162 ondansetron). Patients ranged in age from 64 days to 16.9 years. The majority were male (53.1%) and white (95.1%). The CR rate across the age groups ranged from 53.3%–59.3% for ondansetron, 41.3%–70.4% for PALO 10 mcg/kg and 50.0%–74.1% for 20 mcg/kg. For patients treated with HEC, the CR rate was higher for PALO 10 mcg/kg and 20 mcg/kg (42.6% and 51.0%, respectively) compared with ondansetron (41.2%). For MEC, the PALO 20 mcg/kg CR rate was higher (62.9%), than 10 mcg/kg (59.8%) and comparable to ondansetron (66.7%). The percentage of treatment-emergent adverse events (including prolonged electrocardiogram QT) and serious adverse events, according to age strata and emetogenicity, were similar. All study withdrawals/deaths were unrelated to study drug.
Conclusions: High-dose PALO (20 mcg/kg), given as a single dose, was more effective in preventing CINV in pediatric patients receiving MEC/HEC compared with ondansetron. The results indicate higher-dosage PALO does not require dose adjustment according to patient age. The safety profiles raised no concerns.

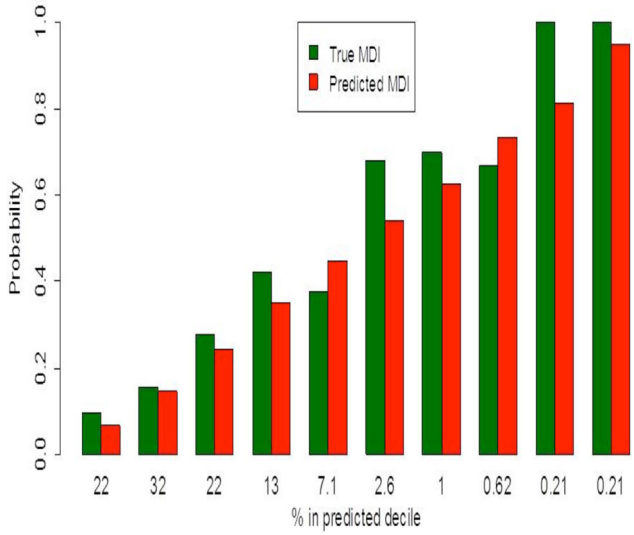
O-010

SIX PRESENTING CLINICAL VARIABLES ROBUSTLY PREDICT THE RISK OF MICROBIOLOGICALLY DEFINED INFECTION IN FEBRILE NEUTROPENIC EPISODES

B. Phillips[1], on behalf of the PICNICC Collaboration[2]

[1]Centre for Reviews and Dissemination, University of York, York, United Kingdom; [2]York, United Kingdom

Objectives: Risk stratified management of febrile neutropenia (FN), also known as "fever with neutropenia", allows intensive management of high-risk cases and early discharge of low-risk cases. No single, internationally validated, prediction rule exists for children and young people. An individual participant data (IPD) pooled analysis was undertaken to devise one.
Methods: The "Predicting Infectious ComplicatioNs In Children with Cancer" (PICNICC) collaboration was formed by engaging international clinical and methodological experts, authors of studies identified in the systematic reviews, parent representatives and healthcare researchers. The PICNICC collaboration consists of 22 different study groups from 15 countries.
Results: IPD information from 5,127 episodes of FN in 3,504 patients was provided for meta-analysis, with 1,070 episodes in 616 patients from 7 studies in higher-income countries suitable for multivariate analysis. Univariate analyses showed anticipated associations between microbiologically defined infection (MDI) and higher temperature, lower white cell counts and a diagnosis of acute myeloid leukaemia. There was no clear relationship demonstrated between age and risk of MDI. Episodes in osteosarcoma/Ewings sarcoma patients and patients with more severe mucositis were associated with a decreased risk of MDI. The multivariable risk prediction model derived from the IPD had six components: Tumour type, temperature, clinically "severely unwell", haemoglobin, white cell count and absolute monocyte count. This model showed moderate discrimination (AUC ROC 0.736) and good calibration (calibration slope 0.95, figure) and was robust to bootstrap and cross-validation sensitivity analyses.



Conclusions: This new risk prediction model for microbiologically defined infection is robust to internal validation techniques but requires prospective validation and studies of implementation. A basic implementation of the model has been made 'live' on: http://tinyurl.com/PICNICC1. When validated this could be adapted to work off a web page or smartphone 'app' to assist clinicians in individualised decision making regarding location and intensity of therapy.

O-011

REDUCTION OF CATHETER ASSOCIATED BLOODSTREAM INFECTIONS IN PAEDIATRIC ONCOLOGY PATIENTS USING ETHANOL LOCKS; A RANDOMIZED CONTROLLED TRIAL

R. Schoot[1], C.H. van Ommen[2], T. Stijnen[3], W.J. Tissing[4], H. Heij[5], J. Lieverst[6], L. Spanjaard[7], H.N. Caron[8], M.D. van de Wetering[8], S. Skion Aristocaths[9]

[1]Paediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [2]Paediatric Hematology, Emma Children's Hospital/Academic Medical Center,

Amsterdam, Netherlands; [3]Biostatistics, University Hospital of Leiden, Leiden, Netherlands; [4]Paediatric Oncology/Hematology, University Hospital of Groningen, Groningen, Netherlands; [5]Paediatric Surgery, Academic Medical Centre and VU Amsterdam, Amsterdam, Netherlands; [6]Datamanagement, Dutch Cancer and Oncology Group, The Hague, Netherlands; [7]Microbiology, Academic Medical Centre, Amsterdam, Netherlands; [8]Paediatric Hematology/Oncology, Emma Children's Hospital/Academic Medical Centre, Amsterdam, Netherlands; [9]Paediatric Oncology, Dutch Cancer Oncology Group, The Hague, Netherlands

Objectives: The prevention of central venous catheter- (CVC-) associated bloodstream infection (CABSI) in pediatric oncology patients is essential. Ethanol locks can eliminate biofilm embedded pathogens and have no known microbial resistance. Up to date no randomized controlled trial in pediatric oncology has been performed on the efficacy of ethanol locks to reduce CABSI. This study's objective was to determine whether 70% ethanol locks can cause a 50% reduction in CABSI in pediatric oncology patients.
Methods: We conducted a randomized, double blind, multicenter trial in pediatric oncology patients (1-18 years) with newly inserted CVCs. Patients were randomly assigned to receive two hour ethanol locks (3 ml 70%) or heparin locks (3 ml 100 IU/ml), maximum frequency once weekly. Primary outcomes were CABSI, CVC removal or death due to CABSI.
Results: We included 307 patients, 153 were allocated to ethanol and 154 to heparin locks. In the ethanol group 16/153 (10%) patients were diagnosed with CABSI versus 29/154 (19%) in the heparin group; incidence was 0.77/1000 and 1.46/1000 catheter days respectively ($p = 0.04$), resulting in a number-needed-to-treat of 12 patients. Particularly Gram-positive CABSIs (ethanol, $N = 8$; heparin, $N = 21$; $p = 0.01$) were reduced. Less CVCs were removed because of CABSI in the ethanol group (ethanol, $N = 5$; heparin, $N = 12$; $p = 0.08$). No patients died because of CABSI. During ethanol locks patients experienced significantly more transient symptoms compared to heparin locks (maximum grade 2) (nausea, $p = 0.03$; taste alteration, $p < 0.001$; dizziness, $p = 0.001$; *blushing, $p < 0.001$), no suspected unexpected serious adverse reactions (SUSAR) occurred.*
Conclusions: This RCT showed that ethanol locks can prevent CABSI in pediatric oncology patients, in particular CABSI caused by Gram-positive bacteria. Implementation of ethanol locks in daily practice should be considered.

O-012

A RANDOMIZED OPEN LABELED PARALLEL GROUP PHASE III STUDY OF ANTIBIOTICS ALONE VS. ANTIBIOTICS PLUS G-CSF IN PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA IN A LOW-INCOME SETTING

B. Arora[1], S. Banavali[1], T. Vora[1], G. Chinnaswamy[1], M. Prasad[1], A. Paradkar[1], P.A. Kurkure[1], R. Havaldar[2], G. Narula[1], S. Talole[3]

[1]Pediatric Oncology, Tata Memorial Hospital, Mumbai, India; [2]Clinical Research Secretariat, Tata Memorial Hospital, Mumbai, India; [3]Biostatistics & Clinical Records, Tata Memorial Hospital, Mumbai, India

Objectives: Granulocyte colony-stimulating factor (G-CSF) use in children with febrile neutropenia (FN) in high-income countries has been shown to decrease the duration of FN, hospital admission, and antibiotics usage with no reduction in infection related complications and mortality. FN in low-income countries (LIC) is associated with higher degree of morbidity and mortality due to limitations in supportive care, limited manpower and host comorbidities such as malnutrition. Hence, reduction in duration of FN by G-CSF in LIC setting may have much more impact on morbidity and mortality and would be potentially more cost-effective.
Methods: In this prospective randomized study, 200 pediatric patients with FN were randomized to receive antibiotics with G-CSF (filgrastim; 5 microgram/kg/d subcutaneously) or antibiotics alone. Children were stratified for their diagnosis and focus of infection. GCSF was started within 24 hr of antibiotics. The study protocol required a resolution of fever and a neutrophil count $>$ or $= 0.2 \times 10$ (9)/L for hospital discharge.
Results: Patients randomized to G-CSF had a shorter duration of neutropenia (median, 5 v 10 days; $P = 0.001$), shorter duration of grade IV neutropenia (median, 2 v 5 days; $P = 0.001$), shorter febrile neutropenia (median, 5 v 6 days; $P = 0.02$), fewer days of total antibiotic use (median, 6 v 8.5 days; $P = 0.01$), and less severe neutrophil nadir (mean, 0.32 vs 0.14; $P = .006$) but there was no difference in ICU admissions, shock or infection related mortality. The reduction in duration of FN did not significantly reduce the cost per patient admission.
Conclusions: GCSF used with antibiotics at the onset of FN in children with cancer in LIC accelerated neutrophil recovery and shortened the duration of febrile neutropenia as well as antibiotic usage but did not reduce hospital admission, cost of therapy and mortality.

LEUKEMIA/MDS AND BONE MARROW TRANSPLANTATION BIOLOGY

O-013

EARLY T-CELL PRECURSOR (ETP) ACUTE LYMPHOBLASTIC LEUKEMIA IS CHARACTERIZED BY ABERRANT ACTIVATION OF THE JAK/STAT PATHWAY AND PROFOUND RESPONSES TO RUXOLITINIB IN XENOGRAFT MODELS

S.L. Maude[1], S. Dolai[2], C. Delgado-Martin[3], S.P. Hunger[4], M.L. Loh[3], C.G. Mullighan[5], M.L. Hermiston[3], S.A. Grupp[1], R. Lock[2], D.T. Teachey[1]

[1]Oncology, Children's Hospital of Philadelphia, Philadelphia, USA; [2]Leukaemia Biology, Children's Cancer Institute Australia for Medical Research, Randwick, Australia; [3]Pediatric Hematology-Oncology, UCSF Benioff Children's Hospital, San Francisco, USA; [4]Pediatric Hematology/Oncology/BMT, Children's Hospital of Colorado, Aurora, USA; [5]Pathology, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Novel therapies are urgently needed for early T-cell precursor (ETP) acute lymphoblastic leukemia (ALL), a recently described subtype of T-ALL with a poor prognosis. Defined by a unique immunophenotype, ETP-ALL expresses myeloid/early progenitor markers in addition to T-lineage markers. While ETP-ALL does not harbor a unifying genetic lesion, a fraction have mutations in genes involved in JAK/STAT signaling. This study sought to determine the dependence of ETP-ALL on JAK/STAT signaling and the activity of JAK-targeted therapy.
Methods: JAK/STAT signaling in 6 primary ETP-ALL samples from pediatric patients was evaluated by phosphoflow cytometry and immunoblot, and xenografts of these samples were established in NOD/SCID/γc null (NSG) mice, under approval of the Institutional Animal Care and Use Committee. Disease burden was monitored by flow cytometry of peripheral blood for human cytoplasmic CD3 (cCD3). Xenografts were randomized to the JAK1/2 inhibitor ruxolitinib or vehicle after they developed >1% peripheral blasts.
Results: We identified aberrant hyperactivation of the JAK/STAT pathway in 6/6 ETP-ALL samples with heterogeneous mutations. ETP-ALL cases had markedly increased levels of pSTAT3 and pSTAT5 compared to non-ETP T-ALL by immunoblot and phosphoflow cytometry. Moreover, ETP-ALL showed hyperactivation of STAT5 in response to IL7, an effect that was abrogated by ruxolitinib. *In vivo*, ruxolitinib displayed activity in 6/6 xenograft models of ETP-ALL, with profound single-agent efficacy in 5/6. Ruxolitinib treatment decreased peripheral blast counts relative to pre-treatment levels and yielded significantly lower peripheral blast counts compared to control ($P < 0.05$) in 5/6 ETP-ALL samples and 75-99% reduction in mean splenic blast counts ($P < 0.01$) in 6/6. Both JAK/STAT pathway activation and ruxolitinib efficacy were independent of the presence of known JAK/STAT pathway mutations.
Conclusions: These results strongly suggest that ETP-ALL blasts are dependent on JAK/STAT signaling and establish ruxolitinib as a potential novel therapeutic option, which should be translated to clinical trials rapidly.

O-014

LOSS OF IKZF1 FUNCTION MEDIATES RESISTANCE TOWARDS GLUCOCORTICOID-INDUCED APOPTOSIS IN BCP-ALL

P. Hoogerbrugge[1], R. Marke[1], J. Havinga[1], J. Cloos[2], L. Yuniati[1], M. Demkes[1], L. Escote[1], D. Ingen[1], E. Sonneveld[3], R. Kuiper[4], G. Kaspers[2], F. Leeuwen[1], B. Scheijen[1]

[1]Pediatric Oncology, Radboudumc, Nijmegen, Netherlands; [2]Pediatric Oncology, VUMC, Amsterdam, Netherlands; [3]Lab, Dutch Childhood Oncology Group, The Hague, Netherlands; [4]Genetics, Radboudumc, Nijmegen, Netherlands

Objectives: Glucocorticoids (GCs) are critical components in the treatment of ALL and the initial response to prednisolone is a major prognostic factor. At relapse, resistance to GCs is common and represents an important determinant in treatment failure. Recent studies performed by us and others have identified *IKZF1* gene deletions and mutations as an independent prognostic factor in children with B cell precursor ALL (BCP-ALL). However, it has not been established whether loss of IKZF1 function directly impacts the response to glucocorticoids.
Methods: We examined whether haplodeficiency for *Ikzf1* gene expression in mouse lymphocytes affects glucocorticoid-induced apoptosis. To assess the effect of IKZF1 overexpression on glucocorticoid receptor (GR) -dependent transcription, luciferase reporter assay were used. Lentiviral-mediated *IKZF1*-shRNA expression in Nalm6 cell line was established to investigate loss of IKZF1 function in a human leukemia cell line. Furthermore, MTT assays were performed on 187 primary leukemia samples after treatment with individual chemotherapeutic agents, comparing *IKZF1*-deleted patient samples with wild-type controls.
Results: B-lymphocytes haplodeficient for IKZF1 showed a significantly enhanced survival after treatment with GCs compared to wild type cells, as measured in an MTS assay and by AnnexinV staining. In case of prednisolone, the inhibitory concentration (IC_{50}) was about ~200-fold higher in the *Ikzf1*$^{+/-}$ splenocytes as compared to the wild-type cells. Gene expression analysis revealed that *Ikzf1*$^{+/-}$ splenocytes displayed lower expression levels as well as diminished transcriptional activation of several GR-induced target genes (i.e. *Sgk1, Irs2, Zfp36L2*). Furthermore, luciferase reporter assay revealed that IKZF1 overexpression enhances GR-mediated transcriptional activation in response to prednisolone. Lentiviral-mediated *IKZF1*-shRNA expression in Nalm6 cell line inhibits prednisolone and dexamethasone-induced apoptosis. Finally, MTT assays on patients samples revealed a significant (30-fold) GC ($P < 0.001$).
Conclusions: Our data provide evidence that loss of IKZF1 function mediates resistance to glucocorticoid-induced apoptosis, which may contribute to the poor outcome of *IKZF1*-deleted BCP-ALL.

O-015

IKZF1 DELETIONS IN PEDIATRIC ACUTE MYELOID LEUKEMIA

J. de Rooij[1], E. Beuling[1], A. Obulkasim[1], J. Trka[2], D. Reinhardt[3], A. Baruchel[4], E. Sonneveld[5], B.E.S. Gibson[6], R. Pieters[1], M. Fornerod[1], M.M. van den Heuvel-Eibrink[1], C.M. Zwaan[1]

[1]Pediatric Oncology/Hematology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Dept of Pediatric Oncology/Hematology, 2nd Medical School Charles University, Prague, Czech Republic; [3]AML-BFM Study Group Pediatric Hematology/Oncology, Medical School Hannover, Hannover, Germany; [4]Dept. of Hematology, Hopital Saint- Louis, Paris, France; [5]Dutch Childhood Oncology Group, The Hague, Netherlands; [6]Dept. of Haematology/Oncology, Royal Hospital for Sick Children, Glasgow, United Kingdom

Objectives: IKAROS family zinc finger 1 (IKZF1) is a zinc finger transcription factor important in lymphoid differentiation that acts as tumor suppressor in acute lymphoid leukemia. Recent studies suggest that IKZF1 is also involved in myeloid differentiation.
Methods: To investigate whether *IKZF1* deletions play a role in pediatric acute myeloid leukemia (AML) we screened a panel of 258 newly diagnosed pediatric AML samples obtained from the DCOG (The Hague, the Netherlands), the AML–Berliner-Frankfurt-Münster Study Group (Germany, Czech Republic), the Saint-Louis Hospital (Paris, France) and the Royal Hospital for Sick Children (Glasgow, United Kingdom) for deletions of the *IKZF1* locus on chromosome 7p12.2 using multiplex ligation-dependent probe amplification (MLPA).
Results: Median age of the patients was 9.5 years (range 0.1-18.5 years), median white blood cell count was 46.7×10^9/L (range $1.2\text{-}483 \times 10^9$/L). All major cytogenetic subgroups were included and patients were treated with intensive cytarabine-anthracycline based pediatric AML protocols. Of 11 patients with an *IKZF1* deletion, 8 cases showed a monosomy 7, and 3 cases showed a focal deletion of *IKZF1*. These deletions included the complete *IKZF1* gene (n = 2) or exons 1-4 (n = 1), leading to a loss of IKZF1 function. The focal deleted cases were an 1.5 year old male diagnosed with fusion of *MNX1/ETV6* who relapsed and died, an 11.3 year old female diagnosed with acute monocytic leukemia who relapsed, and a 2.3 year old male diagnosed with acute myelomonocytic leukemia with a disease-free survival. Genes differentially expressed in monosomy 7 cases significantly correlated with gene expression changes in focal *IKZF1* deleted cases when comparing significant differences to non-deleted samples (n = 247). This suggests that loss of *IKZF1* may be an important determinant in pediatric AML with monosomy 7. Genes increased in expression in *IKZF1* deleted samples included genes involved in myeloid cell cycle and self-renewal.
Conclusions: Our findings suggest evidence for a driving role of *IKZF1* haploinsufficiency in pediatric myeloid leukemias.

O-016

GATA2 DEFICIENCY IN CHILDREN AND ADOLESCENTS WITH MYELODYSPLASTIC SYNDROME

M. Wlodarski[1], S. Hirabayashi[2], J. Stary[3], R. Masetti[4], H. Hasle[5], M. Schmugge[6], M. van den Heuvel[7], M. Dworzak[8], B. De Moerloose[9], C. Niemeyer[2]

[1]Department of Pediatric Hematology and Oncology, University Childrens Hospital Freiburg for EWOG-MDS, Freiburg, Germany; [2]Department of Pediatric Hematology and Oncology, University Childrens Hospital Freiburg, Freiburg, Germany; [3]Dept. of Pediatric Hematology and Oncology, University Hospital Motol Prague, Prague, Czech Republic; [4]Paediatric Oncology and Haematology, Universtiy of Bologna, Bologna, Italy; [5]Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark; [6]Dept. of Pediatrics, Kinderspital Zuerich, Zuerich, Switzerland; [7]Sophia Children's Hospital, University of Rotterdam, Rotterdam, Netherlands; [8]Pediatrics, St. Anna Kinderspital, Vienna, Austria; [9]Dept. of Pediatric Hematology-Oncology, Ghent University Hospital, Ghent, Belgium

Objectives: The etiology of childhood myelodysplastic syndromes (MDS) remains largely unknown. Recently, germline loss-of-function GATA2 mutations were identified in hematopoietic stem cell disorders with variable phenotypes unified by the predisposition for myeloid malignancy. In this study we aimed to define the frequency and clinical characteristics of GATA2 deficiency within primary MDS in children and adolescents.
Methods: We investigated a cohort of 508 consecutive patients with MDS (426 primary and 82 secondary) diagnosed in Germany between 01.01.1998 and 30.06.2013 and enrolled in the studies of the European Working Group of MDS in Childhood (EWOG-MDS) 98 and 2006.
Results: GATA2 mutations were identified in 7% (28/424) of patients with primary MDS and in none of the secondary MDS cases. Interestingly, 20/28 children with mutations had a karyotype either indicating monosomy 7, t1;7, or trisomy 8. We next identified additional 42 cases with GATA2 deficiency (35 EWOG-enrolled and 8 referred for diagnostics), bringing to 71, the total number of GATA2-deficient patients diagnosed at our institution. Intriguingly, of a total cohort of 100 children with monosomy 7, 37 patients (37%) had underlying GATA2 deficiency. While age at diagnosis of MDS was significantly higher in mutated patients (median age at diagnosis 12.5 vs. 4.2 years, $p < 0.01$), the 5-yrs overall survival and event-free survival after HSCT was comparable in patients with monosomy 7 with or without underlying GATA2-deficiency. Investigations of unaffected parents or siblings did not reveal silent exonic mutation carriers.
Conclusions: In summary, GATA2 deficiency accounts for 7% of all primary childhood MDS and a third of all primary MDS cases with monosomy 7. Family investigations imply a full penetrance of MDS for exonic *GATA2* mutations and might help guide clinical decision making in terms of an early transplantation. Further investigations will be critical to better define the clinical penetrance and prognosis of this novel MDS predisposition syndrome.

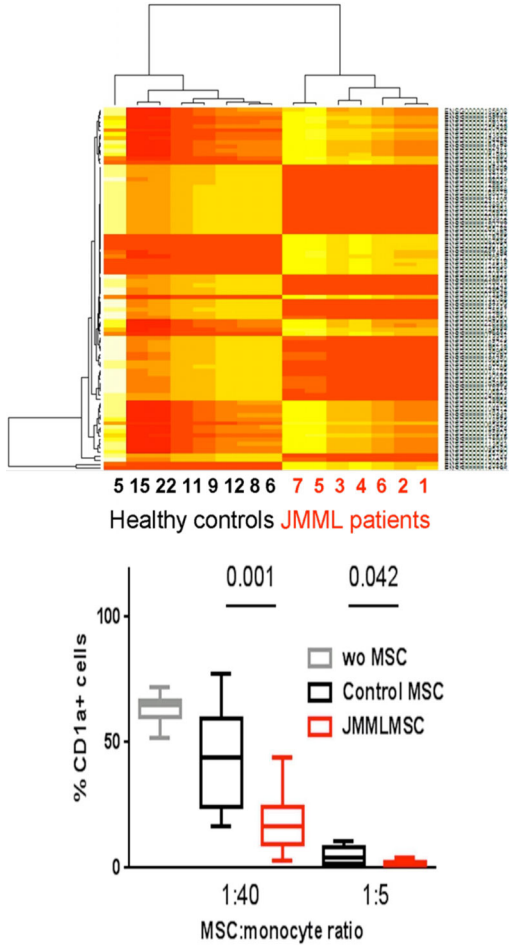
O-017

JUVENILE MYELOMONOCYTIC LEUKEMIA AFFECTS THE FUNCTION AND GENE-EXPRESSION OF MESENCHYMAL STROMAL CELLS

E.G.J. Calkoen[1], C. Vervat[1], P.A.C. 't Hoen[2], M.M. van den Heuvel-Eibrink[3], L.M. Ball[1], M.J.D. van Tol[1], R.M. Egeler[4]

[1]Pediatrics Immunology Hematology/Oncology and Hematopoietic Stem Cell Transplantation, Leiden University Medical Center, Leiden, Netherlands; [2]Department of Human Genetics, Leiden University Medical Center, Leiden, Netherlands; [3]Department of Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands; [4]7Department ofHematology/Oncology and Hematopoietic Stem Cell Transplantation, Hospitalfor Sick Children, Toronto, Canada

Objectives: Aberrant mesenchymal stromal cell (MSC) function was linked to disease and contributed to the pathophysiology of malignant disorders in murine models. Juvenile Myelo-Monocytic Leukemia (JMML) is an aggressive disease affecting young infants and is characterized by presence of a high percentage of blasts. In this study we present the impact of JMML on MSC.
Methods: Bone-marrow samples of children with JMML were collected at diagnosis (n = 9) and after HSCT (n = 7; from 4 patients) for the expansion of MSC. Bone-marrow of 10 healthy pediatric controls was collected at time of stem cell donation. MSC were characterized by phenotyping, differentiation, gene-expression (DeepSAGE) analysis and functional studies assessing immunomodulation and hematopoietic support.
Results: The gene expression profile in JMML-MSC differed significantly from controls (Figure 1). Differential expression was observed a.o. for genes encoding proteins of the IL-1 superfamily and the leptin pathway, and adhesion molecules. Chimerism analysis confirmed the patient origin of MSC expanded from post-HSCT samples. Gene expression of e.g. DKK1, IL-6, CXCL12 and CXCR7 in MSC expanded from bone-marrow of JMML patients after HSCT was comparable to control MSC, but significantly altered compared to MSC of these patients collected at diagnosis.
Whereas hematopoietic support and suppression of PBMC and NK-cell activation was not affected, suppression of differentiation of monocytes towards dendritic cells was significantly stronger by JMML derived MSC compared to healthy controls as depicted in Figure by decreased CD1a expression.



Conclusions: This is the first study to show the impact of leukemic cells on the microenvironment in man. Using MSC from children with JMML at diagnosis and after HSCT treatment, we have shown that these alterations can be partially reversible. Our data shed a new light on the changes occurring in the microenvironment of children with leukemia.

O-018

NATURAL KILLER CELL RECEPTOR GENETIC PROFILING AND THE OUTCOMES OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

R. Faridi[1], T.J. Kemp[1], P. Dharmani-Khan[1], V. Lewis[2], N. Berka[3], J. Storek[4], F. Khan[1]

[1]Department of Pathology and Laboratory Medicine, University of Calgary, Calgary, Canada; [2]Department of Oncology, Alberta Children's Hospital, Calgary, Canada; [3]Department of Pathology and Laboratory Medicine, Calgary Laboratory Services University of Calgary, Calgary, Canada; [4]Department of Medicine, University of Calgary, Calgary, Canada

Objectives: Allogeneic hematopoietic cell transplantation HCT is a curative therapy for hematologic malignancies as well as for numerous life-threatening disorders of hematolymphopoiesis. The most common indication for HCT is acute myeloblastic leukemia (33% of all HCT), followed by lymphoblastic leukemia, chronic myeloblastic leukemia refractory to tyrosine-kinase inhibitors, and lymphoid malignancies. In spite of high resolution HLA matching and optimal care, complications of HCT, including graft versus host disease (GVHD), relapse of the underlying disease and reactivation of otherwise latent viral infections are substantial. Recently, the natural killer (NK) cell genetic system, regulated by the activating and inhibitory Killer Immunoglobulin-like Receptors (KIR) has garnered substantial research interest as a modifier of HCT outcomes. Here we set out to determine the influence of KIR gene repertoires of HCT pairs on HCT complications including GVHD, relapse, posttransplant lymphoproliferative disorder (PTLD) and cytomegalovirus (CMV) reactivation.
Methods: KIR typing was obtained for 100 paediatric and 200 adult HLA- matched allo-HCT pairs in addition to 50 healthy individuals by a Luminex-based rSSO method. Effect of KIR genotypes on HCT outcomes was analysed using binomial regression and Kaplan-Meier tests. Peripheral blood mononuclear cells (PBMNCs) from healthy volunteers were stimulated against different targets to enumerate KIR dependent target specific NK cell responses.
Results: Donor-recipient pairs matched for the KIR-AA and B/x genotypes were significantly protected from GVHD ($HR = 2.224$; $p = 0.01$) without any effect on disease relapse ($HR = 1.098$; $p = 0.934$). Incidence of PTLD was strongly correlated by donor KIR cen-B linkage group ($p = 0.01$), whereas higher activating donor-KIR protected against CMV reactivation ($p = 0.02$). Unique target-induced functional response with higher number of herpes-virus induced functional NK cells in individuals lacking KIR cen-B was observed.
Conclusions: NK cell responsiveness, a function of KIR gene repertoire modified the risk of GVHD, PTLD and CMV reactivation indicating relevance of KIR gene profiling for predicting HCT outcomes.

MEDULLOBLASTOMA – CLINICAL

O-019

METASTATIC MEDULLOBLASTOMA - UK RESULTS WITH INDUCTION AND HIGH DOSE CHEMOTHERAPY WITH HYPERFRACTIONATED ACCELERATED RADIOTHERAPY (THE MILAN STRATEGY)

S. Vivekanandan[1], R. Breene[2], R. Ramanujachar[3], H. Traunecker[4], B. Pizer[5], M. Gaze[6], F. Saran[7], N. Thorp[8], M. English[9], K. Wheeler[10], A. Michalski[11], D.A. Walker[12], D. Saunders[13], F. Cowie[14], A. Cameron[15], V. Lee[16], D. Parashar[17], G. Horan[18], M. Williams[18]

[1]Clinical Oncology, Cambridge University Hospitals NHS Foundation Trust Addenbrookes Hospital, Cambridge, United Kingdom; [2]Paediatric Oncology, Cambridge University Hospitals NHS Foundation Trust Addenbrookes Hospital, Cambridge, United Kingdom; [3]Paediatric Oncology, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom; [4]Paediatric Oncology, Children's Hospital for Wales, Cardiff, United Kingdom; [5]Paediatric Oncology, Alder Hey Children's Hospital NHS Foundation Trust, Liverpool, United Kingdom; [6]Clinical Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [7]Clinical Oncology, The Royal Marsden NHS Foundation Trust, Surrey, United Kingdom; [8]Clinical Oncology, The Clatterbridge Cancer Centre NHS Foundation Trust, Wirral, United Kingdom; [9]Paediatric Oncology, Birmingham Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom; [10]Paediatric Oncology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; [11]Paediatric Oncology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [12]Paediatric Oncology, Nottingham Children's Hospital University of Nottingham, Nottingham, United Kingdom; [13]Clinical Oncology, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom; [14]Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; [15]Clinical Oncology, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; [16]Clinical Oncology, Sheffield Children's NHS Foundation Trust, Sheffield, United Kingdom; [17]Statistics, Cancer Research UK Cambridge Institute University of Cambridge, Cambridge, United Kingdom; [18]Clincial Oncology, Cambridge University Hospitals NHS Foundation Trust Addenbrookes Hospital, Cambridge, United Kingdom

Objectives: Historically, the 5-year overall survival (OS) for metastatic medulloblastoma (MB) is less than 40%. The Milan Strategy of post-operative induction chemotherapy followed by hyperfractionated accelerated radiotherapy (HART) and response directed myeloablative high dose chemotherapy (HDC) or maintenance chemotherapy was reported in a study of 33 patients with metastatic MB to improve 3-year OS to 77% (95% CI 61, 93) and 5-year OS to 73% (59, 87). We report the UK outcomes of this strategy.
Methods: Questionnaires were sent to all 20 UK paediatric oncology centres to collect retrospective data on treatment delivered, toxicity and survival with the Milan strategy.
Results: Between February 2009 and October 2011, 34 patients who fulfilled the entry criteria of the original study, were treated de novo for metastatic MB in 14 centres. The median age at presentation was 7 years (range 3 - 15). Median interval from surgery to HART was 109 versus 85 days in the Milan series. Induction and HDC were toxic with 83-100% incidence of grade 3 toxicities: febrile neutropaenia, blood and platelet transfusion. Response was highly correlated with survival: 16/17 patients who achieved CR by the end of therapy remain alive and in remission but only 3/17 with lesser responses are still alive ($p < 0.0001$). With follow up from induction chemotherapy (as in the Milan study) of 30-60 months, we estimate 3-year overall survival of 55% (95% Cl 38, 71). This result is outside the 95% CI of the Milan results and encompasses the historical result of 40%. We did not observe major late neurotoxicity in this cohort, although some children had residual cerebellar signs and changes on follow up MRI.
Conclusions: We did not replicate the improved results reported by the Milan group. The reasons could include differences in patient sub-groups and protocol compliance in these small cohorts.

O-020

TANDEM HIGH-DOSE CHEMOTHERAPY WITH STEM CELL RESCUE FOLLOWED BY RISK-ADAPTED RADIATION IN CHILDREN WITH HIGH-RISK CEREBRAL PRIMITIVE NEUROECTODERMAL TUMOR: RESULTS OF THE SFCE-TRIAL PNET HR+5

C. Dufour[1], M.B. Delisle[2], A. Geoffray[3], A. Laplanche[2], D. Frappaz[4], C. Icher[5], A.I. Bertozzi[6], P. Leblond[7], F. Doz[8], N. Andre[9], E. DeCarli[10], P. Schneider[11], C. Berger[12], O. Lejars[13], P. Chastagner[14], A. Pagnier[15], C. Soler[16], N. Entz Werle[17], D. Valteau Couanet[1]

[1]Pediatry, Gustave Roussy, Villejuif, France; [2]Epidemiology, Gustave Roussy, Villejuif, France; [3]Radiology, CHU Lenval, Nice, France; [4]Pediatry, Institut d'Hematologie et d'Oncologie Pédiatrique, Lyon, France; [5]Pediatry, CHU, Bordeaux, France; [6]Pediatry, Hopital des Enfants, Toulouse, France; [7]Pediatry, Centre Oscar Lambret, Lille, France; [8]Pediatry, Institut Curie, Paris, France; [9]Pediatry, CHU La Timone, Marseille, France; [10]Pediatry, CHU, Angers, France; [11]Pediatry, CHU, Rouen, France; [12]Pediatry, CHU, Saint Etienne, France; [13]Pediatry, CHU, Tours, France; [14]Pediatry, CHU, Nancy, France; [15]Pediatry, CHU, Grenoble, France; [16]Pediatry, Hopital l'Archet, Nice, France; [17]Pediatry, CHU Haute Pierre, Strasbourg, France

Objectives: To assess the 3-year progression-free survival (PFS) rate of patients with newly diagnosed high-risk medulloblastoma (MB) or supratentorial primitive neuroectodermal tumor (sPNET) between 5-20 years treated according to the prospective multicenter trial PNET HR+5.
Methods: Children received as postoperative induction chemotherapy two cycles of etoposide (500 mg/m^2) - carboplatine (800 mg/m^2), followed by two courses of thiotepa (600mg/m^2 per course) with autologous stem cell rescue. Risk-adapted conventional radiotherapy (RT) was delivered around day 45 after second transplantation. Craniospinal RT dose was 36 Gy for patients with metastatic disease or with unfavourable histology (anaplastic MB, large cell MB, MB with *myc* amplification) followed by a tumor bed boost of 18 Gy. Patients with localized sPNET received focal RT at the dose of 54 Gy. Maintenance treatment with 6 cycles of temozolomide was planned to start between 1-3 months after the end of RT.
Results: From January 2009 to February 2012, 64 patients (MB = 51; sPNET = 13) between 5 and 19 years (median age, 9 years) were enrolled. Five patients didn't received RT due to progressive disease. Maintenance treatment was administered in 42 patients. The median follow-up was 32 months (range, 16-54 months). The 3-year PFS and overall survival (OS) were 80% (95% CI: 68-88%) and 85% (95% CI: 74-92%), respectively. The 3-year PFS was 79% (95% CI: 65-88%) for children with MB and 85% (95% CI: 58-96%) for those with sPNET. No major unexpected toxicities and no treatment-related deaths were reported.
Conclusions: This treatment based on high-dose chemotherapy and conventional RT resulted in a high overall survival rate in children and adolescent with newly diagnosed high-risk cerebral PNET.

O-021

CLINICAL OUTCOMES OF CHILDREN WITH STANDARD RISK MEDULLOBLASTOMA TREATED WITH PROTON AND PHOTON RADIOTHERAPY

B. Eaton[1], N. Esiashvili[1], S. Kim[2], E. Weyman[3], L. Thornton[3], H. Kasper[3], C. Mazewski[4], T. MacDonald[4], D. Ebb[5], S. MacDonald[3], N. Tarbell[3], T. Yock[3]

[1]Radiation Oncology, Emory University, Atlanta, USA; [2]Biostatistics and Bioinformatics, Emory University, Atlanta, USA; [3]Radiation Oncology, Massachusetts General Hospital, Boston, USA; [4]Pediatrics, Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta, Atlanta, USA; [5]Pediatrics, Massachusetts General Hospital, Boston, USA

Objectives: To compare long-term recurrence-free survival (RFS) and overall survival (OS) between children treated with proton and photon radiotherapy (RT) for standard risk medulloblastoma.
Methods: This multi-institution cohort study includes 105 children treated with chemotherapy and proton (n = 45) or photon (n = 60) RT between 1991 and 2009. OS and RFS were estimated by the Kaplan-Meier method and compared with the long-rank test. The effect of RT type and other covariates on each outcome was assessed through multivariable analysis using logistic regression and backward selection method with an alpha level of removal of 0.1.
Results: Median (range) age at diagnosis was 6 yrs (3-21) for proton patients vs. 8 yrs (3-19) for photon patients ($p = 0.002$). Cohorts were similar with respect to gender, histology, extent of surgical resection, craniospinal and total RT dose, and whether the RT boost was delivered to the posterior fossa or tumor bed. The median CSI dose was 23.4 Gy (18-37.2) and the median total dose was 54 Gy (50.4-60). Median follow-up time is 5.7 years (0.6–9.9) for proton patients vs. 8 years (1.3–19.7) for photon patients ($p < 0.001$). There was no significant difference in OS or RFS between patients treated with proton vs. photon RT: 5 yr OS 82.0% (CI 0.65-0.91) vs. 89.4% (CI 0.78-0.95), and 5 yr RFS 82.2% (CI 0.68-0.91) vs. 79.7% (CI 0.67-0.88). On multivariable analysis, female gender ($p = 0.038$) and higher CSI dose ($p = 0.041$) were associated with a better RFS. There was a marginally significant relationship between better OS and older age at diagnosis ($p = 0.054$), classic histology ($p = 0.062$), and female gender ($p = 0.072$). A second primary malignancy occurred in four (6.7%) photon patients, at a median time of 12.7 years (3.7-13.0), vs. no (0%) proton patients ($p = 0.133$).
Conclusions: Disease control with proton and photon radiotherapy appears equivalent for standard risk medulloblastoma.

O-022

THERAPEUTIC IMPLICATIONS OF MEDULLOBLASTOMA SUBGROUPS IN NON-INFANTS: A SINGLE CENTRE POPULATION BASED EXPERIENCE

V. Ramaswamy[1], M. Remke[1], J. Adamski[2], U. Bartels[2], U. Tabori[2], A. Huang[2], M.D. Taylor[1], E. Bouffet[2]

[1]Neurosurgery, The Hospital for Sick Children, Toronto, Canada; [2]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: The advent of integrated genomics has fundamentally changed our understanding of medulloblastoma. Although survival differences have been shown to exist between the four principle subgroups, treatment related differences have yet to be elucidated. We sought to delineate these differences at a large referral centre.
Methods: All patients older than three years of age treated with surgery, craniospinal irradiation, and adjuvant chemotherapy were identified at the Hospital for Sick Children in Toronto from 1998-2012.
Results: Ninety-four patients met our inclusion criteria. Two periods were identified, those patients treated prior to 2006 as per the open protocols of the Children's Oncology Group (CCG9961, POG9631), and patients treated after 2006 treated as per the SJMB03 protocol. Five-year progression free survival over the entire cohort was 78%. When stratified by treatment, 5-year survival pre and post 2006 were identical (76.8% pre-2006 and 79.3% post-2006). When re-analysed in a subgroup specific manner, we find no significant differences in progression-free survival pre and post 2006. Strikingly, we found that Group 3 and 4 patients have excellent survivals compared to those previously reported, with 5 year progression-free survival in average risk Group 4 patients of over 90% and over 75% in average risk Group 3 patients regardless of treatment protocol. Survival of SHH patients was relatively poor across both treatment protocols with 5 year progression free survival of 60% likely owing to a higher proportion of *TP53* mutated patients at our center.
Conclusions: In a cohort of homogenously treated non-infant patients, progression free survival appears to be improved compared to initial reports based on retrospective cohorts. The impact of subgroup affiliation in children over age 3 needs to assessed in large prospectively treated cooperative protocols to determine the prognostic and predictive implications of subgroup affiliation.

O-023

EXPERIENCE WITH A METRONOMIC ANTIANGIOGENIC THERAPY IN CHILDREN WITH RECURRENT MEDULLOBLASTOMA, ATRT, AND VARIOUS OTHER MALIGNANT CNS TUMORS

I. Slavc[1], A. Peyrl[1], M. Chocholous[1], A.A. Azizi[1], T. Czech[2], K. Dieckmann[3], C. Haberler[4], U. Leiss[1]

[1]Pediatrics, Medical University of Vienna, Vienna, Austria; [2]Neurosurgery, Medical University of Vienna, Vienna, Austria; [3]Radiotherapy, Medical University of Vienna, Vienna, Austria; [4]Institut of Neurology, Medical University of Vienna, Vienna, Austria

Objectives: Patients with recurrent malignant CNS tumors have a poor prognosis irrespective of salvage therapy used. We report on an updated and extended series of patients with recurrent medulloblastomas, ATRTs, and various other malignant CNS tumors partly included in a previous publication and treated with an alternative approach consisting of an antiangiogenic combination therapy (1).
Methods: From 11/2006 to 9/2013, 43 patients with various recurrent brain tumors started treatment with an antiangiogenic multidrug-regime consisting of bevacizumab, thalidomide, celecoxib, fenofibrate, and etoposide alternating with cyclophosphamide, with or without intraventricular therapy (etoposide and liposomal cytarabine). Diagnoses were medulloblastoma (n = 9), ATRT (n = 5), ependymoma (n = 4), CNS PNET (n = 3), ETANTR (n = 3), pineoblastoma (n = 2), HGG (n = 2), DIPG (n = 3), NGGCT (n = 2), MPNST (n = 2) and choroid plexus carcinoma, astroblastoma, paraganglioma, meningioma, oncocytoma, epitheloid sarcoma, endolymphatic sac tumor and neuroblastoma in one each.
Results: As of 3/2014, 5/9 patients with medulloblastoma are alive for 67, 63, 63, 37 and 35 months and 3/5 patients with ATRT are alive for 71, 39, and 31 months after their last recurrence, all of them off therapy. Patients with CNS PNET, ETANTR, HGG, DIPG, oncocytoma and neuroblastoma did not appear to respond to this strategy. The two patients with pineoblastoma survived for 38 and 27 months, respectively, despite extensive leptomeningeal disease. The two patients with NGGCT showed a dramatic drop of their Alpha-Fetoprotein levels.
Conclusions: The proposed antiangiogenic regimen that is currently being evaluated for medulloblastomas in an international phase II protocol (MEMMAT; ClinicalTrials.gov Identifier: NCT01356290) seems to be also efficacious in recurrent ATRTs. In a number of other tumor entities time to progression could be prolonged while maintaining good quality of life.
1. Peyrl et al. (2012). *Pediatr Blood Cancer*, 59 (3):511-7.

O-024

LONG TERM NEUROPSYCHOLOGICAL FOLLOW UP OF YOUNG CHILDREN WITH MEDULLOBLASTOMA TREATED ACCORDING TO THE CCG 99703 REGIMEN

T. Fay-McClymont[1], K. Walsh[2], D. Mabbott[3], A. Smith[4], J. Madden[5], S. Chi[6], E. Wells[2], E. Owen[4], R. Packer[2], N. Foreman[5], E. Bouffet[3], L. Lafay-Cousin[1]

[1]Pediatric Hematology Oncology and Bone Marrow Transplantation, Alberta Children's Hospital, Calgary, Canada; [2]Pediatric Oncology, Children's National Medical Center, Washington DC, USA; [3]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada; [4]Pediatric Oncology, Arnold Palmer Hospital for Children, Orlando, USA; [5]Pediatric Oncology, Children's Hospital Colorado, Denver, USA; [6]Pediatric Oncology, Dana Farber Cancer institute, Boston, USA

Objectives: High dose chemotherapy (HDC) strategies were developed in infant brain tumor protocols to prevent neuropsychological (NP) impairments associated with radiation. However comprehensive NP evaluations of young children treated with such strategies remain scant. Our aim was to examine long term NP outcomes in young children with medulloblastoma treated with sequential HDC according to protocol CCG 99703.
Methods: This retrospective study included young children diagnosed with medulloblastoma from 1998-2011 at 6 North American institutions. Neurocognitive data were extracted from institutional NP reports on children old enough to be tested.
Results: The initial cohort included 47 patients. Twenty of the 37 survivors (42%) had at least one NP assessment. This sample was 55% male (n = 11) and mean age at diagnosis was 29.2 months (SD = 14.3). Posterior fossa syndrome (PFs) was reported in five patients (26%). Eight (40%) received radiotherapy (4 Focal, 4 CSI), 2 received IT chemotherapy and 2 received HD MTX during induction. On average, children were assessed 3.2 years (SD = 1.6) post-diagnosis, at 5.7 years of age (SD = 1.7). FSIQ ranged from 67-119 (mean = 94; SD = 16.1). The majority of children had low average to average NP functioning (78%). Four children (3 received RT) accounted for the majority (56%) of the impaired scores ($<10^{th}$ percentile). While sample size limited power, patients treated with radiotherapy had lower working memory scores (WMI; mean = 88 vs. 100; $p = .08$); patients with PFs had lower perceptual reasoning scores (PRI; mean = 85 vs. 100; $p = .09$); and patients with hearing support had lower verbal comprehension scores (VCI; mean = 85 vs. 100; $p = .09$). NP outcomes did not statistically differ by age at diagnosis, gender, extent of resection, metastasis, or histology.
Conclusions: NP data obtained from this sample of survivors of infant medulloblastoma treated according to the 99703 regimen are encouraging and indicate average neurocognitive functioning.

RENAL TUMOR - CLINICAL

O-025

UNILATERAL WILMS TUMOR TREATED BY PARTIAL NEPHRECTOMY ENROLLED ON THE CHILDREN'S ONCOLOGY GROUP (COG) RENAL TUMOR BIOLOGY AND CLASSIFICATION STUDY AREN03B2

P. Ehrlich[1], E.M. Mullen[2], J. Geller[3], A. Naranjo[4], E. Gratias[5], D. Barnhart[6], R. Dasgupta[6], F. Ferrar[6], K. Gow[7], R. Glick[6], T. Hamilton[7], J. Kandel[7], H.E. Ying[8], E. Pearlman[9], J. Kalapurakal[10], J. Dome[11]

[1]Pediatric Surgery, University of Michigan, Ann Arbor, USA; [2]Pediatric Oncology, Boston Childrens, Boston, USA; [3]Pediatric Oncology, Cinncinnati Childrens Hospital, Cinncinnati, USA; [4]Biostatistics, University of Florida, Gainesville, USA; [5]Pediatric Oncology, University of Tennessee, Chattanooga, USA; [6]Pediatric Surgery, Children Onoclogy Group, Philadelphia (COG), USA; [7]Pediatric Surgery, Children Onocology Group, Philadelphia (COG), USA; [8]Biostatistics, University of Florida, Gainesville, USA; [9]Pediatric Pathology, Childrens Oncology Group, Philadelphia (COG), USA; [10]Radiation Oncology, Childrens Oncology Group, Philadelphia (COG), USA; [11]Pediatric Oncology, Childrens National Medical Center, Washington DC, USA

Objectives: The long term renal failure rate in children with unilateral Wilms tumor (WT) is less then 1%. The standard recommended surgical treatment for unilateral WT is a nephroureterectomy with lymph node sampling. Despite this recommendation, some patients with unilateral renal tumors undergo partial nephrectomy. Little is known about the technical considerations and outcomes of these patients. The purpose of this study is to increase that understanding, through report of the operative outcomes, event free survival (EFS) and overall survival (OS) of patients enrolled on AREN03B2 with unilateral WT who have undergone partial nephrectomy.
Methods: Eligible patients enrolled on AREN03B2 from 2/27/2006 to 9/30/2013 with a unilateral surgical review form that indicated partial nephrectomy as the surgical procedure were considered in this analysis. Further eligibility criteria included 1) no enrollment on AREN0534 (bilateral study) and 2) confirmation of histologic diagnosis of WT by central pathology review. Surgical outcomes, EFS and OS were assessed.
Results: In total, 39/4,021 (1.0%) patients with unilateral WT (38 FHWT,1 anaplasticWT) on AREN03B2 underwent a partial nephrectomy. Median tumor weight was 701.1gm (range 133-1870). Local stage distribution was Stage I (15), II (11) and III (11). 13/39 (33%) patients did not have their lymph nodes sampled. Among the patients with stage III disease, 8 had intraoperative tumor spill and 9 had microscopic residual tumor. 9/11 were upstaged. The 5-year EFS and OS estimates were $89.4 \pm 13.0\%$ and $95.7 \pm 8.9\%$.
Conclusions: Patients with unilateral WT undergoing partial nephrectomyhad greater than expected occurrence of microscopic residual disease and intraoperative tumor spill, which resulted in local upstaging and consequent increased therapy. The potential long-term renal benefit of nephron-sparing surgery must be weighed against the potential risks of additional chemotherapy and abdominal radiation in patients who had incomplete surgical resections.

O-026

TREATMENT OF STAGE II-IV DIFFUSE ANAPLASTIC WILMS TUMOR: RESULTS FROM THE CHILDREN'S ONCOLOGY GROUP AREN0321 STUDY

N. Daw[1], J. Anderson[2], J. Kalapurakal[3], F. Hoffer[4], J. Geller[5], E. Perlman[6], P. Ehrlich[7], E. Mullen[8], A. Warwick[9], P. Grundy[10], J. Dome[11]

[1]Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, USA; [2]COG - Data Center (Omaha), Children's Oncology Group, Madison, USA; [3]Radiation Oncology, Children's Oncology Group, Chicago, USA; [4]Quality Assurance Review Ctr, Children's Oncology Group, Lincoln, USA; [5]Hematology/Oncology, Children's Oncology Group, Cincinnati, USA; [6]Pathology, Children's Oncology Group, Chicago, USA; [7]Dept of Ped Surgery, Children's Oncology Group, Ann Arbor, USA; [8]Pediatric Hematology/Oncology, Children's Oncology Group, Boston, USA; [9]Pediatric Hematology/Oncology, Children's Oncology Group, Bethesda, USA; [10]Alberta Health Services, Children's Oncology Group, Edmonton, Canada; [11]Division of Oncology, Children's National Medical Center, Washington, USA

Objectives: In National Wilms Tumor Study-5 (NWTS-5), 4-year relapse-free survival for patients with stages II-IV diffuse anaplastic Wilms tumor (DAWT) treated with vincristine, doxorubicin, cyclophosphamide, and etoposide, plus radiotherapy (XRT) (Regimen I) was 55%. AREN0321 evaluated whether a more intensive regimen containing carboplatin in addition to agents used in Regimen I (Regimen UH-1) improves EFS for these patients.
Methods: Patients with stages II-IV DAWT without measurable disease received Regimen UH-1. Patients with stage IV measurable disease had the option to receive vincristine in combination with irinotecan (VI) in an upfront window; those with partial response (PR) had VI incorporated into Regimen UH-1 (Regimen UH-2). Dosages of doxorubicin, cyclophosphamide and etoposide were reduced mid-study (revised UH-1/UH-2) due to excessive non-hematologic toxicity. The study was designed to detect improvement in EFS compared to historical controls treated with regimen I. The study was approved by the Central Institutional Review Board.
Results: Sixty-six eligible patients were treated: 22 with UH-1, 14 with VI window followed by UH-1/UH-2, and 30 with revised UH-1/UH-2. Nineteen patients had stage IV with measurable disease, 14 of whom participated in VI window; 11/14 (79%) had PR. Three-year EFS for all patients was 69% (95% CI, 56-80%). Nineteen events were observed versus 29 expected based on NWTS-5 data ($p = 0.028$). Four-year EFS was 85% (95% CI, 51-96%) for stage II, 74% (95% CI, 45-89%) for stage III, and 46% (95% CI, 25-65%) for stage IV. For patients with stage IV DAWT, 4-year EFS was 57% (95% CI, 28-78%) for the 14 patients treated with VI window and 33% (95% CI, 8-62%) for the 10 patients treated with UH-1 upfront. Three patients (4.5%) died of toxicity: cardiomyopathy ($n = 1$), pulmonary hypertension ($n = 1$), and pulmonary edema ($n = 1$).
Conclusions: Regimen UH-1/UH-2 appears to produce better EFS for patients with stage II-IV DAWT than Regimen I albeit with increased toxicity.

O-027

MALIGNANT RHABDOID TUMOR OF THE KIDNEY (MRTK) – DATA OF 52 PATIENTS TREATED ACCORDING TO PROTOCOLS OF THE GPOH (GERMAN SOCIETY OF PAEDIATRIC ONCOLOGY AND HEMATOLOGY)

R. Furtwängler[1], N. Nourkamie-Tutdibi[1], I. Leuschner[2], C. Vokuhl[2], F. Niggli[3], L. Kager[4], M.C. Frühwald[5], N. Graf[1]

[1]Pediatric Hematology and Oncology, University Children' s Hospital, Homburg, Germany; [2]Paidopathology, Schleswig Holstein University Hospital Campus Kiel, Kiel, Germany; [3]Pediatric Hematology and Oncology, University Children' s Hospital, Zurich, Switzerland; [4]Pediatric Hematology and Oncology, St. Anna Children's Hospital, Vienna, Austria; [5]Children's Hospital, Swabian's Hospital Augsburg, Augsburg, Germany

Objectives: To analyze the data of 52 consecutive patients having MRTK registered in the framework of SIOP 9/GPO, 93-01/GPOH, 2001/GPOH and EU-RHAB between 1991 and 2013 in Austria, Switzerland and Germany.
Methods: All children having a histologically proven MRTK entered onto above studies were elegible for analysis. Median Follow up was 5.3 years.
Results: 22 patients presented with metastatic disease most frequently to the lungs ($n = 18$). Simultaneous MRTK and AT/RT occurred in 3 patients.1 patient died before treatment. 13 patients underwent upfront surgery and 38 received preoperative treatment (19 Dactinomycin and Vincristine (AV), 18 AV plus Doxorubicin (AVD), 1 unknown). Mean response to AVD was significantly better than to AV (63% volume reduction vs. 15% increase in volume, $p = 0.002$). Local stage distribution after surgery was 5, 13 and 29 for stage 1, 2 and 3 respectively (5 undetermined). 37 patients achieved a complete remission during the treatment course: 20 were in continuous CR at the end of treatment. 29 patients died: 27 due to progressive disease, 2 due to postoperative bleeding. 2 year event free (EFS) and overall survival (OS) were 35 and 39% respectively. Age younger than 10 months (2.7 RR, 95%CI: 1.2-5.7) and local stage III (3.3 RR, 95%CI: 1.4-7.9) are significant risk-factors in Cox-regression analysis. 2y OS for patients with stage IV was 28% ($n = 14/22$) compared to 48% ($n = 15/30$) for localized MRTK. Patients having achieved a macroscopic complete remission and a local stage III had a significantly improved 2y OS if undergoing flank irradiation (36% vs. 18%, $p = 0.05$, $n = 19$). Patients having achieved a macroscopic CR show 52% and 50% 2y OS for localized and metastatic MRTK respectively.
Conclusions: Younger patients especially with metastatic disease still have an apalling prognosis. Early histologic diagnosis and intensive postoperative treatment including irradiation are important in the treatment of MRTK.

O-028

TREATMENT AND OUTCOME OF PATIENTS WITH RELAPSED CLEAR CELL SARCOMA OF THE KIDNEY (CCSK): A COMBINED SIOP AND AIEOP STUDY

S. Gooskens[1], R. Furtwangler[2], F. Spreafico[3], H. van Tinteren[4], J. de Kraker[5], G.M. Vujanic[6], I. Leuschner[7], A. Coulomb-L'Herminé[8], J. Godzinski[9], G. Schleiermacher[10], S. Stoneham[11], C. Bergeron[12], K. Pritchard-Jones[13], N. Graf[2], M.M. van den Heuvel-Eibrink[1]

[1]Department of Pediatric Hematology and Oncology, Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Department of Pediatric Hematology and Oncology, Saarland University, Saarbrucken, Germany; [3]Department of Hematology and Pediatric Onco-Hematology, Fondazione IRCCS Instituto Nazionale dei Tumori, Milano, Italy; [4]Department of Statistics, Netherlands Cancer Institute (NKI-AvL), Amsterdam, Netherlands; [5]Department of Pediatric Hematology and Oncology, Academic Medical Center – Emma Children's Hospital, Amsterdam, Netherlands; [6]Department of Pathology, Cardiff University School of Medicine, Cardiff, United Kingdom; [7]Institute of Pathology, University of Kiel, Kiel, Germany; [8]Department of Pathology, Hopitaux Universitaires Est Parisien, Paris, France; [9]Department of Emergency Medicine / Pediatric Surgery, Medical University of Wroclaw Marciniak Hospital, Wroclaw, Poland; [10]Department of Pediatric Oncology and INSERM U830, Institut Curie, Paris, France; [11]Department of Pediatric and Adolescent Oncology, University College Hospital, London, United Kingdom; [12]Department of Pediatrics, Centre Lyon Berard, Lyon, France; [13]Molecular Hematology and Cancer Biology, Institute of Child Health University College, London, United Kingdom

Objectives: Clear Cell Sarcoma of the Kidney (CCSK) is an uncommon pediatric renal tumor. Relapses occur in about 15% of the patients. Detailed clinical information on relapsed CCSK is scarce. The current study aims to describe outcome of patients with relapsed CCSK treated according to recent European protocols, in order to find a rational for creating future international CCSK relapse treatment protocols.
Methods: We analysed prospectively collected data of all CCSK patients who developed a relapse after complete response to initial therapy, entered onto International Society of Pediatric Oncology (SIOP) and Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP) trials between 1992 and 2012.
Results: Thirty-seven of 237 CCSK patients (16%) treated according to SIOP and AIEOP protocols developed a relapse. Median time from initial diagnosis to relapse was 17 months (range, 5.5 months - 6.6 years). 35/37 relapses (95%) were metastatic; the most common sites of relapse were brain ($n = 13$), lungs ($n = 7$) and bone ($n = 5$). Relapse treatment consisted of chemotherapy ($n = 30$), surgery ($n = 19$) and/or radiotherapy ($n = 18$), followed by high dose chemotherapy and autologous bone marrow transplantation (ABMT) in 14 patients. 22/37

patients (59%) achieved a second complete remission (CR); 15 of whom (68%) developed a second relapse. Five-year event-free survival (EFS) after relapse was 18% (95% CI: 4 - 32%) and 5-year overall survival (OS) was 26% (95% CI: 10 - 42%).
Conclusions: In this largest series of relapsed CCSK patients ever described, overall outcome is poor. Relapses tend to occur late, so extensive follow-up is desirable. Most relapses are metastatic and brain relapses are more common than previously recognized. Intensive treatment aiming for local control, followed by high dose chemotherapy and ABMT, seems to be of benefit to enhance survival. Novel development of targeted therapy is urgently required.

O-029

GAIN OF 1Q AS A BIOMARKER IN PRE-TREATED WILMS TUMOUR IN THE SIOP WT 2001 TRIAL: A SIOP RENAL TUMOURS BIOLOGY CONSORTIUM STUDY

T. Chagtai[1], C. Zill[2], L. Dainese[3], R. Williams[1], J. Wegert[2], M. Maschietto[1], G. Vujanic[4], N. Sebire[5], I. Leuschner[6], P. Ambros[7], L. Kager[8], M. O'Sullivan[9], A. Blaise[3], C. Bergeron[10], D. Gisselsson[11], M. Kool[12], M. van den Heuvel-Eibrink[13], N. Graf[14], H. van Tinteren[15], A. Coulomb[3], M. Gessler[16], K. Pritchard-Jones[1]

[1]Molecular Haematology and Cancer Biology, UCL Institute of Child Health, London, United Kingdom; [2]Wuerzburg University, Theodor-Boveri-Institut fuer Biowissenschaften, Wuerzburg, Germany; [3]Anatomie et Cytologie Pathologiques, Hopitaux Trousseau, Paris, France; [4]School of Medicine, Cardiff University, Cardiff, United Kingdom; [5]Dept of Histopathology, Great Ormond Street Hospital, London, United Kingdom; [6]Dept. of Paediatric Pathology, Kiel University, Kiel, Germany; [7]Childrens Cancer Research Institute, St. Anna Childrens Hospital, Vienna, Austria; [8]Department of Pediatrics, St. Anna Childrens Hospital, Vienna, Austria; [9]Pathology Department, Our Lady's Children's Hospital, Dublin, Ireland; [10]IHOP, Institut d'Hématologie et d'Oncologie Pédiatrie, Lyon, France; [11]Department of Clinical Genetics, Lund University, Lund, Sweden; [12]Division of Pediatric Neurooncology, German Cancer Research Center, Heidelberg, Germany; [13]Paediatric Oncology, Erasmus MC, Rotterdam, Netherlands; [14]Paediatric Oncology, University of Saarland, Homborg, Germany; [15]Department Biometrics, Netherlands Cancer Institute, Amsterdam, Netherlands; [16]Theodor-Boveri-Institut fuer Biowissenschaften, Wuerzburg University, Wuerzburg, Germany

Objectives: To further improve outcomes for Wilms tumor (WT), there is a clinical need for molecular biomarkers with sufficient sensitivity and specificity for use in risk stratification. The SIOPWT2001 trial, that enrolled over 4,000 patients from 261 centres in 28 countries, aimed to evaluate the utility of loss of heterozygosity (LOH) of 1p/16q in relation to histological risk group assessed after pre-operative chemotherapy and incorporate analysis of new potential biomarkers such as gain of 1q.
Methods: The SIOP-RTSG biology consortium contributed 911 frozen tumour samples from SIOPWT2001 trial patients in 7 countries for molecular analysis of 1p/16q LOH (microsatellite analysis) and copy number assessment at 1p/16q, 1q, and several other loci of interest in WT (MLPA analysis). Analyses were conducted in 3 laboratories, with exchange of a blinded quality assurance sample set.
Results: To date, analysis of 365 tumours shows LOH 1p (10%), LOH16q (18%) and combined LOH (3%), with a significant association of LOH 16q with anaplastic histology but not with the SIOP high risk 'blastemal-type' WT. Gain of 1q is found in 98/420 (23%), with increased frequency in blastemal (50%) and anapaestic (44%) WT but similar, lower frequency across all other histological subtypes (mixed:21%; regressive:23%; epithelial:21%; stromal:19%). Preliminary survival analysis of 304 cases showed significant hazard ratios of 3.1 (1.8-5.4) for relapse and 2.7 (1.2-6.2) for death for 1q gain/normal, respectively. Final assessment of 1q gain in multivariate analysis incorporating histological risk group, tumour stage and patient age for all 911 patients is planned for April 2014, once the full molecular dataset is integrated with the international clinical trial database.
Conclusions: Gain of 1q is a potential adverse biomarker for WT. Its association with high risk histological features after pre-operative chemotherapy and independent impact on survival require assessment in a larger number of patients before consideration for clinical use.

O-030

RISK FACTORS FOR CHRONIC KIDNEY DISEASE IN CHILDREN AFTER SURGERY FOR UNILATERAL RENAL TUMOR

D. Cozzi[1], S. Ceccanti[1], S. Frediani[1], I. Falconi[1], D. Morgante[1], R. Iaconelli[1], F. Cozzi[1]

[1]Pediatric surgery unit, Sapienza University of Rome, Rome, Italy

Objectives: Chronic kidney disease (CKD) is associated with increased risk for cardiovascular diseases and overall mortality. We analyzed the characteristics of a cohort of patients with CKD long after surgery for unilateral renal tumor during childhood to identify modifiable risk factors for CKD.
Methods: A single-center observational study of 60 children who underwent nephrectomy and 12 children who underwent nephron-sparing surgery (NSS) for unilateral renal tumor. Glomerular filtration rate was estimated (eGFR) with the Modification of Diet in Renal Study or the Schwartz formulas as appropriate for age. CKD was defined as an eGFR < 90 ml/min/1.73m^2.
Results: At a mean $\pm$ SD age of 27 ± 15 years after surgery, CKD was present in 32 patients (44%). Older age ($p = 0.01$), nephrectomy ($p = 0.008$), pre-operative renal dysfunction ($p = 0.02$), higher tumor stages ($p = 0.001$), blood hypertension ($p = 0.001$), albuminuria ($p = 0.03$), and acquired renal cyst ($p = 0.03$) were more frequently associated with CKD. Adjuvant therapy, second tumor prevalence and co-morbidities did not influence the CKD development.
Conclusions: After surgery for unilateral renal tumor during childhood, main risk factors for CKD in some subjects included 50% ablation of renal parenchyma, age-related decline in renal function, and adaptive renal hyperfiltration.
In children with unilateral renal tumor nephrectomy might no longer be regarded as the gold standard surgical treatment when NSS is feasible.

BRAIN TUMOURS BIOLOGY 1

O-031

MOLECULAR CLASSIFICATION OF EPENDYMAL BRAIN TUMORS

H. Witt[1], M. Sill[2], K. Wani[3], S.M. Mack[4], M.D. Taylor[4], D. Ellison[5], A. Korshunov[6], M. Kool[1], D.T.W. Jones[1], K. Aldape[3], ERC[7], S.M. Pfister[1]

[1]Pediatric Neurooncology, German Cancer Research Center, Heidelberg, Germany; [2]Biostatistics, German Cancer Research Center, Heidelberg, Germany; [3]Neuropathology, MD Anderson, Houston, USA; [4]Brain Tumour Research Centre, The Sick Kids Hospital, Toronto, Canada; [5]Neuropathology, St. Jude Children's Hospital, Memphis, USA; [6]Neuropathology, University Hospital Heidelberg, Heidelberg, Germany; [7]Ependymoma Research Network, Germany

Objectives: Histopathological grading of ependymoma according to the WHO classification of CNS tumors is extremely challenging. A comprehensive molecular stratification scheme is absolutely essential and contemporary, since modern technologies reached routine practise. During the past decade, the biological understanding of ependymomas has improved significantly; especially molecular subgroups based on transcriptomic alterations were defined. Two distinct biological entities of ependymoma were identified by several studies (designated Group-A, CIMP-positive and Group-B, CIMP-negative), which show striking differences in genetic characteristics and clinical outcome. A similar consensus for supratentorial and spinal ependymoma is lacking.
Methods: We studied genome-wide DNA methylation (Illumina HumanMethylation450) in 308 primary ependymal tumors, including ependymomas, subependymomas (SE), and myxopapillary ependymoma (MPE) of distinct localizations. To identify meaningful molecular subgroups, we conducted unsupervised hierarchical clustering. Gene expression profiling was used to validate these molecular subgroups, to identify differentially expressed and epigenetically silenced genes.
Results: DNA methylation data showed that ependymal brain tumors can be classified into several molecular subgroups. Group-A tumors (CIMP-positive), Group-B tumors (CIMP-negative), MPE, and SE formed robust distinct clusters. Supratentorial ependymomas can be classified into two principle molecular subgroups, one of is associated with highly recurrent RELA fusion, displays a poor prognosis, and occur in young children and infants. Notably, a significant number of ependymomas previously classified by histology as WHO Grade II/III look like SE by DNA methylation, and also have extremely good survival.
Conclusions: In summary, using genome-wide DNA methylation analysis we could delineate meaningful molecular subgroups of ependymal brain tumors including supratentorial ependymoma. Diagnoses of tumors with challenging histopathological features can now be supported easily by this DNA methylation technology. Hence, this approach offers the opportunity to replace the current ambiguous histopathological grading system with an unbiased molecular classification that readily distinguishes biologically, genetically, and clinically meaningful subgroups of ependymal brain tumors.

O-032

POSTERIOR FOSSA EPENDYMOMA SUBGROUPS HAVE DISTINCT THERAPEUTIC AND PROGNOSTIC IMPLICATIONS

V. Ramaswamy[1], S.C. Mack[1], E. Bouffet[2], K. Aldape[3], Y. Cho[4], W.A. Weiss[5], X. Fan[6], A. Korshunov[7], S.C. Pfister[7], M. Taylor[8]

[1]Neurosurgery, The Hospital for Sick Children, Toronto, Canada; [2]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [3]Pathology, MD Anderson, Houston, USA; [4]Neurology, Stanford University School of Medicine, Palo Alto, USA; [5]Neurology, University of California, San Francisco, USA; [6]Neurosurgery, University of Michigan, Ann Arbour, USA; [7]Pediatric Neuro-Oncology, German Cancer Research Center, Heidelberg, Germany; [8]Neurosurgery, Hospital for Sick Children, Toronto, Canada

Objectives: Recent integrated genomic studies has shown that posterior fossa ependymoma comprise two distinct molecular subgroups, the CIMP+ve group and CIMP-ve group where CIMP+ve patients are typically younger and have a worse prognosis. Current standard of care for all posterior fossa ependymoma include surgery and conformal external beam radiation to the tumour bed, irrespective of extent of resection or subgroup. We sought to delineate the prognostic implications of external beam irradiation in a subgroup specific manner.

Methods: We assembled a cohort of 83 posterior fossa ependymoma's and were subgrouped using DNA methylation. Clinical details were ascertained through a retrospective chart review.
Results: In order to characterize treatment implications of ependymoma subgroups, overall survival was stratified by treatment with external beam irradiation. When restricting the analysis to CIMP +ve ependymoma with gross total resections, external beam irradiation confers a survival advantage ($p = 0.063$). Subtotally resected CIMP +ve ependymoma have a dismal prognosis without any significant difference in survival with the administration of external beam irradiation ($p = 0.75$). In CIMP –ve patients, administration of upfront external beam irradiation results in improved progression free survival ($p = 0.082$), however, overall survival is 100% across all patients ($p = 1$).
Conclusions: The survival benefit of adjuvant external beam irradiation in posterior fossa ependymoma is highly dependent on subgroup. In CIMP +ve cases, external beam irradiation has no benefit in patients with subtotally resected tumours, and these patients should be considered for enrolment in clinical trials. A significant proportion of CIMP –ve patients can be cured with surgical resection alone, and the remainder can likely be salvaged with irradiation at recurrence.

O-033

EPIGENOMIC ALTERATIONS DEFINE LETHAL CIMP-POSITIVE EPENDYMOMAS OF INFANCY

S.C. Mack[1], H. Witt[2], S.M. Pfister[2], A. Korshunov[2], M.D. Taylor[1], G.E.N.E. Global Ependymoma Network of Excellence[1]

[1]Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada; [2]Division of Pediatric Neurooncology, DKFZ, Heidelberg, Germany

Objectives: Ependymomas are chemo-resistant tumours, which in children, commonly arise in the region of the brain known as the posterior fossa (PF). PF ependymomas comprise two clinically and molecularly distinct diseases termed PFA and PFB. While PFB ependymomas occur most often in older children, exhibit a large degree of chromosomal instability, and have a favorable prognosis, PFA ependymomas arise most often in infants, have very few chromosomal alterations, and are associated with poor survival. The purpose of our study was to characterize the mutational and epigenetic landscape of PF ependymoma to identify drivers of tumourigenesis and targets for therapy.
Methods: We performed whole-genome sequencing of 5 PF ependymomas, and whole-exome sequencing of 42 PF ependymomas. We undertook DNA methylation profiling of 79 ependymomas by MBD2-chip, 48 PF ependymomas by Illumina 450K microarrays, and 6 PF ependymomas by whole-genome bisulfite sequencing. These findings were supported by H3K27me3 ChIP-seq of 11 PF ependymomas.
Results: Our findings reveal that PF ependymoma harbour a stable mutational landscape, exhibiting zero recurrent mutations in coding space. This was in contrast to widespread epigenomic alterations, at the level of DNA and H3K27 methylation, distinguishing between PFA and PFB. We demonstrate that PFA ependymomas are characterized by DNA hypermethylation at CpG islands, described as a CpG island methylator phenotype (CIMP+), and that both DNA and H3K27 methylation converge upon genes known to be silenced by the PRC2 complex in embryonic stem cells. We show that PFA-CIMP+ ependymoma short-term cultures are highly sensitive to inhibitors of DNA methylation and inhibitors of H3K27me3 shown both *in vitro* and *in vivo*.
Conclusions: Our study represents the first subgroup specific therapy shown to be effective in PFA ependymoma, and suggests that agents which target DNA methylation and/or H3K27 tri-methylation in patients harbouring PFA-CIMP+ ependymoma may be efficacious to use in clinical trials.

O-034

COMBINED MODEL OF MOLECULAR AND CLINICAL PROGNOSTIC MARKERS ENHANCES RISK STRATIFICATION OF MEDULLOBLASTOMA

D.J.H. Shih[1], P.A. Northcott[2], M. Remke[1], A. Korshunov[3], D.T.W. Jones[2], M. Kool[2], S.M. Pfister[2], M.D. Taylor[1]

[1]Developmental & Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada; [2]Division of Pediatric Neurooncology, German Cancer Research Center (DKFZ), Heidelberg, Germany; [3]CCU Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany

Objectives: Medulloblastoma comprises four distinct molecular subgroups – WNT, SHH, Group3, and Group4. Current medulloblastoma protocols stratify patients based on clinical features: patient age, metastatic stage, extent of resection, and histological variant. Stark prognostic and genetic differences between the four subgroups suggest that subgroup-specific molecular biomarkers could improve patient prognostication.
Methods: Molecular biomarkers were identified from a discovery set of 673 medulloblastomas from 43 cities around the globe. Combined risk stratification models were designed based on clinical and cytogenetic biomarkers identified by multivariate Cox proportional-hazards analyses. Identified biomarkers were tested using FISH on a non-overlapping medulloblastoma tissue microarray ($n = 453$), with subsequent validation of the risk stratification models.
Results: Subgroup information improves the predictive accuracy of a multivariate survival model compared to clinical biomarkers alone. Most previously published cytogenetic biomarkers are only prognostic within a single medulloblastoma subgroup. Profiling a six-pack of FISH biomarkers (*GLI2*, *MYC*, 11, 14, 17p, and 17q) on FFPE tissues, we can reliably and reproducibly identify very low-risk and very high-risk patients within each of SHH, Group3 and Group4 medulloblastomas.
Conclusions: Combining subgroup and cytogenetic biomarkers with established clinical biomarkers substantially improves patient prognostication, even in the context of heterogeneous clinical therapies. The prognostic significance of most molecular biomarkers is restricted to a specific subgroup. We have identified a small panel of cytogenetic biomarkers that reliably identifies high-risk and low-risk groups of patients and which will make an excellent tool for selecting patients for therapy intensification and therapy de-escalation in future clinical trials.

O-035

MAINTENANCE OF MOLECULAR SUBGROUP AFFILIATION IN METASTATIC MEDULLOBLASTOMA

X. Wang[1], A.M. Dubuc[1], A. Korshunov[2], V. Ramaswamy[1], D. Gendoo[3], S. Mack[1], M. Remke[1], E. Bouffet[4], S.M. Pfister[5], M.D. Taylor[6]

[1]Developmental and Stem Cell Biology, Hospital for Sick Children, Toronto, Canada; [2]CCU Neuropathology, University of Heidelberg, Heidelberg, Germany; [3]Medical Biophysics, Princess Margaret Cancer Centre, Toronto, Canada; [4]Haematology/Oncology, Hospital for Sick Children, Toronto, Canada; [5]Haematology/Oncology, University of Heidelberg, Heidelberg, Germany; [6]Neurosurgery, Hospital for Sick Children, Toronto, Canada

Objectives: Previous genomic and molecular analyses have revealed that medulloblastoma comprises four distinct molecular variants with distinct genetics, transcriptomes, and outcomes. Subgroup affiliation has been previously shown to remain stable at the time of recurrence, which likely reflects their distinct cells of origin. However, an important question that remains unanswered is subgroup stability in the metastatic compartment.
Methods: We assembled a cohort of 12-paired primary-metastatic tumors collected in the MAGIC consortium, and established their molecular subgroup affiliation by performing integrative gene expression and methylation analysis. Frozen tissues were collected and profiled using Affymetrix gene expression arrays and Illumina methylation arrays. Class prediction and hierarchical clustering were performed using existing published datasets.
Results: Our molecular analysis establishes the unequivocal maintenance of molecular subgroup affiliation in metastatic medulloblastoma. We further validated these findings by interrogating a non-overlapping cohort of 19-pairs of primary-metastatic tumors from the Burdenko Neurosurgical Institute using an orthogonal technique of immunohistochemical staining. We confirm the perfect concordance, identified using integrative molecular analysis, between molecular subgroup affiliation at both the primary site and metastatic lesions on the basis of immunohistochemical staining.
Conclusions: This investigation represents the largest reported primary-metastatic paired cohort profiled to-date and provides a unique opportunity to evaluate subgroup-specific molecular aberrations within the metastatic compartment. Although previous studies have shown the existence of clonal evolution of the metastatic compartment from its matching primary tumor, the maintenance of subgroup affiliation presents a treatment opportunity to target subgroup-specific events. Our findings further support the notion that medulloblastoma subgroups arise from distinct cells of origin, which are carried forward from ontogeny to oncology.

O-036

RECURRENT MEDULLOBLASTOMA IS HIGHLY DISTINCT FROM ITS MATCHED PRIMARY TUMOR

L. Garzia[1], S. Morrissy[1], P. Skowron[1], S. Jelveh[2], P. Lindsay[2], L. Collier[3], A. Dupuy[4], D. Lagaerspada[5], R. Hill[2], M.D. Taylor[1]

[1]BTRC, The Hospital for Sick Children, Toronto, Canada; [2]Radiation Oncology, Princess Margaret Cancer Centre, Toronto, Canada; [3]Pharmacology, University of Winsconsin-Madison, Madison, USA; [4]Anatomy & Cell Biology, University of Iowa, Iowa City, USA; [5]Department of Genetics, University of Minnesota, Minneapolis, USA

Objectives: Medulloblastoma (MB) is the most common paediatric malignant brain tumor. By the way of optimal surgery, radiation, and chemotherapy, medulloblastoma can be treated but despite the best therapy the disease recurs in 40% of the cases. We developed a protocol to study the genetic differences between primary and recurrent tumors *in vivo*, using our transposon mutagenesis driven mouse model.
Methods: Our novel murine model of metastatic MB is highly penetrant, has a short latency, and involves random secondary genetic events. The model is based on mobilizing the Sleeping Beauty transposon in the cerebella of $Ptch^{+/-}$ mice. We performed sub-total surgical removal of the murine tumors, and then treated the mice by multi-fraction CT-guided craniospinal irradiation. By the way of next generation sequencing we identified mutated driver genes in the primary tumors as compared to the recurrences.
Results: 70% of the mice treated with surgery and CSI recurred locally, a smaller fraction (30%) recurred distally with recurrent disease on the spinal cord. Recurrences are genetically

divergent from their matched primary tumors. We have sequenced primary and recurrent tumors identifying several potential synthetic lethal genes in the primary and relapse drivers, which are only found mutated in the recurrences. We selected actionable targets and performed *in vitro* radiosensitization assays with small molecules inhibitors of the predicted driver genes, showing a reversal of radiation resistance.
Conclusions: Primary MBs are highly genetically different from the recurrences, urging the scientific community to develop different therapeutic approaches to efficiently target primary and recurrent human tumors. As our mouse model shows the same rate and pattern of recurrence observed in human patients is an extremely valuable translational platform to design new strategy against recurrent MB. Highly targetable events in genes known to play a role in cell-cycle, apoptosis and proliferation, are potential drivers of local and distal MB recurrence.

BONE TUMOUR - FASANELLI SESSION

O-037

ZOLEDRONATE DOES NOT REDUCE THE RISK OF TREATMENT FAILURE IN OSTEOSARCOMA: RESULTS OF THE FRENCH MULTICENTRE OS2006 RANDOMISED TRIAL

L. Brugieres[1], M.C. Le Deley[2], F. Rédini[3], P. Marec-Bérard[4], H. Pacquement[5], C. Lervat[6], J.C. Gentet[7], N. Entz Werle[8], B. Bui[9], N. Corradini[10], E. Bompas[11], N. Penel[6], M.D. Tabone[12], G. De Pinieux[13], P. Petit[14], K. Buffard[15], J.Y. Blay[16], S. Piperno-Neumann[17]

[1]Pédiatrie, Gustave Roussy, Villejuif, France; [2]Epidemiology, Gustave Roussy, Villejuif, France; [3]Laboratoire de Physiopathologie de la Résorption Osseuse et Therapie des Tumeurs Osseuses Primitives, UMR 957, Nantes, France; [4]Pediatry, CHU Lyon, Lyon, France; [5]Pediatry, Institut Curie, paris, France; [6]Pediatry, Centre Oscar Lambret, Lille, France; [7]Pediatry, CHU La Timone, Marseille, France; [8]Pediatry, CHU Strasbourg, Strasbourg, France; [9]Pediatry, CHU Bordeaux, Bordeaux, France; [10]Pediatry, CHU Nantes, Nantes, France; [11]Pediatry, CHU Nantes Unicancer, Nantes, France; [12]Pediatry, APHP Trousseau, Paris, France; [13]Unité d'Anatomie et Cytologie Pathologiques, CHU Tours, Tours, France; [14]Imagerie Médicale, Hôpital d'Enfants la Timone, Marseille, France; [15]Clinical Research, Unicancer, Paris, France; [16]Pediatry, Unicancer CHU Lyon, Lyon, France; [17]Medical Oncology, Institut Curie, Paris, France

Objectives: Based on anti-tumour effect of zoledronate in vitro and in experimental models of rat osteosarcoma, we assessed whether zoledronate (Z) in combination with chemotherapy and surgery improved Event-Free Survival (EFS) in children and adults with osteosarcoma.
Methods: Experimental treatment consisted of 10 Z-injections (4 pre and 6 postoperative), 4 mg/injection in adults, 0.05 mg/kg/injection in younger patients. Chemotherapy included methotrexate-etoposide-ifosfamide +/-adriamycine-cisplatin in children/adolescents, and doxorubicin-ifosfamide-cisplatinum in adults. Balanced randomisation between Z+arm and Z-arm was stratified by centre, age, chemotherapy type and risk group (localised resectable disease versus unresectable primary and/or metastases). The study was planned as an open-label superiority trial, with three interim analyses (early stopping for efficacy or harm) disclosed to an independent data and safety monitoring board (DSMB). 470 patients (170 events) were required to achieve an 80%-power to detect a 13%-improvement of 3-year EFS (H1: 55% versus 68%, HR (event) = 0.65) with zoledronate (2-sided alpha = 0.05).
Results: A second interim analysis was performed after the inclusion of 318 patients (82% with a localised and resectable tumour) recruited between April-2007 and February-2014: 158 Z- and 160 Z+. No significant increase in toxicity was found in Z+, except expected hypocalcemia grade 2-4 ($p < 0.0001$). With a median follow-up of 3.1 years, 106 events and 58 deaths were reported, including one treatment-related death. The risk of failure was not reduced in Z+ compared to Z-: HR (event) = 1.31 [0.79–2.18], p = 0.17; HR (death) = 1.42 [0.70–2.88], p = 0.21. Results were similar after exclusion of eight Z+patients who had received $\leq$1 zoledronate-injection, and were homogeneous across the randomisation strata. Futility analysis, performed on DSMB request, showed that the probability of demonstrating a benefit was <0.0001. Following DSMB recommendation, the trial steering committee decided to stop accrual in the trial.
Conclusions: With current follow-up, the addition of zoledronate to chemotherapy did not reduce the risk of failure in osteosarcoma patients.

O-038

MODELING PRE-CLINICAL STANDARD-OF-CARE THERAPY AND IDENTIFICATION OF NOVEL AND REPURPOSED DRUG CLASSES WITH ACTIVITY AGAINST OSTEOSARCOMA

A.H.P. Loh[1,8], A.A. Shelat[2], C.L. Bradley[3], F.R. Krafcik[3], G.M. Miller[2], D.R. Goshorn[4], E. Stewart[4], V.M. Daryani[5], C.F. Stewart[5], A.J. Funk[6], P. Vogel[7], M.A. Dyer[3]

[1]Department of Surgery, St Jude Children's Research Hospital, Memphis, USA; [2]Department of Chemical Biology and Therapeutics, St Jude Children's Research Hospital, Memphis, USA; [3]Department of Developmental Neurobiology, St Jude Children's Research Hospital, Memphis, USA; [4]Department of Oncology, St Jude Children's Research Hospital, Memphis, USA; [5]Department of Pharmaceutical Sciences, St Jude Children's Research Hospital, Memphis, USA; [6]Animal Resource Center, St Jude Children's Research Hospital, Memphis, USA; [7]Veterinary Pathology Core, St Jude Children's Research Hospital, Memphis, USA; [8]Department of Paediatric Surgery, KK Women's and Children's Hospital, Singapore

Objectives: Treatment outcomes for osteosarcoma have stagnated with current therapies, yet many novel drug classes have not been explored nor integrated into existing regimens. We sought to screen novel agents and repurposed drugs for cytotoxicity against osteosarcoma, and to develop a preclinical model of human standard-of-care therapy, in order to integrate candidate compounds into existing treatment regimens.
Methods: With IACUC approval, orthotopic xenografts of human osteosarcoma were created in athymic nude mice. Femoral tumors and pulmonary metastases developed, recapitulating human disease. Early phase cultures of xenograft tumors and osteosarcoma cell lines were exposed to compounds from focused drug libraries in graded concentrations, both in insolation and in combination with standard-of-care agents. After 72 hours' exposure, an ATP cell viability assay was used to determine ec50 values and relative activity compared against a reference dose-response curve.
Results: 373 compounds in 432 formulations were screened with this high-throughput assay. Drug sensitivity profiles of primary and metastatic tumors showed minimal differences. Using ec50 <10uM and relative activity >50% as a threshold, sensitivity and activity were highest with HDAC and proteasome inhibitors, and inhibitors of PI3K with MEK and PI3K with mTOR, and lowest with PARP, RAF, ERK and MEK inhibitors. Panobinostat and CUDC-907 were the HDAC inhibitors with greatest potency. As a class, HDAC inhibitors showed additive effects when combined with doxorubicin. Separately, using area-under-concentration-time-curve (AUC) -guided dosing, mice were subjected to a multimodal standard-of-care regimen incorporating methotrexate with leucovorin rescue, doxorubicin, cisplatin, ifosfamide and etoposide, and hind limb amputation for local control.
Conclusions: We identified classes of novel and repurposed drugs with activity against human osteosarcoma cells. HDAC inhibitors have particular efficacy, and their effects are potentiated when combined with doxorubicin. These and other identified compounds can be further tested using our preclinical standard-of-care regimen to prioritize agents for introduction into existing clinical protocols.

O-039

WHOLE GENOME AND EXOME SEQUENCING REVEALS THE HETEROGENOUS LANDSCAPE OF CANCER GENES IN OSTEOSARCOMA

S. Behjati[1], P.S. Tarpey[1], M.R. Stratton[1], A.M. Flanagan[2], P.C. Campbell[1]

[1]Cancer Genome Project, Wellcom Trust Sanger Institute, Cambridge, United Kingdom; [2]Cancer Institute, University College London, London, United Kingdom

Objectives: The aim of this study was to describe through unbiased next generation sequencing the somatic alterations that drive osteosarcoma.
Methods: A series of 126 osteosarcoma tumours along with normal tissue DNA from the same patients was selected based on the availability of DNA and subjected to whole genome (n = 39) or whole exome (n = 87) massively parallel sequencing. The series comprised paediatric / adolescent (n = 67) and adult (n = 59) osteosarcoma. Ten cases arose secondary to radiation or to an underlying cancer predisposition syndrome. All classes of mutations, i.e. substitutions, small insertion and deletions (indels), structural rearrangements, and copy number changes were called using the analysis pipeline of the Cancer Genome Project.
Results: The overall configuration of the genomes varied greatly, in terms of mutation burden, mutational signatures and processes including chromothripsis and kataegis, with no striking differences found between paediatric/adolescent and adult osteosarcoma. Focusing the analysis on the cancer gene landscape, cancer genes mutated at a high frequency included established osteosarcoma drivers such as *TP53* or *RB1*. Novel cancer genes such as *H3F3A*, previously not implicated in the pathogenesis of osteosarcoma, were also identified. However, these were generally mutated at a low frequency. A number of potential therapeutic targets were identified, including mutations in different tyrosine kinase receptors.
Conclusions: The landscape of cancer genes driving osteosarcoma was markedly heterogeneous. Although our study identified cancer genes not previously implicated in the pathogenesis of osteosarcoma, no novel driver mutated at a high frequency was identified. This lack of an osteosarcoma specific driver distinguishes osteosarcoma from other bone tumours that we and others have studied by unbiased sequencing. Nevertheless, our findings may guide efforts that utilise targeted therapeutics in osteosarcoma. Furthermore, our findings enable studies of clinical cohorts by targeted sequencing of the cancer genes we describe here, to investigate whether tumour genotype accurately predicts clinical outcome.

O-040

LONG-TERM FOLLOW-UP OF THE CESS 81 AND CESS 86 EWING SARCOMA TRIALS

H. Juergens[1], C. Hoffmann[1], U. Dirksen[1], M. Paulussen[2], A. Ranft[1]

[1]Pediatric Hematology and Oncology, University Hospital, Muenster, Germany; [2]Vestische Kinder- und Jugendklinik, Witten/Herdecke University, Datteln, Germany

Objectives: Since 1980 patients with Ewing sarcoma have been treated according to consecutive protocols (CESS) of the German Society of Pediatric Oncology and Hematology (GPOH) *. Post treatment surveillance also includes long term follow-up**.

Methods: 673 patients (pts) entered into the CESS 81 (n = 183) (1980-1985) and CESS 86 (n = 490) (1985-1992) Ewing sarcoma trials were analyzed. 375 pts (59%) were male, 278 (41%) female. 549 pts (82%) had localized, 124 (18%) metastatic disease. The median age at diagnosis was 14.8 years (range 0.7 - 41.4). The median age of survivors at last time of observation was 28.9 years (range 8.8 - 63.3). Median follow-up time of survivors was 15.5 years (range 0.3 - 30.6).
Results: 315 pts (47%) were alive at last follow-up. Events were observed in 361 pts: local relapse in 19%, distant relapse in 64%, combined relapse in 13%, and secondary malignancies in 4%. 10-year event-free survival (EFS) was 0.49 (SE = 0.02) in localized, and 0.21 (SE = 0.04) in metastatic disease. 10-year overall survival (OS) was 0.54 (SE = 0.02) in localized, and 0.23 (SE = 0.04) in metastatic disease. Self-reported late morbidity was available from 128 of 315 survivors: 19.5% cardiovascular and 2% renal abnormalities, and secondary amputation (3.9%). 19.8% of the former patients rated their health status as less good or poor. 7.3% have been unemployed more than 1 year in the last 5 years. 62.2% had a handicapped pass, 9.9% with 100%.
Conclusions: Long-term observation is crucial in pediatric cancer survivors. Nearlyhalf of patients of the earliest phase III Ewing sarcoma trials are long-term survivors. Of patients with recurrence approx. 90% died from disease. Patient-related outcome scores are currently investigated in a long-term observation study for inclusion into long-term follow-up guidelines and to better predict the long-term quality of survivorness.
*supported by Deutsche Krebshilfe **supported by BMBF/DLR 01ER0807

O-041

PROGNOSIS OF CHILDREN AND ADOLESCENTS WITH SOFT TISSUE EWING TUMORS (STET) TREATED IN 3 CONSECUTIVE, PROSPECTIVE STUDIES OF THE COOPERATIVE WEICHSTEILSARKOM STUDIENGRUPPE (CWS)

E. Koscielniak[1], T. Dantonello[1], B. Blank[1], G. Seitz[2], I. Leuschner[3], B. Kazanowska[4], R. Ladenstein[5], G. Ljungman[6], F. Niggli[7], S. Bielack[8], E. Hallmen[8], T. Klingebiel[9]

[1]Pediatric Oncology/Hematology and Immunology, Olgahospital Klinikum Stuttgart, Stuttgart, Germany; [2]Department of Pediatric Surgery and Pediatric Urology, University Children's Hospital, Tuebingen, Germany; [3]Department of Paidopathology, University Hospital, Kiel, Germany; [4]Department of Paediatric Bone Marrow Transplantation Oncology and Hematology, Medical University, Wroclaw, Poland; [5]Children's Cancer Research Institute, St. Anna Children's Hospital, Vienna, Austria; [6]Department of Pediatric Haematology and Oncology, Children's University Hospital, Uppsala, Sweden; [7]Department of Pediatric Haematology and Oncology, Children's University Hospital, Zürich, Switzerland; [8]Department of Pediatric Oncology/Hematology and Immunology, Olgahospital Klinikum Stuttgart, Stuttgart, Germany; [9]Department of Pediatric Oncology/Hematology and Hemostasis, University Children's Hospital, Frankfurt, Germany

Objectives: Intensive chemotherapy (CHT) and aggressive local therapy are regarded as a golden standard in the treatment of Ewing sarcoma. However, the optimal CHT-intensity and the extent of local modalities are still not known. Different Ewing Sarcoma studies differ concerning CHT intensity and recommendation for local therapy. We present the therapy results of patients with STET treated in the three consecutive CWS-Studies CWS--91, -96 and 2002.
Methods: 244 pts aged 1-21 yrs were registered in the CWS-91 (n = 84), CWS-96 (n = 116) - or CWS 2002P (n = 44). 19 pts were in IRS Group I, 55 in II and 170 in III. In the CWS -91 a combination EVAIA (Ifo, Vcr, Dox, ActD, VP16) was used. In the CWS-96 the patients were randomized between a 4 drug combination VAIA (Ifo, Dox, ActD, VCR) vs. 6 drug CEVAIE (Epi-Dox instead of Dox, plus carboplatin and VP16). In CWS 2002P, VAIA plus maintenance CHT with Cyclophosphamid and Vinblastine were recommended. Irradiation was recommended depending on results of the primary or secondary resection.
Results: 5 yr event-free-survival (EFS) and OS (overall survival) were 62.8% and 73.2%. The EFS and OS by study were: CWS-91 64.1% and 71.9%, CWS-96 56.9% and 70.1%, CWS 2002P 78.5% and 86.1% respectively. The 5 yr EFS for the VAIA was: 66.3% for the CEVAIE: 51.7% (p = 0.053), the OS - 85.6% vs. 57.2% (p = 0.032). 5yr EFS and OS for irradiated (n = 172) vs. not irradiated patients were 63.0% vs. 61.7%, and 71.6% vs. 79.5% respectively.
Conclusions: The prognosis improved from CWS-91/96 to CWS 2002P. The CEVAIE was inferior in OS in comparison to the standard regimen VAIA. The stratification criteria allowed for the correct allocation to irradiation. The addition of maintenance CHT in the CWS 2002P may be associated with improved prognosis and should be examined in a randomised way.

O-042

DOES INTENSITY OF SURVEILLANCE AFFECT SURVIVAL AFTER SURGERY FOR SARCOMAS? RESULTS OF A RANDOMIZED NONINFERIORITY TRIAL

A. Puri[1], A. Gulia[1], R. Hawaldar[1], P. Ranganathan[1], R. Badwe[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: We hypothesized that a less intensive follow up protocol would not be inferior to the conventional follow up protocol in terms of overall survival (OS). We asked whether a chest radiograph follow up group was inferior to a CT scan follow up group in terms of detecting pulmonary metastasis; and whether a less frequent (6 monthly) follow up interval was inferior to a more frequent (3 monthly) follow up group in terms of detecting pulmonary metastasis and local recurrence.
Methods: A prospective randomized single-center non inferiority trial was conducted between January 2006 and June 2010. 500 non metastatic patients were randomized to demonstrate non inferiority by a margin (delta) of 10% (hazard ratio [HR], 1.36). The primary end point was OS at 3 years.
Results: At minimum follow up of 30 months (median, 42 months; range, 30–81 months), 3 year OS and DFS for all patients was 67% and 52%, respectively. OS was 67% and 66% in chest radiography and CT groups, respectively (HR, 0.9; upper 90% confidence interval [CI], 1.13). DFS rate was 54% and 49% in chest radiography and CT groups, respectively (HR, 0.82; upper 90% CI, 0.97). OS was 64% and 69% in 6-monthly and 3-monthly groups, respectively (HR, 1.2; upper 90% CI, 1.47). DFS was 51% and 52% in 6-monthly and 3-monthly groups, respectively (HR, 1.01; upper 90% CI, 1.2).
Conclusions: Inexpensive imaging will detect the vast majority of recurrent disease in patients with sarcoma without deleterious effects on eventual outcomes. Although less frequent visits adequately detected metastasis and local recurrence, this trial could not conclusively demonstrate non inferiority in OS for a 6-monthly interval of follow up visits against 3 monthly. This might have been a function of a small sample size; longer follow up in larger populations may confirm this finding.

SUPPORTIVE CARE AND LATE EFFECTS

O-043

STANDING ON PINS AND NEEDLES? PATTERNS AND SEVERITY OF VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA DURING THE FIRST YEAR OF TREATMENT

E. Smith[1], L. Lang[2], R. Ho[3], E.M. Wells[4], R.J. Hutchinson[5], J. Skiles[6], A. Chakraborty[7], C.W. Chiang[7], K. Thomas[1], J. Renbarger[8]

[1]School of Nursing, University of Michigan, Ann Arbor, USA; [2]Department of Medical and Molecular Genetics Center for Computational Biology and Bioinformatics School of Medicine, Indiana University, Indianapolis, USA; [3]Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, USA; [4]Department of Neurology and the Brain Tumor Institute, Children's National, Washington D.C., USA; [5]Department of Pediatrics, University of Michigan School of Medicine, Ann Arbor, USA; [6]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [7]Department of Medical and Molecular Genetics Center for Computational Biology and Bioinformatics, Indiana University School of Medicine, Indianapolis, USA; [8]Indiana University School of Medicine/ Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, USA

Objectives: The study purpose was to describe vincristine-induced peripheral neuropathy (VIPN) patterns and severity in children with preB acute lymphoblastic leukemia (ALL) during the first year of treatment.
Methods: 128 newly diagnosed children 1-18 years of age receiving vincristine 1.5 mg/M_2 (2mg maximum) per Children's Oncology Group (COG) treatment trials were recruited from four sites (Indiana University, University of Michigan, Vanderbilt University, Children's National). Neurologist-trained evaluators quantified VIPN based on patient-reported symptoms and physical examination using the Total Neuropathy Score-Pediatric Vincristine (TNS©-PV). Additional assessments were conducted using the NCI-CTCAE v.4.0. VIPN was assessed over the first year of therapy. Data were analyzed using descriptive statistics, correlations, paired t-tests, and cluster analysis. Vincristine dose density curves were calculated using the kernel density function.
Results: VIPN assessments (N = 1961) were performed on equal numbers of males and females. Most were Caucasian (87.7%) and non-Hispanic (78.1%). Mean age was 6.16 (SD 4.96) years (range 1-18). TNS©-PV and NCI-CTCAE score patterns were similar, but TNS©-PV scores revealed more granular details regarding specific signs and symptoms. Reflexes were affected most (mean/SD = 1.63/0.05, range 0-4). VIPN scores peaked 5-6 months post-diagnosis, approximately two months after reaching the maximum vincristine dose density, illustrating a coasting effect. VIPN did not improve in months 8-12 despite decreasing dose density. VIPN scores were positively associated with age ($p = .0095$) but not gender. Cluster analyses results revealed that some children ($n = 7$) experienced severe VIPN unrelated to dose density.
Conclusions: VIPN is most severe six months from the onset of ALL treatment and does not improve over the first year of treatment despite decreasing dose density. Cluster analysis identifies a cohort of children at risk for developing severe VIPN. Further research is ongoing to elucidate a baseline predictive signature for identifying high-risk patients.

O-044

GENETIC VARIANTS IN *SLC22A17* AND *SLC22A7* ARE ASSOCIATED WITH ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN CHILDREN

H. Visscher[1], C.J. Ross[2], S.R. Rassekh[3], G.S. Sandor[4], H.N. Caron[5], E.C. van Dalen[5], H.J. van der Pal[5], L.C. Kremer[5], B.C. Carleton[6], M.R. Hayden[2]

[1]Department of Pediatrics, Amalia Children's Hospital/Radboud University Medical Centre, Nijmegen, Netherlands; [2]Centre for Molecular Medicine and Therapeutics Child & Family

Research Institute, University of British Columbia, Vancouver, Canada; [3]Division of Pediatric Hematology/Oncology/BMT Department of Pediatrics, University of British Columbia, Vancouver, Canada; [4]Division of Pediatric Cardiology Department of Pediatrics, University of British Columbia, Vancouver, Canada; [5]Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [6]Division of Translational Therapeutics Department of Pediatrics, University of British Columbia, Vancouver, Canada

Objectives: The risk of anthracycline-induced cardiotoxicity (ACT), a serious adverse drug reaction of cancer therapy, is in part mediated by genetic variation. Recently, several genetic variants predictive of ACT in children were identified and replicated. This study was aimed to identify additional genetic variants associated with ACT and to assess whether these variants could improve a genotype-guided ACT risk prediction model.
Methods: We carried out a case-control association study in a discovery cohort of 78 serious ACT cases and 266 controls with replication in an independent cohort of 56 cases and 162 controls. Samples were genotyped for more than 4,500 single nucleotide polymorphisms (SNPs) in over 300 key genes pre-selected for relevance in drug transport, metabolism or toxicity. Predictive models including genetic and clinical risk factors were trained in the discovery cohort and assessed in the replication cohort.
Results: We identified significant genetic associations with ACT in the discovery cohort for two SNPs in *SLC22A17* (rs4982753) and *SLC22A7* (rs4149178) ($P = 0.0078$ and $P = 0.0034$, respectively), that were subsequently replicated ($P = 0.0071$ and $P = 0.047$; combined odds ratio 0.50 [95% CI 0.33-0.75] and 0.45 [95% CI 0.26-0.75]). Additional evidence for association was found for variants in *SULT2B1* and several genes related to oxidative stress. Adding the two *SLC22* variants to a risk prediction model improved the discriminative ability (Area Under Curve (AUC) from 0.75 to 0.78 for combined cohorts [$P = 0.029$]).
Conclusions: We identified and replicated two novel genetic variants predictive of ACT. Addition of these variants to a risk prediction model further improved this model, which could be used for risk stratification of patients who may benefit from alternative treatment strategies, more intensive cardiotoxicity monitoring or preventive treatment measures.

O-045

METABOLIC SYNDROME AND CARDIAC DYSFUNCTION IN ADULT SURVIVORS OF CHILDHOOD CANCER: RESULTS FROM THE ST. JUDE LIFETIME COHORT STUDY

G.T. Armstrong[1], V. Joshi[2], K. Ness[1], N. Zhang[3], D. Srivastava[3], D.A. Mulrooney[4], T.H. Marwick[5], M.M. Hudson[4], L.L. Robison[1], J.C. Plana[6]

[1]Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [2]Pediatric Cardiology, University of Tennessee Health Sciences, Memphis, USA; [3]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA; [4]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [5]Cardiology, Menzies Research Institute, Hobart, Australia; [6]Cardiology, Cleveland Clinic, Cleveland, USA

Objectives: Cardiac dysfunction after anthracycline chemotherapy and chest-directed radiotherapy (RT) is well established. The additional contribution of traditional cardiovascular risk factors and metabolic syndrome in aging survivors is less well defined.
Methods: Analysis included 1,679 ≥10 yr survivors (median age 31 yrs, range 18-59;. Echo included systolic (3D EF, abnormal <50%), diastolic function (grades 1-3 abnormal), global longitudinal (>-18.9) and circumferential (>-22.1) myocardial strain. Metabolic syndrome defined using NCEP-ATP III criteria. Logistic regression or Poisson regression was adjusted for current age, age at diagnosis, race/ethnicity, sex, chest RT and anthracycline exposure to calculate odds ratios (ORs) or relative risk (RR) and 95% confidence intervals (CI).
Results: Systolic dysfunction was detected in 5.1%, diastolic dysfunction in 10.2%, and abnormal strain in 43.1% (longitudinal) and 58.1% (circumferential). 27.8% of survivors had metabolic syndrome (obesity 29.2%, triglycerides >150mg/dl 25.3%. HDL cholesterol abnormal 36.7%, hypertension 45.6% and diabetes 32.1%). Metabolic syndrome was associated with increased risk for diastolic dysfunction (OR 2.6, CI 1.8-3.7) and strain abnormalities (longitudinal RR 1.6, CI 1.4-1.8; circumferential RR 1.1, CI 1.0-1.2), but not reduced EF (OR 1.2, 95% CI 0.7-2.1).
Conclusions: Although EF is preserved, metabolic syndrome increases risk for diastolic dysfunction and systolic dysfunction detected by longitudinal myocardial strain, independent of chest RT and anthracycline exposure. Interventions that prevent metabolic syndrome may reduce cardiac risk and should be considered.

O-046

ADVERSE SOCIAL OUTCOMES IN SURVIVORS OF CHILDHOOD CANCER: A MEDICAL RECORD LINKAGE STUDY

A. Font-Gonzalez[1], E.A.M. Feijen[1], E. van Dulmen-den Broeder[2], H.J. van der Pal[3], M.L. Essink-Bot[4], R.B. Geskus[5], H. Maurice-Stam[6], M.A. Grootenhuis[6], H.N. Caron[1], L.C. Kremer[1]

[1]Department of Pediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [2]Department of Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [3]Department of Medical Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [4]Department of Social Medicine, Academic Medical Center, Amsterdam, Netherlands; [5]Department of Clinical Epidemiology Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, Netherlands; [6]Pediatric Psychosocial Department, Academic Medical Center, Amsterdam, Netherlands

Objectives: To determine the likelihood of adverse social outcomes such as not being married/registered partner, not living independently and using social benefits in adult childhood cancer survivors (CCS) compared to the general Dutch population.
Methods: We linked a complete cohort of 5-year CCS treated at Emma Children's Hospital/Academic Medical Center (N = 1,647) with two administrative registers, the Municipal Personal Records Database (Dutch acronym: GBA) and the Social Economic Categories register (Dutch acronym: SECMBUS). We included CCS diagnosed between 1966-2001, aged above 18 years during the study period and alive at 1st January 1999. We retrieved anonymous social outcomes data from the last year that a person was registered in the GBA during 1999-2009 and compared it to a randomly selected sample of the general Dutch population obtained from GBA, matched on gender, year of birth and calendar year per CCS retrieved (sampling rate 1:20 at maximum). We conducted multivariate logistic regression analysis to estimate the likelihood of not being married/registered partner, not living independently and using social benefits compared to the general Dutch population. Furthermore, we used multivariate logistic regression within the CCS group to analyze patient-, cancer- and treatment-related associated risk factors for adverse social outcomes.
Results: After complete linkage, we obtained a group of 1,283 unique CCS and 25,188 reference persons (81% and 97.8% respectively, of individuals retrieved from GBA) with information on social outcomes. CCS had higher likelihood (odds ratio, 95% confidence interval) of not being married/registered partner (1.2, 1.1-1.4), not living independently (1.6, 1.3-1.9) and using social benefits (2.4, 2.0-2.8) compared to the general population. Radiotherapy (with or without surgery) increased the likelihood of using social benefits (2.6, 1.2-5.0) as well as a central nervous system tumor diagnosis (1.9, 1.1-3.4).
Conclusions: Targeted prevention of adverse social outcomes needs consideration to increase possibilities for survivors to develop socially in line with their peers.

O-047

HOSPITALIZATIONS AMONG ADULT SURVIVORS OF CHILDHOOD CANCER TREATED WITH STEM CELL TRANSPLANTATION

T. Schechter[1], P.C. Nathan[1], A. Gassas[1], M. Ali[1], M. Agha[2], M.L. Greenberg[2], J. Pole[2]

[1]Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Research Unit, Pediatric Oncology Group of Ontario, Toronto, Canada

Objectives: Knowledge regarding the burden of morbidity after HSCT once pediatric cancer survivors reach adulthood is sparse. Frequency of hospitalizations can serve as a proxy measure of morbidity. population. The aim of the study was to assess the number of hospitalization episodes in long-term adult survivors of childhood malignancies treated with HSCT.
Methods: We used record linkage between the SickKids' clinical transplant database, the Canadian Province of Ontario's pediatric cancer registry (POGONIS) and health care utilization data housed at the Institute for Clinical Evaluative Sciences (ICES). The study population included all adult (>5 years post transplant) survivors of childhood cancer treated with allogeneic/autologous HSCT at SickKids.
Results: 242 long-term adult survivors were followed for a mean of 12.3 years (148 allogeneic and 86 autologous HSCT). Mean age at HSCT was 11.5y (SD: 4.7) and 11.0y (SD: 5.3) for the allogeneic and autologous groups, respectively. 262 hospitalizations were documented in adults post allogeneic HSCT, representing a rate of 0.15 hospitalizations per follow-up year. Univariate analysis revealed that age >10 years at cancer diagnosis (RR = 3.53, 95% CI: 2.34-5.33), age >10 years at HSCT (RR = 5.88, 95% CI: 2.89-11.85), and female gender (RR = 1.70, 95% CI: 1.33-2.18) were associated with an increased rate of hospitalization. The underlying diagnosis, ALL vs. AML was not associated with increased rate of hospitalization despite the use of TBI among ALL patients. 106 hospitalizations were documented in adults post autologous HSCT, representing a rate of 0.09 hospitalizations per follow-up year. Age >10 y-o at time of HSCT (RR = 2.29, 95% CI: 1.29-4.04) and female gender (RR = 1.70, 95% CI: 1.15-2.52) were associated with increased rate of hospitalization.
Conclusions: Age > 10 years at time of HSCT and female gender were associated with increased risk for hospitalization. Our future studies focus on length of stay and the indications for these hospitalizations.

O-048

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDERS IN PEDIATRIC TRANSPLANT RECIPIENTS

C. Sergi[1], D. Yu[1], S. Girgis[1], B. Chiu[1]

[1]Department of Lab Med and Pathology, University of Alberta Hospital, Edmonton, Canada

Objectives: Recipients of solid organ transplantation (SOT) carry a substantially increased risk to develop posttransplant lymphoproliferative disorders (PTLD). Excess risk of cancer is

largely due to immunosuppression and oncogenic virus infection. Objective: We performed a clinicopathological review of PTLD in pediatric transplantations in our institution.
Materials and Methods
Recipients of pediatric (age at transplantation <21 years) SOT were reviewed and PTLD were classified using the WHO criteria: PTLD, early, or PTLD, monomorphic; and the organ/sites of involvement as nodal or extranodal.
Results: In over 500 SOT performed, there were 40 PTLD developed in 26 patients, patient's age (mean 13.6, range 1 to 29) with 11 cases classified as early PTLD, and 29 cases as monomorphic PTLD. The latency period of PTLD onset ranged from 10 months to 11 years, involving nodal sites 16, extranodal sites 24, with GI tract, lung, upper aerodigestive tract and liver most commonly involved. Diffuse large B-cell lymphoma with 23 cases (79%) was the most common cancer type and associated with EBV infection. The cumulative incidence rate of PTLD in pediatric heart transplant and lung transplant recipients were 8.5% and 5.9% respectively.
Conclusions: PTLD are relatively common in pediatric recipients of SOT and commonly involving nodal and extranodal sites, and in particular, in organs with mucosa-associated lymphoid tissues (MALT). Oncogenic viruses, especially EBV play an etiologic role in the development of PTLD in the pediatric transplant population.

NEUROBLASTOMA 2

O-049

A NEUROBLASTOMA RISK CLASSIFICATION MODEL FOR DEVELOPING COUNTRIES: A STUDY FROM THE INTERNATIONAL NEUROBLASTOMA (NB) RISK GROUP (INRG) DATABASE

W. London[1], V. Moroz[2], B. Hero[3], J.R. Park[4], D. Valteau-Couanet[5], A. Nakagawara[6], F. Berthold[7], K.K. Matthay[8], G. Schleiermacher[9], D. Machin[10]

[1]Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston MA, USA; [2]Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom; [3]Pediatric Oncology, University Children's Hospital, Koln, Germany; [4]Pediatric Hematology/Oncology, Seattle Children's Hospital, Seattle WA, USA; [5]Pediatric and Adolescent Oncology, Gustave Roussy Institute Universite Paris-Sud, Villejuif, France; [6]Pediatric Oncology, Chiba Cancer Research Institute, Chiba, Japan; [7]Pediatric Oncology, University of Cologne, Cologne, Germany; [8]Pediatric Hematology/Oncology, University of California San Francisco, San Francisco, USA; [9]Pediatric Oncology and INSERM U830, Institut Curie, Paris, France; [10]Biostatistics, University of Leicester, Leicester, United Kingdom

Objectives: Current methods for stratifying NB patients at diagnosis to INRG risk/pre-treatment groups are based on prognostic clinical, genomic, and histologic factors [Cohn et al, JCO 2009]. In developing countries, testing tumors for genomic biomarkers or histologic features is not possible; however, clinical tests serum ferritin and serum lactate dehydrogenase (LDH) are likely available.
Methods: Retrospective analysis included INRG patients with sufficient data for clinical risk factors and event-free survival (EFS). Survival tree regression was performed, considering only age (<18 months; ≥18 months), INSS stage (4; not 4), ferritin (<92; ≥92ng/mL), and LDH (<587; ≥587U/L). Patients were categorized into clinical pre-treatment risk groups by 5-yr EFS: very low (>85%), low (>75–≤85%), intermediate (≥50–≤75%), or high risk (<50%). EFS time was from diagnosis until first event (relapse/progression, second malignancy, death), or until last contact if no event occurred.
Results: From 8,800 INRG patients, 7,679 were able to be risk classified according to INRG definitions, including genomic and histological factors. Of 7,679, 3,509 had known age/stage/LDH/ferritin, and a clinical pre-treatment risk group was assigned: very low (n = 1319), low (n = 379), intermediate (n = 550), and high (n = 1261), with 5-yr EFS of 90 ± 1%, 80 ± 3%, 65 ± 3%, and 27 ± 2%, respectively. The clinical risk classification was the same as (58.1%) or similar to (12.8%) the INRG in 70.9% of patients. Based on 5-year EFS: INRG overestimated risk but clinical factors correctly assigned risk in 18.9% of patients; clinical factors overestimated (3.7%) or underestimated (6.4%) risk but INRG correctly assigned risk in 10.1% of patients.
Conclusions: In 89.9% of patients, clinical factors (age, stage, ferritin, LDH) do as well or better than clinical, genomic, and pathologic factors currently used in INRG risk/pre-treatment group assignment. The INRG-clinical pre-treatment risk stratification shows promise for developing countries to assign treatment intensity, whereby very low-risk patients can be spared unnecessary, expensive chemotherapy.

O-050

RISK FACTORS WITHIN THE EUROPEAN HIGH RISK NEUROBLASTOMA HR-NBL1/SIOPEN TRIAL

R. Ladenstein[1], U. Poetschger[1], R. Luksch[2], M. Elliot[3], V. Castel[4], I. Yaniv[5], V. Papadakis[6], J. Malis[7], P. Kogner[8], D. Valteau-Couanet[9]

[1]Studies and Statistics on Integrated Research, Children's Cancer Research Institute, Vienna, Austria; [2]Paediatric Oncology Haematology, Istituto Nazionale Tumori di Milano, Milano, Italy; [3]Paediatric Oncology Haematology, Leeds General Hospital, Leeds, United Kingdom; [4]Paediatric Oncology Unit, Hospital La Fe Valencia, Valencia, Spain; [5]Paediatric Oncology Haematology, Schneider Children's Medial Center of Israel, Petach Tikvah, Israel; [6]Paediatric Oncology Haematology, Agia Sofia Children's Hospital, Athens, Greece; [7]Paediatric Oncology Haematology, University Hospital Motol, Prague, Czech Republic; [8]Paediatric Oncology Haematology, Karolinska Hospital, Stockholm, Sweden; [9]Paediatric and Adolescent Oncology Department, Institut Gustave Roussy, Villejuif, France

Objectives: Evaluation of the unselected patient cohort of the HR-NBL1/SIOPEN trial including all non-randomised patients.
Methods: Since 02/02/2002, the trial accrued in 21 countries (175 centres) 2242 patients (pts) of whom 2022 had INSS stage 4 (eligibility <1year only pts with MycN amplification (MNA)) and 220 stage 2&3 with MNA of any age. The median age is 3.6yrs (range,1 day-20yrs). Four randomised questions are addressed (R0/R1/R2/R3). After Rapid Cojec or modified N7 induction (R0/R3), pts with insufficient response received additional 2nd line treatments (i.e. TVD 2- 4 courses) to proceed to myeloablative therapy (MAT/R1; BUMEL, CEM or mIBG containing regimes). Local control aimed at complete surgical resection (achieved in 76%) and radiotherapy of 21 Gy only to the primary tumour site. Till 2007 maintenance treatment was 13cis RA alone. In 2007 ch14.18/CHO mAb based immunotherapy (IT) was introduced with a modification towards a randomised IL2 question in 2009 (R2). To date 428pts received ch14.18/CHO based IT by the 8 hour infusion scheme.
Results: In stage 4 pts MNA frequencies are: 66% in 1-1.5 yrs (116/177, 66%), 44% in 1.5-5yrs (449/1108) and 22% (79/363) > 5yrs. The 5-yrs EFS&OS for all pts is 0.31 ± 0.01/0.41 ± 0.01 with rates of 0.28 ± 0.01/0.38 ± 0.01 for stage 4, but 0.63 ± 0.04/0.68 ± 0.04 in MNA stages 2&3 with lower rates in 24 infants (0.44 ± 0.12/0.43 ± 0.12). In stage 4 pts prognosis declines with age: infants and pts 1-1.5 yrs showed comparable outcomes (n = 186, 0.39 ± 0.07/0.47 ± 0.08), followed by pts of 1.5-5yrs (n = 1234, 0.30 ± 0.02/0.40 ± 0.02) and pts>5yrs (n = 402, 0.15 ± 0.02/0.28 ± 0.03). Partial response or better was more frequently observed in younger children with the following rates: 90%, 84%, 82%, 66%, 56% and 41% for age groups of 114 yrs of age.
Conclusions: Stage and age remain major prognostic factors whilst MNA pts clearly benefit from intensification.

O-051

IMAGE DEFINED RISK FACTORS (IDRF) IN NEUROBLASTOMA: INCIDENCE, EVOLUTION DURING TREATMENT AND CORRELATION WITH SURGICAL OUTCOME

L. Pio[1], C. Granata[2], G. Erminio[3], K. Holmes[4], H. Rubie[5], P. Buffa[6], V. Castel[7], D. Valteau-Couanet[8], S. Sarnacki[9], R. Haupt[3]

[1]Pediatric Surgery Unit, Istituto Giannina Gaslini DINOGMI University Of Genoa, Genoa, Italy; [2]Pediatric Radiology Unit, Istituto Giannina Gaslini, Genoa, Italy; [3]Epidemiology Biostatistics and Committees Unit, Istituto Giannina Gaslini, Genoa, Italy; [4]Department Pediatric Surgery, St George's Hospital, London, United Kingdom; [5]Hemato-Oncology Unit, Children's Hospital Toulouse, Toulouse, France; [6]Pediatric Surgery Unit, Istituto Giannina Gaslini, Genoa, Italy; [7]Pediatric Oncology Unit, Hospital La Fe, Valencia, Spain; [8]Département d'oncologie pédiatrique, GHU Paris-Sud - CLCC Institut de cancérologie Gustave Roussy, Paris, France; [9]Pediatric Surgery Department, Necker Enfants Malades Hospital Paris Descartes University, Paris, France

Objectives: Describe IDRF prevalence among patients enrolled in the European Unresectable Neuroblastoma (EUNB) study, evaluate their modification after chemotherapy, and how influenced surgical outcome.
Methods: IDRF were those reported by the treating physicians, but imaging reports were reviewed for those coded as "other" and a more specific IDRF was assigned. When the only IDRF was related to the size of the tumour (big), the patient was exluded from the study. Surgical outcomes were related with IDRF response to chemoterapy.
Results: Of the 160 patients enrolled in the EUNB study, 17 were excluded (8 no imaging pre second surgery, 6 "big tumor", 3 stage 3 after first surgery). The 143 evaluable patients had a total of 228 IDRF. The most frequent were: encasement of carotid sheath in cervical tumours (n = 4); infiltration of the left costo-vertebral junction in thorax (n = 9); and infiltration of renal pedicles in abdomen (n = 50).
Following chemotherapy 76 (33%) IDRF disappeared, but 33 new appeared. Complete IDRF disappearance was observed in 33 patients (23%), decrease in number but persistence in 13 patients (9%), no change in 70 (49%), disappearance of some but appearance of new IDRF in 15 (10%), and IDRF number increase in 12 (8%). Second surgery was not performed in 18 patients (3 because of CR or MRD after chemotherapy, and 15 because still inoperable). Of the 125 patients who underwent second surgery, 6 (5%) had a further biopsy, 30 (24%) had incomplete tumor excision; 36 (29%) had minimal residual, while 53 (42%) had complete resection. Complete resection or minimal residual were more frequent among children who had numerical reduction of IDRF (P = 0.002).
Conclusions: Chemotherapy was effective in 33% of IDRF, but in 27 patients (19%) new IDRF appeared despite chemotherapy. Second surgery was more successful in patients/tumors in which some chemotherapy related response was documented.

O-052

REVISED RISK ESTIMATION AND TREATMENT STRATIFICATION OF LOW- AND INTERMEDIATE-RISK NEUROBLASTOMA PATIENTS BY INTEGRATING CLINICAL AND MOLECULAR PROGNOSTIC MARKERS

M. Fischer[1], A. Oberthuer[1], D. Juraeva[2], R. Schmidt[3], A. Faldum[3], F. Berthold[1], F. Westermann[4], B. Brors[2], T. Simon[1], B. Hero[1]

[1]Pediatric Oncology, University of Cologne, Cologne, Germany; [2]Theoretical Bioinformatics, German Cancer Research Center, Heidelberg, Germany; [3]Biostatistics and Clinical Research, University of Muenster, Muenster, Germany; [4]Tumor Genetics, German Cancer Research Center, Heidelberg, Germany

Objectives: Precise risk estimation is essential to avoid under- and overtreatment of neuroblastoma patients. To optimize neuroblastoma treatment stratification, we aimed at developing a novel risk estimation system by integrating gene expression-based classification and established prognostic markers.
Methods: Microarray-based gene expression profiles were generated from 709 primary neuroblastomas. Classification models were built using a training set of 75 tumors with contrasting courses of disease, and subsequently validated in an independent test set ($n = 634$). Kaplan-Meier estimates and multivariate Cox regression analyses were used to assess the prognostic variables under investigation.
Results: The best-performing classifier (SVM_th10) consisted of 194 probes corresponding to 139 genes, and predicted patient outcome with an accuracy of 0.95 (sensitivity 0.93, specificity 0.97) in the validation cohort. The highest potential clinical value of the classifier was observed in current low- and intermediate risk (LR and IR, respectively) patients, in which the classifier significantly distinguished patients with diverging outcome (LR, 5-year OS 0.99 ± 0.01 *vs* 0.76 ± 0.11; IR, 5-year OS 1.0 *vs* 0.70 ± 0.09; both $p < 0.001$). In multivariate Cox regression models for non-high risk patients, the classifier outperformed risk assessment of the current German trial NB2004 (EFS, HR 5.07, 95%-CI 3.20-8.02, OS, HR 25.54, 95%-CI 8.40-77.66; both $p < 0.001$). Based on these findings, we developed a revised risk stratification system for LR/IR neuroblastoma patients by integrating established prognostic markers and the SVM_th10 classifier. According to this system, we newly identified patient subgroups with poor outcome (5-year EFS $18.5 \pm 7.8\%$), for whom we propose intensified treatment, and patient subgroups with beneficial outcome (5-year EFS $87.4 \pm 5.3\%$), who may benefit from treatment de-escalation.
Conclusions: Integration of gene expression-based classification and established prognostic markers improves risk estimation of LR/IR neuroblastoma patients. We propose to implement our revised risk assessment and treatment stratification system in the upcoming prospective clinical trial NB2013 LR/IR.

GERM CELL AND SEX CORD-STROMAL TUMOURS

O-053

MATURE AND IMMATURE TERATOMA: RESULTS OF THE SECOND PEDIATRIC AIEOP (ASSOCIAZIONE ITALIANA DI EMATOLOGIA ONCOLOGIA PEDIATRICA) ITALIAN STUDY

M. Terenziani[1], G. Cecchetto[2], A. Inserra[3], F. Siracusa[4], R. Boldrini[5], P. Dall'Igna[2], G. Riccipetitoni[6], G. Bisogno[7], M. Conte[8], P. Indolfi[9], M.D. De Pasquale[10], F. Spreafico[1], P. Tamaro[11], P. D'Angelo[12]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Pediatric Surgery Unit, Azienda Ospedaliero-universitaria, Padova, Italy; [3]Pediatric Surgery Division, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Italy; [4]Pediatric Department, Università di Palermo, Palermo, Italy; [5]Pathology Unit, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Italy; [6]Pediatric Surgery Unit, Ospedale Dei Bambini Buzzi, Milano, Italy; [7]Hematology-Oncology Division, Azienda Ospedaliero-universitaria, Padova, Italy; [8]Hematology-Oncology Division, Istituto Giannina Gaslini, Genova, Italy; [9]Pediatric Oncology Unit, Seconda Università degli Studi di Napoli, Napoli, Italy; [10]Hematology-Oncology Division, Ospedale Pediatrico Bambino Gesù IRCCS, Roma, Italy; [11]Hematology-Oncology Division, Ospedale Pediatrico Burlo Garofalo, Trieste, Italy; [12]Hematology-Oncology Division, Ospedale Pediatrico G. di Cristina, Palermo, Italy

Objectives: Teratomas (T) demonstrate a benign clinical behavior, however they may recur with malignant components or as T only, and in a small group of patients prognosis can be fatal. In the Protocol for Malignant Germ Cell Tumor (MGCT), in the context of AIEOP, we collected patients with T to evaluate prognostic factors, type of relapse and outcome.
Methods: All 209 patients were enrolled from 2004 to 2013. Initial evaluation and follow-up included clinical examination, tumour markers and imaging procedures. Surgical resection was recommended as unique treatment. Immature T (IT) were classified as grading 1–3.
Results: Mature T (MT) and IT were diagnosed in 139 and 70 patients, respectively (median age 42 months; F:M ratio 2.4:1). 113 patients had gonadal tumor (91 ovarian, 22 testicular) 96 extragonadal (61 sacrococcyx (SC), 12 mediastinum, 9 retroperitoneum, 14 other sites). 10 patients (4.8%) showed associated congenital malformation-syndromes. A tumor complete resection was performed in 175 patients, a partial resection in 21 and a biopsy in one. 15 events occurred: 4 patients had contralateral metachronous ovarian T; 1 with SC-MT developed an adrenal neuroblastoma; 10 patients relapsed locally (2/139 MT and 8/70 IT) within a median time of 7 months from diagnosis: 6 with MGCT component, 1 with malignant transformation and 3 with T only. Two patients died, one of progressive IT grade 3 and 1 for surgical complications. At a median follow-up of 60 months, the EFS, RFS and OS are as follows: 87%, 91% and 95%, respectively. Analyzing MT and IT separately, OS is 100% and 95% and EFS 96% and 86%, respectively.
Conclusions: T show good prognosis, especially the M ones. Surgery and follow-up remain the standard approaches, however, in some rare cases, especially with partial resection, IT may progress, representing a real challenge in term of treatment.

O-054

OUTCOME OF CHILDHOOD MALIGNANT GERM CELL TUMOR (MGCT) TREATED ON CARBOPLATIN BASED CHEMOTHERAPY –SINGLE CENTRE EXPERIENCE IN PAKISTAN

R. Khan[1], M. Ashraf[1]

[1]Children Cancer Hospital, Children Cancer Hospital, Karachi, Pakistan

Objectives: To study the clinicopathological features and outcome of children with MGCT treated on Carboplatin, Etoposide and Bleomycin (JEB) at CCH, Pakistan.
Methods: A retrospective study at CCH on children less than 16 years diagnosed with extracranial Germ cell tumor between January 1998 till 2013. They were treated on Carboplatin based chemotherapy including Etoposide and Bleomycin (JEB) without risk stratification. The demography, clinical presentations and primary site, histopathology, staging and treatment received, were reviewed. Outcome was analyzed.
Results: Total 75 patients included with male to female ratio 1:1. Median age of presentation was 3 years (range 1 month to 16 years). Median duration of symptoms was 2 months (15 days – 2 years). Abdominal distention and pain were the most common symptoms. 48/75 patients (64%) were Gonadal Germ Cell Tumor (GGCT) with 19 (25%) ovarian and 29 (39%) testicular tumors. Extragonadal tumors were 27 (36) with sacrococcygeal teratoma (20%) being most common. Yolk sac tumor was the most common (56%) histopathological diagnosis followed by mixed GCT 16%, teratoma 12%, and dysgerminoma 9.3%. 14 gonadal tumors did not receive chemotherapy. 61/75 patients received 3-6 cycles of JEB chemotherapy. 51 patients (84%) completed the treatment, 1 left and 2 died during chemotherapy, 7 (12%) had progressive disease. 20 patients had Stage I disease, 6 stage II,18 stage III and 17 had stage IV disease, with 100%, 60%, 71% and 59% overall survival (OS) respectively. For patients who received chemotherapy, OS is 76%; for GGCT 89% and for extragonadal 58%. OS of whole cohort is 81% (59/75).
Conclusions: Carboplatin based chemotherapy has shown good survival for children with GGCT. The suboptimal survival in extragonadal cases could be due to advanced disease and poor local control.

O-055

OVARIAN SERTOLI LEYDIG CELL TUMORS IN CHILDREN AND ADOLESCENTS: AN ANALYSIS OF THE EUROPEAN COOPERATIVE STUDY GROUP ON PEDIATRIC RARE TUMORS (EXPERT)

D.T. Schneider[1], D. Orbach[2], G. Cecchetto[3], T. Stachowicz-Stencel[4], I.B. Brecht[5], B. Brummel[1], G. Bisogno[6], A. Ferrari[7], Y. Reguerre[8], J. Godzinski[9], G. Calaminus[10], C. Patte[11]

[1]Clinic of Pediatrics, Klinikum Dortmund, Dortmund, Germany; [2]Pediatric Oncology, Institut Curie, Paris, France; [3]Pediatric Surgery, University of Padova, Padova, Italy; [4]Pediatric Hematology Oncology and Endocrinology, Medical University Gdansk, Gdansk, Poland; [5]Pediatric Hematology and Oncology, University of Erlangen, Erlangen, Germany; [6]Pediatric Oncology, University of Padova, Padova, Italy; [7]Pediatric Oncology, Istituto Nazionale Tumori, Milan, Italy; [8]Pediatric Oncology, Centro hospitalo-universitaire, Angers, France; [9]Pediatric Surgery, Wroclaw Medical University, Wroclaw, Poland; [10]Pediatric Hematology and Oncology, University of Münster, Münster, Germany; [11]Pediatric Hematology and Oncology, Institut Gustave Roussy, Paris, France

Objectives: To analyze ovarian Sertoli-Leydig cell tumors (SLCTs) for potential prognostic markers and their use for treatment stratification.
Methods: Forty-four patients were included. Patients were prospectively reported to the German MAKEI studies ($n = 23$), French TGM protocols ($n = 10$), Italian TREP registry ($n = 6$), and the Polish Pediatric Rare Tumor Study group ($n = 5$). Tumors were classified according to WHO and staged according to FIGO.
Results: Median age was 13.9 (0.5–17.4) years. All patients underwent resection by tumor enucleation ($n = 8$), ovariectomy ($n = 17$), adnectomy isolated ($n = 18$) or with hysterectomy ($n = 1$). FIGO-stage: Ia 24 pts, Ic 17 pts, II/III 3 pts. One patient had bilateral tumors. Four patients (stage Ia: 3, stage Ic: 1) developed a metachronous contralateral tumor. Otherwise, all stage Ia patients remained in complete remission. Among 20 patients with incomplete resection or tumor spread (stage Ic-III), 8 relapsed, and 5 patients died. Eleven patients were initially treated with 2–6 cycles of cisplatin-based chemotherapy. Of these, seven patients are in continuous remission. Poor histological differentiation was associated with higher relapse rate (5/13) compared to intermediate (3/18) and high differentiation (0/4). Tumors with retiform pattern or heterologous elements showed a high relapse rate, too (5/11). After a median follow-up of 62 months, event-free survival is 0.70 ± 0.07, relapse-free survival 0.81 ± 0.06, and overall survival 0.87 ± 0.05.
Conclusions: Prognosis of SLCTs is determined by stage and histopathologic differentiation. Complete resection with careful avoidance of spillage is a prerequisite of cure. The impact of chemotherapy in incompletely resected and advanced stage tumors remains to be evaluated.

O-056

SEX CORD STROMAL TUMORS IN CHILDREN AND TEENAGERS: RESULTS OF THE TGM95 STUDY

B. Fresneau[1], D. Orbach[2], C. Faure-Conter[3], C. Verite[4], M.P. Castex[5], N. Kalfa[6], H. Martelli[7], C. Patte[1]

[1]*Pediatric Oncology, Gustave Roussy, Villejuif, France;* [2]*Pediatric Oncology, Institut Curie, Paris, France;* [3]*Pediatric Oncology, Institut d'Hématologie et d'Oncologie Pédiatrique, Lyon, France;* [4]*Pediatric Oncology, Centre Hospitalier Universitaire, Bordeaux, France;* [5]*Pediatric Oncology, Centre Hospitalier Universitaire, Toulouse, France;* [6]*Pediatric Surgery, Centre Hospitalier Universitair, Montpellier, France;* [7]*Pediatric Surgery, Centre Hospitalier Universitair, Le Kremlin-Bicetre, France*

Objectives: Sex cord stromal tumors (SCT) are rare in children and teenagers, accounting for 2% of malignant gonadic tumors. We present the results of the National SFCE TGM95 trial for ovarian and testicular SCT.
Methods: Between 1995 and 2005, in France, children (<18years) with ovarian and testicular SCT were prospectively registered. Primary gonadal resection was recommended whenever feasible with complete and "non-mutilating" surgery. Patients with disseminated disease or incomplete resection received neoadjuvant or adjuvant 4-6 cycles of VIP (etoposide 75mg/m^2/D1-5, ifosfamide 3g/m^2/D1-2, cisplatinum 20/mg/m^2/D1-5, every 3 weeks).
Results: Thirty-eight ovarian SCT were registered. Median age was 10.7y [0.58-17.7]. Endocrine symptoms were present in 21 cases. Histological diagnoses were: juvenile (23) and adult (3) granulosa cell tumors, Sertoli-Leydig cell tumors (11), and mixed germ cell-SCT (1). Primary oophorectomy +/salpingectomy led to complete resection in 23 patients who did not receive adjuvant treatment. Two relapsed after 4-5 years (1 peritoneal and 1 contralateral) and achieved 2nd complete remission with surgery and VIP. Fifteen patients had primary incomplete resection due to tumor rupture and/or malignant ascites: 11 received VIP and had no recurrence (median follow-up: 5.8y), 4 did not receive chemotherapy and relapsed between 2-18 months, with fatal outcome in 2 cases with Sertoli-Leydig cell tumors. Five-year OS and EFS were 94.4% and 85.3%. Eleven patients had localized testicular tumors (median age 0.83y [0-8.8]): juvenile granulosa cell tumors (4), Sertoli and/or Leydig cell tumors (5), and not otherwise specified SCT (2). Treatment was surgery alone with inguinal orchiectomy. None relapsed (median follow-up 5.3y).
Conclusions: In childhood ovarian SCT, surgery should be complete and non-mutilating. If complete resection is non-feasible, neoadjuvant chemotherapy is necessary. Tumor rupture is a formal indication for adjuvant chemotherapy which is efficient to prevent recurrences. In childhood testicular SCT, prognosis is excellent with inguinal orchiectomy, raising the debate on testis sparing surgery.

EPIDEMIOLOGY 2

O-057

EARLY DIAGNOSIS: THE INFLUENCE OF TRAINING OF PRIMARY HEALTH CARE PROFESSIONALS FOR SUSPICION OF PEDIATRIC CANCER IN BRAZIL

V. Junqueira[1]

[1]*Project, Instituto Ronald McDonald, Rio de Janeiro, Brazil*

Objectives: In Brazil, cancer is the leading cause of death by disease among children and adolescents 1-19 years for all regions. As in Brazil the time between symptoms and diagnosis of pediatric cancer is long and many patients are referred to treatment at advanced stages, NGO Instituto Ronald McDonald (IRM) developed the Early Diagnosis Program to build capacity of primary health care workers. In the context of primary health care, the program called Family Health Strategy (ESF) covers approximately 50% of the population. Thus, it is considered crucial for changing this scenario, the dissemination of knowledge about the main signs and symptoms of the disease among these professionals, evaluating the performance of health primary care professionals in suspicion of pediatric cancer in Brazil.
Methods: Training health workers in order to promote early diagnosis of childhood cancer. The live learning course has a 24 hour workload per training within weeks. The classes include discussions with health managers on local content that covers everything from the organization of the national policy for cancer care, to the role of each ESF professional in early diagnosis of cancer. The book, freely distributed by IRM, was developed in partnership with Brazilian Society of Pediatric Oncology and National Cancer Institute. Besides, a multicenter survey to measure the impact of the program in each location where the projects were executed was performed.
Results: The program exists since 2008 and already trained 14,885 professionals of 2,254 teams in 14 states. It impacted 2,367,089 0-19 years children and adolescents with an investment of R$ 4.748.825,25 (US$ 2,016,101.06).
Conclusions: In regions where the program was implemented there was a 23% increase in the number of children referred with suspected cancer. The average delay time of referral for diagnosis fell by 61% in those who received the training (13-5 weeks).

O-058

FETAL MACROSOMY AS A RISK FACTOR FOR CHILDHOOD NON-HODGKIN LYMPHOMA: A NATIONWIDE SWEDISH COHORT STUDY

A. Skalkidou[1], E. Petridou[2], T. Sergentanis[2], C. Antonopoulos[2], N. Dessypris[2], T. Svensson[3], O. Stephansson[3], H. Kieler[3], K. Smedby[3]

[1]*Dept of Women's and Children's Health, Uppsala University, Uppsala, Sweden;* [2]*Dept of Hygiene Epidemiology and Medical Statistics, University of Athens Medical School, Athens, Greece;* [3]*Unit of Clinical Epidemiology and Centre for Pharmacoepidemiology Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden*

Objectives: Birth weight has been explored as a risk factor for several types of childhood (0-14 years) cancer. This nationwide Swedish cohort study aims to evaluate the association between crude and adjusted characteristics of fetal growth (birth weight, length, head circumference, ponderal index, small-SGA, appropriate-AGA and large for gestational age-LGA) and non-Hodgkin lymphoma (NHL) risk.
Methods: All 3,444,136 singleton live births were included, among whom 515 incident NHL cases aged 0-14 years were diagnosed in 1973-2007, as identified through linkage with the Swedish Cancer Register. Proportional hazards models were used to estimate the Hazard Ratio (HR) and 95% confidence intervals (95% CI) of NHL. The core multivariable model included infant sex, maternal education and maternal age at delivery, birth order of the index child (1+ child) and gestational age, the latter omitted in the analyses with SGA, AGA, LGA variables, as appropriate.
Results: Male sex was associated with a doubled NHL risk (HR = 2.00, 95% CI: 1.66-2.41). LGA birth weight, but not birth weight *per se*, was associated with an 80% increase in NHL risk (HR = 1.83, 95%CI: 1.20-2.79). In the subgroup analyses by sex, the latter association was confined particularly to females (HR = 3.37, 95% CI: 1.90-5.97). Other growth variables were not consistently associated with NHL risk, prossibly due to smaller variation or measurement errors.
Conclusions: Fetal macrosomy seems to represent a considerable risk factor for childhood NHL, whereas its effect may differ by gender. An approach to assess the association solely using crude birth weight, as a proxy, seems inadequate, given that more elaborate LGA indices may portray accelerated intrauterine growth as a more meaningful component. Future studies should aim at disentangling the physiological mechanisms underlying the relevance of sex-specific associations.

O-059

LATE MORTALITY AMONG 5-YEAR SURVIVORS OF EARLY ONSET CANCER: A POPULATION-BASED REGISTER STUDY

A. Kero[1], L.S. Järvelä[1], M. Arola[2], N. Malila[3], L.M. Madanat-Harjuoja[3], J. Matomäki[1], P.M. Lähteenmäki[1]

[1]*Pediatrics, Turku University Hospital, Turku, Finland;* [2]*Pediatrics, Tampere University Hospital, Tampere, Finland;* [3]*Finnish Cancer Registry, Helsinki, Finland*

Objectives: To investigate cause-specific long-term mortality among 5-year survivors of early onset cancer (aged 0-34 years at diagnosis), with follow-up for death extending from 1971 through 2012.
Methods: The 5-year survivor cohort was identified via the Finnish Cancer Registry. Mortality data was extracted from National Death Certificate files of Statistics Finland.A total of 16,769 cancer survivors who survived for at least 5 years and were aged less than 35 years at cancer diagnosis were identified. A healthy sibling cohort and general population data served as reference.
Cause-specific cumulative mortality among 5-year cancer survivors, standard mortality rates (SMRs) compared to general population data and hazard ratios (HRs) for causes of death compared to the healthy sibling cohort were analyzed.
Results: The overall standardized mortality ratio (SMR) of cancer patients was 4.6-fold, (95% CI 4.4-4.8). Highest SMRs were found for malignancies (12.8, 95% CI 12.3-13.3), infectious (4.8, 95%CI 2.9-6.7) and cardiovascular diseases (1.9, 95% CI 1.7-2.1). Malignancies and cardiovascular diseases accounted for largest death numbers. Childhood and YA cancer survivors with the same primary cancer diagnosis displayed elevated overall SMRs in the same range, with the exception of markedly higher values after childhood Hodgkin lymphoma. The highest cumulative non-malignancy-related mortality was due to cardiovascular disease with a steady rise throughout the follow-up, but strongly dependent on the primary cancer diagnosis and age at diagnosis. Different from survivors of YA malignancies, no reduction of cumulative cardiovascular mortality was observed in childhood cancer survivors towards the recent treatment periods. However, overall and malignancy-related mortality showed a declining tendency towards the most recent periods after both, childhood and YA cancer.
Conclusions: Our findings on non-malignancy-related mortality stress the need to set up long-term individual follow-up with a focus on cardiovascular late effects for early onset cancer survivors, especially for YA cancer survivors still lacking those.

O-060

CREATION OF COMPOSITE INDICES TO ASSESS THE IMPACT OF ECONOMIC AND CULTURAL FACTORS ON OUTCOMES IN PEDIATRIC HEMATOLOGIC MALIGNANCIES

B. Truong[1], P. Friedrich[2], K. Bona[2], C. Rodriguez-Galindo[2], K. Ribeiro[3]

[1]Medical Sciences, Harvard Medical School, Boston, USA; [2]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [3]Department of Social Medicine, Faculdade de Ciências Médicas da Santa Casa, Sao Paulo, Brazil

Objectives: The contribution of socioeconomic factors to racial and ethnic disparities in pediatric cancers remains understudied, partly due to the complexity of synthesizing the effects of multiple individual factors. In this study, we aimed to construct and utilize a composite index to analyze the impact of socioeconomic factors on survival in common pediatric hematologic malignancies.
Methods: Standardized values of seven different county-based disparity variables from the U.S. Census were utilized to calculate two indices: economic index (utilizing levels of poverty, income, education, crowding, and unemployment) and cultural index (utilizing levels of language isolation and immigration), with high values indicating greater social disadvantage. Selection of factors included test for face validity through consensus, evaluation of correlations between factors, and confirmation of pre-established domains using principle component analysis (PCA). We obtained survival outcomes from 18 SEER registries for all patients under the age of 19 who were diagnosed with acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), Hodgkin-lymphoma (HL), or non-Hodgkin lymphoma (NHL) from 2000–2010. Survival distribution functions of disadvantaged and advantaged counties were compared using Log-rank test. Cut-off values for comparisons were defined as the median of each index within the cohort.
Results: The construction of the two indices was supported by PCA, which revealed two main latent variables from the set of seven chosen variables. Economic disadvantage (high index score) was associated with lower survival rates for ALL ($p < 0.001$), AML ($p = 0.005$), HL ($p = 0.036$), and NHL ($p = 0.02$). Differences were not significant when counties were stratified by cultural domain.
Conclusions: Our study resulted in the creation of an index that synthesizes a variety of census-derived measures of SES. Economic factors showed strongest impact during validation. Cultural factors appear less significant in mediating outcomes, but may be combined with economic factors to create a composite index in the future.

NEUROBLASTOMA 3

O-061

INTEGRATED ANALYSES OF EPIGENETIC REGULATORY GENES IN NEUROBLASTOMA

N. Hoshino[1], S. Masafumi[2], K. Yoshida[3], M. Kato[4], R. Nishimura[2], S. Miyano[5], Y. Hahashi[6], A. Oka[2], T. Iwanaka[1], S. Ogawa[7], J. Takita[2]

[1]Dept. of Pediatric Surgery, The University of Tokyo, Tokyo, Japan; [2]Dept. of Pediatrics, The University of Tokyo, Tokyo, Japan; [3]Department of Pathology and Tumor Biology, Graduate School of Medicine Kyoto University, Kyoto, Japan; [4]Dept. Cell Therapy and Transplantation Medicine, The University of Tokyo, Tokyo, Japan; [5]Laboratory of DNA Information Analysis Human Genome Center, Institute of Medical Science The University of Tokyo, Tokyo, Japan; [6]Department of Hematology/Oncology, Gunma Children's Medical Center, Shibukawa, Japan; [7]Department of Pathology and Tumor Biology, Graduate School of Medicine Kyoto University, Tokyo, Japan

Objectives: Neuroblastoma (NB) is one of the aggressive pediatric solid tumors of childhood. Because NB displays remarkable clinical heterogeneity, heterogeneous genetic targets have been implicated in their pathogenesis. Recently, high-throughput genome-wide screenings have been applied to discover tumor-specific mutations of ALK, ATRX, and ARID1A/B in NB. However, since overall frequencies of recurrent mutation rate of these genes are relatively low, molecular basis of NB has not been completely elucidated. Meanwhile, previous genome-wide methylation studies suggest epigenetic aberrations may be also important, but little is known about their roles in the pathogenesis of NB. To elucidate the role of epigenetic regulators in the pathogenesis of NB, target capture 'deep' sequencing which enabled minor clones detections and array based methylation analysis were carried out.
Methods: Target capture followed by deep sequencing of 80 epigenetic regulatory genes using next-generation sequencing (Iliumina Hiseq 2000) was performed in 24 NB specimens. An extended cohort of 96 NB specimens was analyzed for deep sequencing of selected genes. Additionally, genome-wide methylation analysis (Iliumina Infinium HumanMethylation450 BeadChip Kit) was performed in 50 NB specimens.
Results: Among the 80 epigenetic regulators, 9 genes including polycomb and trithorax group related genes were mutated in 24 cases. Although these mutations were mostly found in single cases, ASH1L mutations were detected in two cases. Subsequent deep sequencing revealed that novel ASH1L mutations were observed in total of 9/197 (4.5%) cases of NB. On the other hand, based on the methylation profiles, 50 NB cases were divided into 2 subgroups independently of the clinicopathological findings, such as age, stage, and MYCN status.
Conclusions: Our results indicated that not only genetic alterations but also epigenetic regulation may play important roles in the pathogenesis of NB. Comparing expression patterns, genetic alterations, and methylation plofiles would be necessary to disclose the roles of epigenetic regulation in NB.

O-062

SURVIVAL FOLLOWING LONG-TERM INFUSION OF ANTI-GD2 ANTIBODY CH14.18/CHO IN COMBINATION WITH INTERLEUKIN-2 IN A PILOT COHORT OF HIGH-RISK NEUROBLASTOMA PATIENTS CORRELATES WITH FC-GAMMA RECEPTOR POLYMORPHISMS

H.N. Lode[1], C. Jensen[1], S. Endres[1], L. Pill[1], N. Siebert[1], P. Brock[2], D. Valteau-Couanet[3], H. Loibner[4], R. Ladenstein[5], I. Müller[1]

[1]Pediatric Hematology/Oncology, University Medicine Greifswald, Greifswald, Germany; [2]Pediatric Hematology/Oncology, Great Ormond Street Hospital, London, United Kingdom; [3]Pediatric Hematology/Oncology, Institut Gustave Roussy, Villejuif, France; [4]Apeiron, Biologics, Vienna, Austria; [5]Pediatric Hematology/Oncology, Children's Cancer Research Institute, Vienna, Austria

Objectives: Treatment using long-term infusion (LTI) of anti-GD_2 antibody ch14.18/CHO and subcutaneous interleukin-2 (IL-2) may improve outcome in high risk neuroblastoma (NB).
Methods: 53 NB patients received 5/6 cycles of 6×10^6 IU/m^2 s.c. IL-2 (d1-5; 8-12), LTI of 100 mg/m^2 ch14.18/CHO (d8-17) and 160 mg/m^2 oral 13-cis-RA (d19-32) in a single center program. Effector cells (NK- and T-cell subsets), ch14.18/CHO levels and GD_2 specific killing of neuroblastoma cells by ADCC and CDC were analyzed. KIR/KIRL mismatch and Fcγ-receptor polymorphisms were determined with a validated PCR-based method for, KIR, HLA, FCGR2A (H131R), -3A (V158F) and -3B (NA1/NA2). Clinical response was assessed following INRG criteria by mIBG, MRI/CT, BM and catecholamines.
Results: LTI of ch14.18/CHO translated into the expansion of effector NK- (3x) and T-cells (2x) combined with a pro-inflammatory cytokine response (IL-2, IL-6, IL-8, IFNγ). Effective levels of ch14.18/CHO (12.48 ± 0.93 (g/ml) at the end of antibody infusion was associated with GD_2 specific activity against NB cells in functional assays (CDC, ADCC, WBT). Interestingly, ch14.18/CHO levels and functional parameters before subsequent treatment cycles indicate persistent anti-NB activity measurable for the entire treatment period of 6-7 months. Response rates were 41.7% in mIBG (15/36), 31.8% MRI/CT (7/22), 28.6% bone marrow- (6/21) and 38.1% in catecholamines (8/21). An overall response of 30% (12/40), EFS of 32.4% (observation 3.2 years, mean: 1.6 years) and an OS of 66.8% (observation 3.9 years, mean: 3.1 years) was observed. Patients with high affinity FCGR alleles are associated with a longer event-free survival ($P = 0.025$), which supports NK-cell mediated ADCC as the mechanism of action.
Conclusions: Survival following LTI of ch14.18/CHO correlates with high affinity FCGR supporting ch14.18/CHO mediated ADCC as the primary mechanism of action.

O-063

MYELOABLATIVE THERAPY (MAT) AND IMMUNOTHERAPY (IT) WITH CH14.18/CHO FOR HIGH RISK NEUROBLASTOMA: UPDATE AND NEWS OF RANDOMISED RESULTS FROM THE HR-NBL1/SIOPEN TRIAL

R. Ladenstein[1], U. Poetschger[1], R. Luksch[2], M. Elliot[3], V. Castel[4], I. Yaniv[5], G. Laureys[6], W. Balwierz[7], H.N. Lode[8], D. Valteau-Couanet[9]

[1]Studies and Statistics on Integrated Research, Children's Cancer Research Institute, Vienna, Austria; [2]Paediatric Oncology Haematology, Istituto Nazionale Tumori di Milano, Milano, Italy; [3]Paediatric Oncology Haematology, Leeds General Hospital, Leeds, United Kingdom; [4]Paediatric Oncology Unit, Hospital La Fe Valencia, Valencia, Spain; [5]Paediatric Oncology Haematology, Schneider Children's Medical Center of Israel, Petach Tikvah, Israel; [6]Paediatric Oncology Haematology, University Hospital Gent, Gent, Belgium; [7]Paediatric Oncology Haematology, Jagiellonian University Medical College, Krakow, Poland; [8]Paediatric Oncology Haematology, University of Greifswald, Greifswald, Germany; [9]Paediatric and Adoloscente Oncology Department, Institut Gustave Roussy, Villejuif, France

Objectives: The HR-NBL1/SIOPEN trial randomised 2 essential treatment concepts: Randomisation R1 investigated BUMEL superiority whilst randomisation R2 tested the benefits of adding subcutaneous interleukin 2 (scIL2) to ch14.18/CHOmAB immunotherapy (IT).
Methods: After Rapid Cojec induction patients (pts) were randomised in R1 (296 BuMel, 302 CEM) till 09/2010. Median follow up is 6.2 years. Eligibility included complete bone marrow remission and ≤ 3, but improved mIBG positive spots. Local control included surgery and radiotherapy of 21 Gy. R2 was initiated in 2009 aiming at 400pts receiving ch14.18/CHOmAB as 8-hour infusion with 20mg/m^2 over 5 days and 13 cis RA over a total of 5 IT cycles. The schedule requires high dose morphine to control for neuropathic pain. R2 addressed a scIL2 question, using a dose of 6×10E6/m^2/day over 5 days twice in a weekly interval, given in week 2 in parallel with ch14.18/CHOmAb.
Results: The superiority of BuMel in EFS and OS over CEM (3-years EFS&OS 50%/61% vs. 38%/52%; $p < 0.001$) is maintained with a significantly lower relapse and progression rate with BuMel (48% vs. 58%) as major factor. Severe toxicity rates (ICU, toxic deaths) are below 10%, but are higher for CEM ($p = 0.012$). Hence the MAT toxicity profile favours BuMel in spite of a VOD rate of 24% (grade 3: 4%) vs. 10% in CEM (Grade3: 1%). In August 2013, R2 reached the target and the randomisation is currently suspended with last patient out in 01/2014. The R2 population undisclosed for treatment arms shows currently a 2 year EFS/OS of 56%/68%. The scIL2 arm carries a significantly higher toxicity burden

related to IL2 associated side effects like fever and capillary leak with a number of pts in the IL2 arm stopping treatment early.
Conclusions: BuMel is maintained as SIOPEN standard treatment whilst disclosed and detailed R2 results are expected for SIOP2014.

O-064

SIGNIFICANT PROGNOSTIC RESULTS OF THE SIOPEN MIBG SCORING METHOD IN 2 COOPERATIVE INDEPENDENT HIGH RISK NEUROBLASTOMA TRIALS

R. Ladenstein[1], A. Boubaker[2], B. Lambert[3], M.R. Castellani[4], Z. Bar-Sever[5], A. Oudoux[6], A. Kaminska[7], S.G. Kreissman[8], K.K. Matthay[9], U. Poetschger[10]

[1]Studies and Statistics on Integrated Research, Children's Cancer Research Institute, Vienna, Austria; [2]Nuclear Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [3]Nuclear Medicine, Ghent University Hospital, Ghent, Belgium; [4]Nuclear Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [5]Nuclear Medicine, Schneider Children's Medical Center, Petach Tivka, Israel; [6]Nuclear Medicine, Centre Oscar-Lambret, Lille, France; [7]Nuclear Medicine, Children's Memorial Health Institute, Warsaw, Poland; [8]Pediatrics Hematology Oncology, Duke University Medical Center, Durham, USA; [9]Pediatric, San Franscisco School of Medicine, San Francisco, USA; [10]Studies and Statistics on Integrated Research and Projects, Children's Cancer Reserach Institute, Vienna, Austria

Objectives: Harmonised evaluation standards of MIBG scintigraphy for (re) staging of neuroblastoma (NB) are an international aim. In the HR-NBL1/SIOPEN trial population a SIOPEN score (SISCO) >3 was associated with a significantly poorer event free survival (EFS) on pre and post induction mIBG. This analysis validates the SISCO prognostic value in the independent dataset (DS) of the Children's Oncology Group (COG) protocol A3973.
Methods: SIOPEN scoring evaluates mIBG uptake in 12 skeletal regions (scored 0-6/region, maximum of 72), MIBG scans from mIBG-avid stage 4 NB pts in 2 collaborative trials were reviewed by the SIOPEN Nuclear Medicine review committee: the COG-A3973 (DSA; n = 216) and SIOPEN HR-NBL1 trial (DSB; n = 343). Predefined categories from DSB were used with a SISCO of 0, 1-3, 4-17 and ≥18. The median follow-up time was 7.1 and 5.5y, respectively.
Results: Both DS showed a significantly superior EFS with a SISCO ≤3 at diagnosis [5-yr EFS in DSA: 51% ± 7% vs 34% ± 4%, p = 0.047 and in DSB 47% ± 7% vs 26% ± 3%, p = 0.007]. A post induction SISCO of ≤3 also revealed a significant superior outcome [5-yr EFS in DSA: 43% ± 5% vs 16% ± 6%, p = 0.004 and in DSB 36% ± 4% vs 14% ± 4%, p < 0.001]. Pts with a SISCO of 0 post induction have the best outcome in both DS. In MYCN amplified pts, the pre and post-induction SISCO of ≤3 showed a significant impact in both groups, whilst in MYCN non-amplified pts this effect is only seen post induction. A SISCO ≤3 has independent statistical significance in Cox models including age and MYCN.
Conclusions: A SIOPEN score ≥ 3 of mIBG scans carries relevant prognostic significance for the management of patients with high-risk NB at diagnosis and at the end of induction chemotherapy in the HRNBL1/SIOPEN trial and was confirmed in the independent COG A3973 data set.

O-065

HISTORICAL GOLD STANDARD FOR TIME-TO-PROGRESSION (TTP) AND PROGRESSION-FREE SURVIVAL (PFS) FROM RELAPSED/REFRACTORY NEUROBLASTOMA MODERN ERA (2002-14) PATIENTS

W.B. London[1], R. Bagatell[2], B. Weigel[3], E. Fox[2], C. Van Ryn[4], A. Naranjo[4], M.D. Krailo[5], C.H. Ahern[6], J.R. Park[7]

[1]Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston MA, USA; [2]Pediatric Hematology/Oncology, The Children's Hospital of Philadelphia, Philadelphia PA, USA; [3]Pediatric Hematology/Oncology, University of Minnesota, Minneapolis MN, USA; [4]Children's Oncology Group Statistics and Data Center, University of Florida, Gainesville FL, USA; [5]Children's Oncology Group Statistics and Data Center, University of Southern California, Monrovia CA, USA; [6]Biostatistics, Baylor College of Medicine, Houston TX, USA; [7]Pediatric Hematology/Oncology, Seattle Children's Hospital, Seattle WA, USA

Objectives: Early phase trials of investigational agents in pediatric patients (pts) with relapsed neuroblastoma (NB) historically used a "response" (RECIST) endpoint, which is challenging because NB in bone and bone marrow isn't 'measureable'. TTP and PFS are better suited to measure therapeutic benefit in NB, especially for targeted agents and immunotherapies. Historical data on PFS/TTP exist in small potentially biased cohorts. We studied the largest cohort to date of relapsed/refractory NB pts, treated with modern era frontline and relapse therapy. We determined PFS, OS, & TTP, for use as historical comparators in future Phase 2 studies.
Methods: All 489 enrollments (consecutive 11/2002-1/2014), from 384 distinct pts, on 36 Phase 1 (27) or 2 (9) Children's Oncology Group trials were analyzed for PFS (relapse, progression, disease death), overall survival (OS) (any death), & TTP, starting from Phase 1,2 trial enrollment. If pts were on multiple trials, enrollments were analyzed as if independent. For PFS, non-disease deaths were censored. Using RECIST, only 2 Phase 2 trials met the prospective response rate bar for success. For high-risk pts, planned frontline therapy included HSCT; 11.6% received ch14.18 antibody.
Results: From relapse study enrollment: 1-year & 4-year PFS/OS were 19 ± 2% & 8 ± 3%/56 ± 3% & 14 ± 4%, respectively; median TTP was 63 days (95% CI: 56,79). Median follow-up in pts without progression was 9.7 mos. Risk factors at diagnosis within subgroups were: 88% of 230-INSS stage 4; 92% of 230-≥18 mos old; 18% of 189-*MYCN* amplified; 49% of 180-diploid; 94% of 172-unfavorable histology. Only *MYCN*amplification was prognostic of worse PFS after relapse study enrollment ($p < 0.001$). Median time from diagnosis to first relapse/progression was 22 mos (95% CI: 19,25) (n = 214).
Conclusions: PFS/TTP/OS from this representative comprehensive historical COG early-phase trial NB cohort should be used in Phase 2 trials as the gold standard comparator to identify promising new agents for NB.

O-066

HUMANIZED ANTI-GD2 ANTIBODY (HU14.18K322A) GIVEN WITH CHEMOTHERAPY +/- PARENTAL NATURAL KILLER (NK) CELLS IN CHILDREN WITH RECURRENT OR REFRACTORY NEUROBLASTOMA

S. Federico[1], W. Leung[1], A.S. Pappo[1], F. Navid[1], V.M. Santana[1], J. Wu[1], B. Shulkin[1], D.R. Shook[1], P.M. Sondel[1], W.L. Furman[1]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Preclinical studies demonstrate that anti-GD2 antibodies, acting via antibody-dependent cell-mediated cytotoxicity (ADCC), enhance the effects of chemotherapy; however, it is unknown if chemotherapy combined with Hu14.18K322A is feasible and effective in children with neuroblastoma. This study evaluates the safety and feasibility of administering a unique humanized anti-GD2 antibody (Hu14.18K322A) with chemotherapy and parental NK cells to enhance ADCC.
Methods: Pediatric patients with recurrent or refractory neuroblastoma were eligible to receive six courses of Hu14.18K322A (40mg/m^2/dose, days 2-5) in combination with alternating courses of cyclophosphamide/topotecan (courses 1,2), irinotecan/temozolomide (courses 3,4) and ifosfamide/carboplatin/etoposide (courses 5,6). Parental NK cells were administered with courses 2, 4 and 6.
Results: Ten heavily pretreated patients, median age 6.5 years (range, 2.8–13.5), including 7 with prior anti-GD2 treatment, completed 40 courses. One patient developed unacceptable toxicity characterized by prolonged thrombocytopenia (>35 days). Four patients came off study for adverse events (hu14.18K322A allergy, prolonged viral infection, surgical death and myelodysplastic syndrome). Common toxicities included grade 3-4 myelosupression (10/10 patients) and grade 1-2 pain (10/10 patients). Eight patients received 19 NK cell infusions. The median number of NK cells infused per dose was 18.2×10^6/kg (range, 6.2×10^6/kg-47.8×10^6/kg). Responses to therapy included: 2 complete responses (CR), 1 very good partial response (VGPR), 2 partial responses (PR) and 5 with stable disease (SD). Five patients (2CR, 1VGPR, 1PR, 1SD) and 2 patients (1CR, 1VGPR) who received NK cell infusions had measureable donor NK cells on days 7 (chimerism range, 2%-100%) and 14 (chimerism range, 1%-64%) respectively. None of the patients progressed on therapy. One patient remains in CR 9 months after completing therapy.
Conclusions: Administration of concurrent chemotherapy, Hu14.18K322A and parental NK cells is safe, feasible and resulted in clinically meaningful responses in patients with neuroblastoma. Accrual to the trial is ongoing.

BRAIN TUMOURS BIOLOGY 2

O-067

MICRORNA EXPRESSION IN ATYPICAL TERATOID/RHABDOID TUMORS (AT/RT): NEW POTENTIAL THERAPEUTIC TARGETS?

K. Patel[1], M.D.F. Bonaldo[2], C.C. Huang[3], T. Tomita[4], S.T. Sredni[5]

[1]Neurosurgery, Ann & Robert H. Lurie Childrens Hospital of Chicago, Chicago, USA; [2]Cancer Biology and Epigenomics Program, Ann & Robert H. Lurie Childrens Hospital of Chicago, Chicago, USA; [3]Biostatistics, Joseph J. Zilber School of Public Health, Milwaukee, USA; [4]Neurosurgery, Feinberg School of Medicine, Chicago, USA; [5]Neurosurgery, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, USA

Objectives: Atypical Teratoid/Rhabdoid Tumors (AT/RT) are aggressive pediatric tumors of the central nervous system. As there is no effective treatment, new therapeutic options are needed. MicroRNAs (miRNAs) are small noncoding RNAs that post-transcriptionally modulate entire sets of genes. Modulating miRNAs may provide a new avenue on cancer treatment.
Methods: We compared the miRNA expression profiles of 10 AT/RT to 4 Meduloblastoma (MB) and the gene expression (GE) profiles of 14 AT/RT to 6 MB. Illumina V2 MicroRNA Chips and Illumina HT-12 whole genome expression arrays (Illumina, Inc., CA, USA) were used for analysis. Total RNA was isolated using Trizol Reagent (Invitrogen, CA, USA). Fold changes (FC) were calculated, and *t-test* was applied to assess the significance of differentially expressed genes. MiRNAs with $-1.5 \leq FC \geq 1.5$ (p-value<0.05) and mRNAs with $-2 \leq FC \geq 2$ (p-value<0.05) were selected. Ingenuity Pathway Analysis (IPA, www.ingenuity.com) was used to determine pairing of highly predicted miRNA-mRNA with inverse expression

correlation and to determine enriched biological functions of differentially expressed genes. Selective miRNA/mRNAs were validated by real-time PCR.
Results: Among 85 differentially expressed miRNAs and 1002 differentially expressed mRNAs, miRNAs-mRNAs pairs were established with 10 miRNAs and 53 mRNAs. Among them, miR- 663 was the most up-regulated in AT/RT (FC = 4.81). Accordingly, the following predicted targets were found to be significantly down-regulated: CDK5R1 (FC = −5.24) that regulates expression of CDK5, and NCAM1 (FC = −4.51), both of them essential for neural development.
Conclusions: The down-regulation of genes involved in neural development regulated by miR-663 in AT/RT may indicate that this miRNA might be concurring for the poor differentiated nature of these tumors. We speculate that manipulating this specific miRNA could induce differentiation of AT/RT cells lowering its aggressive behavior.
A*cknowledgments
Research Funded by The Rally Foundation for Childhood Cancer Research in memory of Haley Trainer and Dr. Ralph and Marian C. Falk Medical Research Trust.

O-068

USING *DROSOPHILA MELANOGASTER* FOR THE IDENTIFICATION OF GENES INVOLVED IN THE BIOLOGY OF ATYPICAL TERATOID/RHABDOID TUMORS

K. Eikmeier[1], A. Linge[1], A. Jeibmann[1], M. Kool[2], M. Frühwald[3], W. Paulus[1], M. Hasselblatt[1]

[1]Institute of Neuropathology, University Hospital Münster, Münster, Germany; [2]Division of Pediatric Neurooncology, German Cancer Research Center DKFZ, Heidelberg, Germany; [3]Swabian Childrens' Cancer Center, Childrens' Hospital Augsburg and EU-RHAB Registry working group, Augsburg, Germany

Objectives: The majority of atypical teratoid/rhabdoid tumors (AT/RT) is characterized by inactivation of one single gene, *SMARCB1*. However, only little is known on targetable downstream pathways. We therefore aimed to perform a broad functional screen of genes potentially involved in the detrimental effects of SMARCB1 deficiency.
Methods: Using *Drosophila melanogaster* andthe Gal4-UAS system, amodifier screen was performed in order to identify pathways involved in the phenotype associated with ubiquitous or glial-specific knockdownof *snr1*, the fly homolog of *SMARCB1*. The functional role of identified genes and pathways was investigated in human rhabdoid tumor cell lines BT16, A204 and G401 as well as AT/RT tumor samples from the European Rhabdoid Tumor Registry EURHAB.
Results: Silencing of *snr1* expression in *Drosophila melanogaster* resulted in a lethal phenotype as well as increased volume and proliferation of the larval fly brain. Crossing *snr1* knockdownflies with strains expressing specific RNAi shifted the lethal phenotype in 70/1015 screened candidate genes. These included *merlinkibra* and *expanded*, whose products represent a key upstream regulator of the hippo pathway. In *SMARCB1*-deficient human rhabdoid tumor cell lines, silencing of *NF2*, *WWC1* and *FRMD6*, the homologues of *merlin*, *kibra* and *expanded*, resulted in reduced proliferative activity on MTT and BrdU assay, while cytotoxicity was unaltered. Furthermore, YAP1, the main effector of the hippo pathway was over-expressed in AT/RT and associated with shorter progression-free survival and overall survival.
Conclusions: Highlighting the role of hippo signaling in *SMARCB1*-deficiency and the biology of AT/RT, these results demonstrate that fly models can be employed for the identification of clinically relevant pathways in human cancer.
Supported by IZKF Münster (Ha3/016/11).

O-069

DELINEATING TRANSFORMING MECHANISMS AND THERAPEUTIC TARGETS OF THE C19MC ONCOMIR CLUSTER

P. Sin-Chan[1], M. Lu[1], C. Kleinman[2], D. Picard[1], T. Spence[1], K.C. Ho[1], J. Chan[3], C. Hawkins[1], J. Majewski[2], N. Jabado[2], P. Dirks[1], A. Huang[1]

[1]Arthur and Sonia Labatt Brain Tumor Research Centre, The Hospital for Sick Children, Toronto, Canada; [2]Department of Human Genetics, McGill University, Montreal, Canada; [3]Department of Pathology and Laboratory Medicine, University of Calgary, Calgary, Canada

Objectives: Central nervous system-primitive neuro-ectodermal tumors (CNS-PNETs) represent a distinctly aggressive and clinically heterogeneous class of embryonal brain tumors with poorly understood biology. We have recently shown that CNS-PNETs with *C19MC* amplification and/or high LIN28 expression comprise a single molecular entity that spans various histologic categories and anatomic compartments. These tumors, classified as 'Group 1', are distinguished by highly primitive neural gene signatures. Taken together with our prior observations that C19MC miRNAs alters human neural stem cell (hNSC) phenotypes, these findings suggest C19MC OncoMiRs may critically modulate cell differentiation and growth pathways to promote tumorigenesis.
Methods: To elucidate molecular mechanisms of C19MC-mediated tumorigenesis, we combined miRNA target prediction algorithms with comparative gene expression analyses of primary C19MC amplified tumors and hNSCs with stable expression of 5-oncogenic C19MC miRNAs.
Results: These analyses revealed multiple cell cycle regulatory tumor suppressors as candidate C19MC gene targets including p21, p27 and p130 (RBL2), which displayed highly conserved C19MC binding sites. We observed that p21, p27 and RBL2 were directly and synergistically targeted by C19MC miRNAs in cell lines with stable 5-C19MC OncomiRs expression. Significantly, miRNA *in-situ* hybridization and immuno-histochemical analyses confirmed p21, p27 and RBL2 as bonafide gene targets in primary C19MC-amplified human tumor cells. We observed stable 5-C19MC miRNA expression conferred a proliferative phenotype in hNSCs, thus suggesting C19MC OncomiRs may synergize to activate pro-growth pathways. Recently, we identified gene fusions of C19MC and *TTYH1* and demonstrated that the distinct methylation landscape of Group 1 CNS-PNETs correlated with C19MC targeting of RBL2 with consequent up-regulation of DNMT3B. Consistent with these observations, growth of primary Group 1 CNS-PNET cells was robustly inhibited by 5-azacytidine and Vorinostat treatment.
Conclusions: These studies collectively suggest that C19MC OncoMiRs promote tumorigenesis by targeting cell cycle regulators to modulate the epigenome and provides one of the first rational therapeutics for these devastating tumors.

O-070

SIGNIFICANCE OF TUMOR ASSOCIATED MACROPHAGES IN MEDULLOBLASTOMA

A. Margol[1], N. Robison[1], J. Gnanachandran[1], G. Dhall[1], R. Drissi[2], M. Fouladi[2], F. Gilles[3], A. Judkins[3], R. Sposto[1], S. Asgharzadeh[1]

[1]Pediatrics -Hematology-Oncology, Children's Hospital Los Angeles, Los Angeles, USA; [2]Pediatrics -Hematology-Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [3]Pathology, Children's Hospital Los Angeles, Los Angeles, USA

Objectives: Children with medulloblastoma can be subgrouped into at least four molecular categories, offering the potential for targeted therapeutic approaches to reduce treatment related morbidities. Little is known about the role of tumor microenvironment in medulloblastoma or its contribution to these molecular subgroups. Tumor microenvironment has been shown to be an important source for therapeutic targets in both adult and pediatric neoplasms. In this study, we investigated the hypothesis that expression of genes related to tumor-associated macrophages (TAMs) correlate with the medulloblastoma molecular subgroups and contribute to a diagnostic signature.
Methods: Gene expression profiling using Human Exon Array (n = 168) was analyzed to identify medulloblastoma molecular subgroups and expression of inflammation-related genes. Expression of 45 tumor-related and inflammation-related genes was analyzed using a custom-built TaqMan Low Density Array (TLDA) card in 83 medulloblastoma samples to build a gene signature predictive of molecular subgroups. TAMs in medulloblastomas (n = 54) comprising the four molecular subgroups were assessed by immunohistochemistry (IHC).
Results: A 31-gene medulloblastoma subgroup classification score inclusive of TAM-related genes (*CD163, CSF1R*) was developed with a misclassification rate of 2%. Tumors in the Sonic Hedgehog (SHH) subgroup had increased expression of inflammation-related genes and significantly higher infiltration of TAMs than tumors in the Group 3 or Group 4 subgroups ($p < 0.0001$ and $p < 0.0001$, respectively). IHC data revealed a strong association between location of TAMs and proliferating tumor cells.
Conclusions: Our study reports the first evidence of the presence of TAMs in medulloblastomas and provides a novel 31-gene TLDA signature that accurately determines medulloblastoma molecular subgroups. These data suggest that SHH tumors have a unique tumor microenvironment and interactions of TAMs and SHH tumor cells may contribute to their pathogenesis revealing TAMs as a potential therapeutic target.

O-071

H-PRUNE, THROUGH NEGATIVE REGULATION OF NM23-H1, ENHANCES TGF-β SIGNALING IN MEDULLOBLASTOMA

M. Zollo[1]

[1]Medicina Molecolare e Biotecnologie Mediche, University of Naples Federico II, Naples, Italy

Objectives: Brain tumors are the most common cause of childhood oncological death and medulloblastoma (MB) is the most frequent and highly invasive embryonal tumor that arises in the cerebellum and disseminates through the cerebrospinal fluid to coat the brain and spinal cord. Recent studies have revealed that MB comprises at least four distinct molecular sub-entities, which differ in terms of cell-of-origin, clinicopathologic features and disease outcome. Within these molecular groups, metastatic disease at diagnosis was characteristic in Group-3 subtype even though the mechanisms of metastatic cells dissemination are still poorly studied.
Methods: In our study, we identified h-Prune as one of the most differentially expressed and functionally relevant genes in MB Group-3. In this group TGFBR1 is highly amplified and network analysis studies illustrate that TGF-β signaling activation is unique to Group-3. Moreover the Group-3-enriched MB oncogene OTX2 is a prominent target of TGF-β signaling in the developing nervous system.

Results: H-Prune, was identified as NM23-H1-binding protein and NM23-H1 was found as negative regulator TGF-β signaling by preventing activation of SMADSs proteins. Here we found that h-Prune through negative regulation of NM23-H1 enhance TGF-β signaling, while h-Prune silencing by RNA interference in several well established MB cell lines resulted in a strong inhibition of cell migration, proliferation and adhesion, suggesting that h-Prune is required for growth of MB cells. Further, we demonstrated that h-prune silencing negatively regulate OTX 2 protein quota in MB immortalized cell line, and finally knockdown of h-prune model impairs the tumor engraftment in orthotopic xenograft.
Given the relevance of h-Prune in MB, accordingly with the effects of its silencing, *in vitro* and *in vivo*, we also presented a new drug against h-prune able to impair its protein stability.
Conclusions: Our findings in primary tumors, together with functional studies in MB cell lines, provide strong evidence for an important role of h-Prune in the progression and metastatic dissemination, suggesting future ways for rational tailored-pharmacological therapy for Molecular Group-3 MBs.

O-072

CHROMOSOME ENGINEERING AND STEM CELL DIFFERENTIATION TECHNOLOGIES TO MODEL SOMATIC COPY NUMBER ABERRATIONS IN MEDULLOBLASTOMA

J. Peacock[1], T. Wataya[1], K. Zane[1], M.D. Taylor[2]

[1]Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada; [2]Division of Neurosurgery, The Hospital for Sick Children, Toronto, Canada

Objectives: Medulloblastoma is the most common malignant brain tumour of childhood and a major cause of oncologic death in children. Recent progress in genetic analysis has revealed a number of chromosome abnormalities in medulloblastoma. Chromosome 17 aberrations including loss of 17p, gain of 17q and isochromosome i17q, are seen across medulloblastoma subgroups. A chromosome "17p deletion" knock-out mouse model has been developed, however, this model is embryonic lethal at an early stage of development likely due to haploinsufficiency of critical developmental genes, it is unclear if neuronal precursors can form when mouse 17p equivalent region is deleted. Mouse embryonic stem cells cultured under serum-free of embryoid body-like aggregates (SFEBq) conditions can differentiate into many cell types of the brain including cerebellar progenitor cells. We hypothesize that differentiation of 17p deletion ES cells into cerebellar progenitor cells is not embryonic lethal.
Methods: The SFEBq method was optimized for use with chromosome engineered mouse embryonic stem cells harboring an 18 million bp deletion equivalent to human 17p deletion. EBs were differentiated into cerebellar progenitor cells and intracranially injected into NOD scid gamma (NSG) immunodeficient mice.
Results: Mouse ES cells with 17p equivalent deletion were successfully differentiated into cerebellar precursors *in vitro*. 17p deletion cells were more proliferative in Ki67 staining comparing to the parental floxed cells without 17p deletion. Immunoflorescence staining with Math1 and Neph3 demonstrates "17p deletion" ES cells give rise to granule cell precursor, purkinje cells and other GABAergic neurons.
Conclusions: SFEBq allows us to generate cell types of the cerebellum chromosome engineered with a mouse equivalent 17p deletion. These cells are more proliferative but insufficient to cause medulloblastoma. The addition of Oncogene overexpression or gene knockouts will allow us to model the events that transform cerebellar progenitors into medulloblastoma.

RARE TUMOURS

O-073

PEDIATRIC MALIGNANT MESOTHELIOMA: THE EUROPEAN EXPERT GROUP EXPERIENCE

M. Ben Arush[1], D. Orbach[2], G. Bisogno[3], V. Bajciova[4], T. Stachowicz-Stencel[5], P. Leblond[6], R. Dvir[7], I. Brecht[8], N. André[9]

[1]Pediatric Hematology and Oncology, Children's Hospital Rambam Medical Center, Haifa, Israel; [2]Pediatric Hematology and Oncology, Institut Curie, Paris, France; [3]Dipartimento di Pediatria, Clinica di Oncoematologia, Padova, Italy; [4]Pediatric Oncology Department, Childrens Oncology Hospital, brno, Czech Republic; [5]Pediatric Oncology Department, Medical University, Gdansk, Poland; [6]Pediatric Oncology Department, Centre Oscar Lambret, Lille, France; [7]Pediatric Oncology Department, Sourasky Medical Center, Tel Aviv, Israel; [8]Pediatric Oncology Department, Children's Hospital, Erlangen, Germany; [9]Pediatric Oncology Department, Children's Hospital of La Timone, Marseille, France

Objectives: Mesothelioma is an exceptional tumor that arises from the surfaces of the pleural and peritoneal cavities, pericardium, or tunica vaginalis. In adults, most patients need medical oncological therapies and long-term survival is very uncommon. Very little is known about the characteristics of this tumor in a pediatric setting.
Methods: The European EXPeRT group of pediatric very rare tumors reviewed retrospectively children and adolescents (< 18 year) diagnosed in Europe with mesothelioma between 1987 and 2013.
Results: 22 patients (pts) were identified, 6 males and 16 females, mean age 11.2 years (range 3 months-17.9 y). Primary tumour was located into the peritoneum in 13 pts, pleura in 3, vagina in 1 case, pericardium in 1, and multiple sites in 4 pts. Metastasis at diagnosis were present in 9 patients. Histology was epithelioid for all cases. Chemotherapy was delivered to 19 patients, cisplatin-based regimen, added to Pemetrexed in 9 patients. Additional cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (cCHIP) was performed in 6 patients as first line therapy, and for 3 patients after relapse or progressive disease. Ten patients went into complete remission after cCHIP and cisplatin-based chemotherapy. At a median of 59 months follow-up, 10 patients remain in first complete remission, 4 with residual stable images, one with progressive disease, 5 patients died, two patients are lost of follow-up.
Conclusions: Mesothelioma is a very rare tumour in pediatric population. Pediatric mesothelioma seems to be different from its adult counterpart with less primary pleural localization and a much better outcome despite frequent relapses.
This series provides interesting insight into the safety and effectiveness of treatment of pediatric mesothelioma patients highlighting the role chemotherapy cisplatin based with pemetrexed, cCHIP. Establishment of European recommendations are recommended.

O-074

PEDIATRIC MELANOMA: ANALYSIS OF 52 CASES FROM THE FRENCH PEDIATRIC RARE TUMOR GROUP (FRACTURE)

M. Vittaz[1], L. Martin[2], C. Robert[3], D. Orbach[4], C. Bodemer[5], C. Mateus[3], S. Fraitag[6], D. Plantaz[7], P. Lutz[8], E. Plouvier[9], J. Rakotonjanahary[10], Y. Réguerre[11]

[1]Pediatric Clinic, CHU, Angers, France; [2]Dermatology Department, CHU, Angers, France; [3]Dermatology Unit, Gustave Roussy Cancer Center, Villejuif Paris Sud, France; [4]Pediatric Adolescent and Young Adult Department, Curie Institute, Paris, France; [5]Dermatology Department, Necker Hospital APHP, Paris, France; [6]Department of Pathology, Necker Hospital APHP, Paris, France; [7]Pediatric Oncology Department, CHU Grenoble, Grenoble, France; [8]Pediatric Oncology Department, CHU, Strasbourg, France; [9]Pediatric Oncology Department, CHU, Besançon, France; [10]Pediatric Oncology Department, CHU, Angers, France; [11]Pediatric Oncology Department, CHU, Saint Denis, France

Objectives: To describe the clinical presentation, treatment and evolution of malignant skin melanomas (MM) occurring in children.
Methods: A descriptive, retrospective, multicenter national study of children and adolescents.
Results: 52 patients from 7 French centers were included. The median age was 15 years (ranges: 5-18), 12 were less than 10 years old. 45% of the tumors were amelanotic and 84% were raised. The Breslow thickness was >4mm for 35% of tumors. Histology showed superficial spreading (n = 16), spitzoid (n = 15) or nodular presentation (n = 13). At diagnosis, the disease was localized in 40 patients, and 2 had metastasis. Clinical lymph node involvement was present in 5. Primary excision was performed in 49 patients. Sentinel lymph node biopsy was performed in 19 patients and was positive in 5. Sixteen patients relapsed and 10 died after progressive disease despite various treatments (surgery, chemotherapy, and immunotherapy). The five-year event-free (EFS), relapse-free (RFS) and overall (OS) survivals were respectively 62.7% [95%CI: 45.3 – 76.0], 72.3% [95%CI: 55.6 – 83.7] and 75.5% [95%CI: 56.8 – 87.1]. On Cox univariate analysis, older age at diagnosis had a negative impact on OS (HR: 1.3 [95%CI: 1.1 – 1.7], p: 0.04). Clark level (II/III vs. IV/V), Breslow thickness and AJCC staging were not significant prognostic factors for EFS and OS. Differences between children and adolescents will be discussed.
Conclusions: Pediatric melanoma is a very rare pathology. It can be amelanotic and concerns mainly adolescents. Primary surgical resection of primary and involved nodes is the optimal management for early stages. Therapy for advanced stages or relapses is unclear and prognosis remains dismal. As efficacy of targeted therapy is unknown in pediatric MM, international cooperative clinical and biological studies are warranted.

O-075

NASOPHARENGEAL CARCINOMA IN CHILDREN AND ADOLESCENTS 1989-2014: DEMOGRAPHIC, CLINICAL, THERAPEUTICAL CHARACTERISTICS AND LONG TERM OUTCOME

R. Kebudi[1], R. Meral[2], O. Gorgun[1], B. Cakir[3], S. Celikarslan[2], I. Ayan[4], F. Yaman Agaoglu[2], E. Darendeliler[2], B. Zulfikar[1], M. Altun[2]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute, Istanbul, Turkey; [2]Radiation Oncology, Istanbul University Oncology Institute, Istanbul, Turkey; [3]Pediatric Hematology - Oncology, Bezmialem Vakif University Medical Faculty, Istanbul, Turkey; [4]Pediatric Hematology - Oncology, Istanbul University Oncology Institute, Istanbul, Turkey

Objectives: The aim of this study was to evaluate the demographic, clinical and therapeutic characteristics and long-term outcome in childhood and adolescent nasopharyngeal carcinoma (NPC) retrospectively in a single center.
Methods: From November 1989 to January 2014 the files of 85 patients <18 years with NPC were treated in Istanbul University Oncology Institute. All patients received three courses of neoadjuvant chemotherapy (1989-1994; cisplatinum-based regimens; 1995-2008: Bleomycin, etoposide and cisplatinum- BEP; since 2008-:EP) followed by radiotherapy given both to the primary tumor and to the metastatic cervical lymph nodes.

Results: Sixty-four males and 21 females, median age 14 yrs (6-18), presented mostly with a lump in the neck, headache, and ear and nose problems. Median follow-up time was 118 months (1mo.-24 years). Eighty-eight% of the biopsies (n = 75) of NPC were WHO type III tumors. Most patients had advanced stage tumors (III = 40, IVA = 17, IVB = 23) with 2 distant metastatic sites (IVC = 2) according to AJCC staging system. Chemotherapy was followed with radiotherapy 60Gy to the primary tumor and involved lymph nodes, and 50-54Gy to the cervical nodal region. The 10-year overall (OS) and event-free survival (EFS) rates were 79.5% and 78.7%, respectively. When patients before 1994 were excluded from the analysis, there was no significant difference in 10 yr-OS and EFS in patients who received BEP or EP (88.6 vs 87.1 and 86.2 vs 88.5, respectively). Eight patients died due to relapse disease. Secondary malignancy developed in two patients. Two others died with causes unrelated to malignancy. Late effects included hypothyroidism, neck fibrosis, xerostomia, bony hypoplasia, skin problems and hearing loss.
Conclusions: Children and adolescents with advanced NPC had a relatively good rate of long-term survival. Neoadjuvant therapy and radiotherapy leads to high locoregional control and thus survival in advanced stage NPC; EP seems to be as effective as BEP. Survivors should be followed for long-term morbidities.

O-076

SALIVARY GLAND CARCINOMAS IN CHILDREN AND ADOLESCENTS: THE ITALIAN TREP PROJECT EXPERIENCE

S. Chiaravalli[1], M. Guzzo[2], G. Bisogno[3], M.D. De Pasquale[4], R. Migliorati[5], F. De Leonardis[6], P. Collini[7], M. Casanova[8], G. Cecchetto[9], A. Ferrari[1]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Otorhinolaryngology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [3]Hematology-Oncology Division, Clinica di Oncoematologia Pediatrica - Università di Padova, Padova, Italy; [4]Hematology-Oncology Division, Ospedale Pediatrico Bambino Gesù, Roma, Italy; [5]Pediatric Oncology Division, Ospedale Pediatrico Pausillipon, Napoli, Italy; [6]Pediatric Hematology-Oncology Division, Università di Bari, Bari, Italy; [7]Soft Tissue and Bone Pathology Histopathology and Pediatric Pathology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [8]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [9]Pediatric Surgery, Ospedale Universitario di Padova, Padova, Italy

Objectives: Salivary glands carcinomas (SGC) are extremely rare in pediatric age, with an annual incidence of 0.8-1.4 per million persons <20 years. We report clinical features of a series of children/adolescents with SGC prospectively registered in the Italian TREP (*Rare Tumors in Pediatric Age)* project.
Methods: Diagnostic/therapeutic guidelines were developed and disseminated between Italian pediatric oncology/surgical centers. In the 2000-2012 period, 720 cases of rare pediatric tumors by 39 different centers were registered: 17 patients had SGC. The number of SGC expected each year in Italy is 6.8 in the 0-17 years population, so the observed/expected ratio was 0.19.
Results: SGC mainly arose in the parotid (14 cases), in most cases they were low-grade tumor (14 cases); clinical presentation was often favorable, with low-stage disease; they had low-grade tumor (12 T1 tumor, i.e. size <2 cm, without extraparenchymal extension, 4 regional nodal involvement). All patients underwent surgical resection, achieving histologically-free margins in 9/17. Concerning patients with parotid gland tumor, 13/14 received parotidectomy (10 total, 3 superficial), 1 had a tumorectomy. Post-operative facial nerve injury was reported in 2 cases. Adjuvant radiotherapy was given to 6 cases, due to incomplete resection associated to N1 tumor and/or T3 tumor. The overall prognosis was good: only one patient with a huge high-grade T4N3 tumor had tumor progression and died of disease. The other 15 cases were alive in first continuous remission, 1-8 years after diagnosis. Noteworthy, in 4/17 cases SGC was a second tumor, 6-9 years after a primary cancer (i.e. acute lymphoblastic leukemia, osteosarcoma, Ewing sarcoma and Hodgkin disease).
Conclusions: This series represents the firstly-reported prospective national-based cooperative series of pediatric SGC. The compliance to TREP recommendations was high. These tumors are rarely managed by pediatric oncologists/surgeons. Larger international cooperation and networking with otolaryngologists/head-neck surgeons expert on adult SGC are advisable.

O-077

TRACHEOBRONCHIAL MUCOEPIDERMOID CARCINOMA IN PEDIATRIC POPULATION- KEY CLINICAL PATHOLOGICAL ISSUES

R. Fan[1]

[1]Pathology, Indiana University School of Medicine, Indianapolis, USA

Objectives: Mucoepidermoid carcinoma was first identified as malignant tumor of major salivary glands, and later also described in tracheobronchial tree, from submucosa mucous glands. Though extremely rare in the pediatric population, tracheobronchial is the second most common primary neoplasm for the location. The most common for is carcinoid tumor. Large series study of this entity in childhood is very scarce in medical literature and the molecular mechanism.
Methods: We retrieved 40 pediatric cases of tracheobronchial mucoepidermoid carcinoma from literature and our institution and analyzed their most relevant clinicopathological features. The age cutoff is 20 years old.
Results: The gender distribution appears to be equal in this population. Presentation age ranges from 3 months to 20 years (mean = 9 year). Pneumonia, especially recurrent pneumonia manifested by cough and fever is the most salient presentation feature. Less than one third of the cases have hemoptysis. The typical endoscopic finding is a well-defined polypoid endobronchial/intraluminal mass. The intermediate grade cases were more frequently encountered in pediatric population (about 50%), but no high grade case was observed. One case regional lymph node metastasis was identified. All study group patients survived with surgical resections alone. On molecular pathology level, translocation t (11;19) and t (1;11) have been detected, some associated with cyclin D1 immuno positivity. 30% of the cases tested were positive for EGFR gene mutation L861Q. One case was tested positive for ERCC1.
Conclusions: Slow growth, insidious course featuring recurrent pneumonia is characteristic of pediatric mucoepidermoid carcinoma. The most important differential diagnosis to be considered include: carcinoid, adenoid cystic carcinoma. The other differentials include-inflammatory myofibroblastic tumor, histoplasmosis nodules, chondroid hamartoma, infantile fibrosarcoma, neurofibroma, hemangioma, and bronchogenic cyst. Mucoepidermoid carcinoma is resistant to radiotherapy and chemotherapy, surgical options do well. In term of prognosis, compared with adult cases, pediatric cases fared better, with 100% survival rate and rare recurrences.

O-078

CLINICAL ANALYSIS OF PLEUROPULMONARY BLASTOMA IN THE LARGER CHINESE PEDIATRIC HEMATOLOGY AND ONCOLOGY CENTER

X. Ma[1], X.S. Wang[1], X.F. Sun[2], S. Wang[3], J.Y. Tang[4], M. Jin[5], D.W. Zhang[5], W. Zhao[5]

[1]Hematology Oncology Center, Beijing Children's Hospital Capital Medical University, Beijing, China; [2]Hematology Oncology Center, Sun Yat-sen University, Guangdong, China; [3]Oncological Surgery, The Children's Hospital of Chongqing Medical University, SiChan, China; [4]Hematology Oncology Center, Shanghai Children's Medical Center Shanghai Jiaotong University School of Medicine, ShangHai, China; [5]Hematology Oncology Center, Beijing Children's Hospital Capital Medical University, Beijing, China

Objectives: Retrospectively analyzed pleuropulmonary blastoma (PPB) in 4 larger Chinese Pediatric Oncology center in recent years. And provide a basis for multi-center collaborative treatment of PPB in China.
Methods: The clinical features, pathological findings and outcome of PPB cases observed from 1999 to 2011. Clinical data, surgical notes and summaries of treatment were taken from the charts and correlated with outcome by standard statistical methods.
Results: The series included 30 patients (12 males, 18 females) with a median age of 36 months (19∼156months), a median of 15 days (5-180days) from onset to diagnosis. In ten patients developed with lung involvement only. Site of extrapulmonary involvement have mediastinal, pleura, pericardial, abdominal lymph nodes and liver. Tumor size was between 5 and 10 cm in seven patients, more than 10 cm (max $16\times15\times12$ cm^3) in nine patients, and unknown in fourteen patients. Two patients had type 1, eight patients type 2, and thirteen patients type 3. Histologic subtype was unknown in seven patients.
At diagnosis, twelve patients had total resection, 2 had recurrences and died, 2 had lost, 8 were complete remission (CR); three patients had partial resection. The remaining patients had biopsy only at initial surgery. Of fourteen patients were treated by chemotherapy. Nine patients received CAV/IE regimen for 3-8 courses. Three received IVAD regimen and Cisplatin for 7-12 courses. Two received IVADand IVA regimen for 12 courses. 6 got CR, 1 partial remission, 6 had recurrences and died, 1 was lost. Those patients had total surgery or partial resection before and/or after chemotherapy.
Conclusions: PPB is an aggressive neoplasm. Achieving total resection of the tumor at any time of treatment (both before and/or after chemotherapy) resulted in a significantly better prognosis, whereas extrapulmonary involvement at diagnosis resulted in a significantly worse prognosis.

LEUKEMIA/MDS/BONE MARROW TRANSPLANTATION – CLINICAL

O-079

TO COMPARE ROLE OF HYDROXYUREA AND HYPERHYDRATION VERSUS HYPERHYDRATION ALONE TO DECREASE TOTAL LEUKOCYTE COUNT IN CHILDREN OF ACUTE LEUKEMIA WITH HYPERLEUKOCYTOSIS: A RANDOMIZED CONTROL TRIAL

M. Sharma[1], A. Singh[1], R. Seth[1], R. Kumar[2], S. Kabra[1], R.M. Pandey[3]

[1]Pediatrics, All India Institute of Medical Sciences, Delhi, India; [2]Laboncology, All india Institute of Medical Sciences, Delhi, India; [3]Biostatistics, All india Institute of Medical Sciences, Delhi, India

Objectives: Acute leukemia with hyperleukocytosis (TLC > 1,00,000/cu.mm) is an oncological emergency. Hydroxyurea is used to treat hyperleukocytosis, but evidence is limited.

1. To demonstrate that addition of hydroxyurea to conventional management causes a significant decline in total leukocyte count when compared to conventional therapy alone in newly diagnosed children of acute leukemia with hyperleukocytosis.
2. To demonstrate difference in complications (tumor lysis, pulmonary complications, CNS complications, hemorrhagic complications and mortality) and time taken to initiate chemotherapy in both the groups.
Methods: All 48 children were randomized in two groups. One group received conventional treatment (intravenous fluids 3 liter/m^2 as 5% dextrose saline with 40 meq/liter of sodium bicarbonate and oral Allopurinol 300 mg/m^2/day). Other group in addition received hydroxyurea (75mg/kg/day).
Results: Treatment response in hydroxyurea group was seen in (83.3%) patients, were as in conventional group it was (29.2%). The difference was significant (P value < 0.05). There was no significant difference in complications (P value > 0.05). Bleeding complication were petechiae (25%), ecchymosis (16.7%), melena (8.3%), epistaxis (6.3%) and retinal hemorrhage (6.3%). Respiratory complications were tachypnea (41.7%), cough (22.9%), respiratory acidosis (10.4%) and infiltrate on chest radiograph (10.4%). CNS complications were papilledema (8.3%), photophobia (8.3%) and headache (4.2%). Median duration to start chemotherapy was less in hydroxyurea group (P value < 0.05). There was no significant adverse drug effects of hydroxyurea observed.
Conclusions: Addition of hydroxyurea to conventional treatment leads to rapid and early decline in TLC without any significant adverse drug effect. Hydroxyurea treatment should be given with standard conservative treatment including intravenous fluids, alkalinization and allopurinol.

O-080

MONITORING MRD IN CHILDHOOD AML USING A SET OF SEVEN GENES – A SIMPLE METHOD WITH STRONG PROGNOSTIC IMPACT

D. Steinbach[1], P. Bader[2], A. Willasch[2], S. Bartholomae[1], K.M. Debatin[1], M. Zimmermann[3], U. Creutzig[3], D. Reinhardt[3], B. Gruhn[4]

[1]Pediatric Oncology, University Medical Center, Ulm, Germany; [2]Pediatric Oncology, University Medical Center, Frankfurt, Germany; [3]Pediatric Oncology, Medical School, Hannover, Germany; [4]Pediatric Oncology, University Medical Center, Jena, Germany

Objectives: This study evaluated the prognostic impact of a simple and highly standardized assay for monitoring minimal residual disease (MRD) in acute myeloid leukemia (AML).
Methods: The expression of seven leukemia associated genes (WT1, PRAME, CCL23, GAGED2, MSLN, SPAG6, and ST18) was measured by TaqMan Low Density Arrays in bone marrow of 114 children with AML and 52 healthy controls. Patients were treated according to multicenter study AML-BFM 2004. Samples were collected and analyzed prospectively at standard time points (diagnosis, day15; day28). The lab that measured the MRD was blinded to the clinical course of the patients.
Results: Relapse free survival (RFS) was 95% ($n = 19$; $SE = 5\%$) if expression of all genes was down to normal by day15, 63% ($n = 41$; $SE = 8\%$) if expression was elevated on day15 but normalized by day28, and 38% ($n = 21$; $SE = 11\%$) in patients who still showed elevated expression of at least one gene on day28 ($p < 0.001$). The prognostic impact was still highly significant ($p = 0.002$) when patients were stratified for established risk factors. Day15 was the most relevant time point for measuring treatment response.
Conclusions: This method is strongly predictive of outcome in childhood AML. It can easily be adopted by other groups because TaqMan Low Density Arrays are a commercially available, fully standardized method.

O-081

TOXICITY IS ASSOCIATED WITH AGE IN NOPHO-AML 2004

D.J.A. Løhmann[1], J. Abrahamsson[2], S.Y. Ha[3], O.G. Jónsson[4], M. Koskenvuo[5], B. Lausen[6], J. Palle[7], B. Zeller[8], H. Hasle[9]

[1]Department of Paediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark; [2]Department of Pediatrics, Institution for Clinical Sciences Queen Silvia Children's Hospital, Gothenburg, Sweden; [3]Department of Pediatrics, Queen Mary Hospital and Hong Kong Pediatric Hematology & Oncology Study Group (HKPHOSG), Hong Kong, China; [4]Department of Pediatrics, Landspitalinn, Reykjavik, Iceland; [5]Department of Pediatrics, Turku University Hospital, Turku, Finland; [6]Department of Pediatrics and Adolescent Medicine, Rigshospitalet University of Copenhagen Denmark, Copenhagen, Denmark; [7]Department of Woman's and Children's Health, Uppsala University, Uppsala, Sweden; [8]Department of Pediatric Medicine, Oslo University Hospital, Oslo, Norway; [9]Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark

Objectives: Due to the high intensity treatment of childhood acute myeloid leukemia (AML) almost all patients experience severe toxicities, some life threatening. Children $\geq$10 years with AML have worse outcome compared to younger children, in part due to treatment related mortality. We investigated if a range of toxicities were age-dependent in the NOPHO-AML 2004 protocol.
Methods: We reviewed toxicities registered in the database of the NOPHO-AML 2004 protocol, including all protocol patients from the Nordic countries and Hong Kong ($n = 320$) censoring patients at time of HSCT.
Results: Treatment-related mortality (after day 10 of diagnosis) occurred in 11/315 (3.5%). During therapy, sepsis/septic shock was significantly more common in 10-17 year olds compared to 2-9 year olds (22% vs 8.5%, $p = 0.01$). Admission to the intensive care unit was more common in 10-17 year olds compared to 2-9 year olds (24% vs 13%, $p = 0.051$). This difference was also seen for infants compared to 2-9 year olds, but not significantly (13% vs 23%, $p = 0.28$). Other noteworthy differences were seen that did not reach significance: assisted ventilation was more common in infants and 10-17 year olds compared to 2-9 year olds (13% and 12% vs 6.8%); Creatinine was elevated to more than 3 x normal more often in infants and 10-17 year olds compared to 2-9 year olds (6.7% and 3.7% vs 0.8%); Bilirubin was elevated to more than 3 x normal more often in infants compared to 2-9 year olds (10% vs 2.6%). The only toxicity seen more often in 2-9 year olds was central neurotoxicity (7.6% vs 1.9% for 10-17 year olds, $p = 0.094$).
Conclusions: Infants and 10-17 year olds experienced more toxicity during AML treatment. This was especially true for admission to the ICU, sepsis and assisted ventilation.

O-082

MOLECULAR AND CYTOGENETIC ANALYSES OF PEDIATRIC ACUTE MYELOID LEUKEMIA PATIENTS WHO DID NOT OBTAIN COMPLETE REMISSION AFTER INDUCTION THERAPY: A REPORT FROM JPLSG AML-05 STUDY

Y. Hara[1], K. Ohki[2], N. Shiba[1], A. Shimada[3], D. Tomizawa[3], T. Taga[3], S. Adachi[3], H. Arakawa[1], A. Tawa[3], Y. Hayashi[2]

[1]Pediatrics, Gunma University Hospital, Maebashi-shi, Japan; [2]Hematology/Oncology, Gunma Children's Medical Center, Shibukawa-shi, Japan; [3]Pediatric Hematology/Oncology, Japanese Pediatric Leukemia/Lymphoma Study Group, Nagoya, Japan

Purpose: Recent improvement of risk-stratified chemotherapy has increased the long-term survival rate of the patients with pediatric acute myeloid leukemia (AML). However, some subgroups still have poor prognosis despite intensive chemotherapy with hematopoietic stem cell transplantation (HSCT), indicating the necessity of more specific identification of the subgroups. Prognosis of the patients with non-complete remission after induction therapy (non-CR) is considered to be extremely poor, but little is known about the molecular characteristics. In this study, we report the molecular identification of pediatric AML cases with non-CR.
Patients & Methods: We analyzed 369 pediatric AML cases enrolled in the AML-05 study in Japan. After induction therapy, 53 of the cases (19.6%) did not achieve CR. AML1-ETO, CBFB-MYH11, MLL-rearrangement, NUP98-NSD1, CBFA2T3-GLIS2, NUP98-JARID1A, FLT3-ITD, KIT, N-RAS, WT1, MLL-PTD, and NPM1 were detected by RT-PCR and MLPA methods.
Results: WBC count was significantly higher in non-CR cases (48,200 vs 18,250) (p
Conclusions: Conventional chemotherapy and HSCT were thought to be insufficient for pediatric AML patients with non-CR, who had distinct biology. Therefore, novel targeted therapies against such genetic mutations are expected.

O-083

REFRACTORY CYTOPENIA OF CHILDREN AND ACQUIRED APLASTIC ANEMIA: A CLINICAL AND PATHOLOGICAL STUDY OF 130 CASES

X. Qin[1], I. Baumann[2], J. Chen[1], P. Shen[3], J.F. Chen[3], M.Z. Yin[3]

[1]Department of Hematology and Oncology, Shanghai Children's Medical Center affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China; [2]Department of Pathology, Boeblingen Hospital, Boeblingen, Germany; [3]Department of Pathology, Shanghai Children's Medical Center affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

Objectives: Explore the clinical characteristics and histopathological morphology features of bone marrow biopsies between refractory cytopenia of children (RCC) and acquired aplastic anemia (AAA), and facilitate the diagnosis, differential diagnosis and treatment of RCC and AAA.
Methods: We retrospectively analyzed clinical data and histopathological morphology of bone marrow biopsies in RCC or AAA patients from January 2011 to December 2012 in our hospital.
Results: There were totally 130 patients studied. The final diagnoses of them were RCC in 78 cases (60.0%) and AAA in 52 cases (40.0%). The ratio of RCC and AAA in this study was 1.5:1. The median WBC count, absolute neutrophil count, blood platelet count, hemoglobin level, and reticulocyte count were all higher in RCC children than AAA (*P*micromegakaryocyte was found in 61.5% (48/78) of them. In AAA group, 88.5% (46/52) of them had cellularity of bone marrow biopsy specimens under 5%; megakaryocyte was not found in 98.1% (51/52) of them. The response rates of immunosuppressive therapy (IST) using CSA $\pm$ rabbit anti-thymocyte globulin for patients with RCC and AAA at 3 months were 59.5% and 26.9% ($P = 0.011$), and at 6 months 75.0% and 38.1% ($P = 0.007$).
Conclusions: RCC and AAA are not uncommon in childhood bone marrow failure disorders. RCC patients showed milder cytopenia and bone marrow hyperplasia than AAA. Patchy distribution of hematopoietic cells, erythroid islands with a marked left shift and micromegakaryocytes are decisive histomorphological patterns used to separate RCC from SAA. IST is an effective therapy in patients with RCC and AAA, and the outcome of IST for patients with RCC is superior to that of patients with AAA.

O-084

CHEMOTHERAPY-BASED CONDITIONING FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AS PREPARATIVE REGIMEN FOR ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANTATION: AN EBMT PAEDIATRIC DISEASES WORKING PARTY STUDY

C. Peters[1], N. Zubarovskaya[1], P. Bader[2], J.H. Dalle[3], A. Hamidieh[4], C. Heredia-Diaz[5], A. Lankester[6], F. Locatelli[7], J. Wachowiak[8], A. Yassilibek[9]

[1]Stem Cell Transplantation Unit, St. Anna Children's Hospital, Vienna, Austria; [2]Stem Cell Transplantation Unit, University Hospital Frankfurt, Frankfurt, Germany; [3]Stem Cell Transplantation Unit, University Hospital Paris Debre, Paris, France; [4]Stem Cell Transplantation Unit, University Hospital Teheran, Teheran, Iran; [5]Stem Cell Transplantation Unit, University Hospital Barcelona, Barcelona, Spain; [6]Stem Cell Transplantation Unit, University Hospital Leiden, Leiden, Netherlands; [7]Stem Cell Transplantation Unit, Hospital Bambini Gesu, Rome, Italy; [8]Stem Cell Transplantation Unit, University Hospital Poznan, Poznan, Poland; [9]Stem Cell Transplantation Unit, University Hospital Ankara, Ankara, Turkey

Objectives: Total body irradiation (TBI) is the backbone for conditioning regimen in children with high risk acute lymphoblastic leukemia (ALL). Some situations preclude the application of TBI, e.g. young patient's age, pre-existing morbidities or centre's facilities. To get detailed outcome information of children who received non-TBI conditioning, the EBMT Paediatric Diseases Working Party initiated a longitudinal retrospective study.
Methods: We identified 1728 children and adolescents with ALL who received a first HSCT between 2000 and 2012 and who were registered in the EBMT data base with a majority transplanted from unrelated donors and bone marrow.
Results: The stem cell source was bone marrow in 43,6% and peripheral blood stem cells in 37,8%. 18,1% received cord blood. For 90,8% of patients the centres intended a myeloablative conditioning, and for 9,8% a reduced toxicity or a reduced intensity conditioning regimen was chosen. The preferred non-TBI conditioning regimen was a combination of busulfan and cyclophosphamide (48%), followed by a triple-drug regimen consisting of busulfan, cyclophosphamide and etoposide; the remaining patients received different combinations like fludarabine/thiotepa/melphalan or treosulphan. At time of analysis, 51,4% of patients were alive. Causes of death were relapse (49,8%) or transplant related complications (42,7%). Patients transplanted after 2008 had an overall survival of 60,9% with comparable relapse incidence but lower incidence of non-relapse mortality. Compared to the whole cohort, children who were transplanted below the age of 4 years had a lower relapse incidence (28,6%) and an overall survival of 56,3%.
Conclusions: More than 50% of children with ALL who received a TBI-free conditioning regimen for allogeneic HSCT from different donors in different remission status are alive. This observation justifies and requests a prospective evaluation whether TBI is still superior compared to conditioning regimen with chemotherapy only in comparable cohort of patients.

LIVER TUMOURS

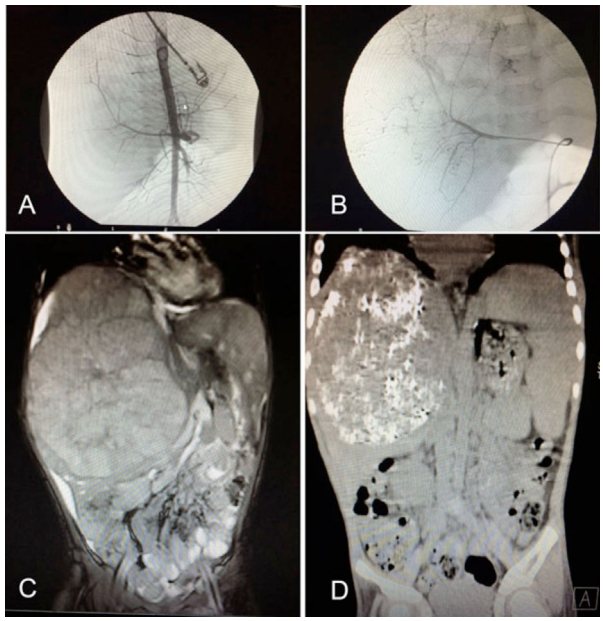
O-085

TRANSARTERIAL EMBOLIZATION FOR PRIMARY HEPATIC MALIGNANT TUMOR IN PEDIATRIC PATIENTS: A 10-YEAR SINGLE INSTITUTION EXPERIENCE

J. Wang[1], Q. Shu[1], M. Li[1], Q. Xiong[1], Y. Lou[1], M. He[1]

[1]Pediatric Oncology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China

Objectives: The purpose of this study is to evaluate the feasibility and efficacy of transarterial chemoembolization (TACE) in treating pediatric primary hepatic malignant tumor (PHMT).
Methods: From 2000 to 2009, 29 patients (age between 4 months and 14 years) with initially unresectable PHMT were enrolled in this study. Twenty-four cases were hepatombalstoma (HB); 3 cases were hepatic carcinoma (HC); 2 cases were undifferentiated embryonal liver sarcoma (UELS). After percutaneous puncture biopsy, all patients received TACE (1-3 times), chemotherapy, and surgery. Follow-up materials were obtained in all patients. The tumor response, survival rate, and complications were analyzed.
Results: Following TACE, there was a visible reduction in tumor size as well as a dramatic decrease in AFP levels (in patients with hepatoblastoma). The tumor volumes (evaluated using CT or MRI) decreased by between 50.1 and 81.3%, with a mean value of 67%. Multiple metasatsis masses were found in one patient with HB after TACE; 2 patients with PRETEXT stage IV tumor (1 HB and 1 HC) remained unresectable after 2 times of TACE. Complete surgical resection was achieved in other 26 patients (89.7%). All patients who underwent surgery (26 cases) received a follow-up at least 5 years. One patient was found to have lung metastasis lesion 6 months after surgery. The 5-year event free survival (EFS) rate was 86.2% (25/29). Complications included fever, transient impairment of hepatic function and abdominal pain.
Conclusions: TACE is a safe and promising method with a low rate of severe complication in treating pediatric PHMT.



O-086

RESULTS OF SURGICAL TREATMENT IN CHILDREN WITH HEPATOBLASTOMA IN THE NETHERLANDS (1990-2013): A NATION WIDE ANALYSIS

M. Wijnen[1], L. Busweiler[2], J. Wilde[2], J. Ziros[3], C. Terwisscha van Scheltinga[4], R. Bakx[5], H. Heij[5]

[1]Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [2]PediatricSurgery, Pediatric Surgical Center of Amsterdam Emma Children's Hospital AMC and VU Medical Center, Amsterdam, Netherlands; [3]Pediatrics, Pediatric Surgical Center of Amsterdam Emma Children's Hospital AMC and VU Medical Center, Amsterdam, Netherlands; [4]Pediatric Surgery, Erasmus Medical Center, Rotterdam, Netherlands; [5]Pediatric Surgery, Pediatric Surgical Center of Amsterdam Emma Children's Hospital AMC and VU Medical Center, Amsterdam, Netherlands

Objectives: Surgical resection remains the cornerstone for a successful treatment in hepatoblastoma. A better insight in the results of surgery may improve the outcomes for hepatoblastoma patients even more. Therefore, the aim of this study was to review the results of surgery in the treatment of hepatoblastoma in the Netherlands retrospectively, focusing on surgery related complications, complete resection of the intrahepatic tumour, morbidity, surgical mortality and long term survival.
Methods: A retrospective chart review was performed on all patients treated for hepatoblastoma at one of the Paediatric Surgical Centers at the Academic Hospitals in Amsterdam, Nijmegen, Groningen and Rotterdam between 1990 and 2013.
Results: A total of 100 patients were included. Among the 73 patients who underwent partial liver resection, pathology report showed complete tumour resection in 64 patients and microscopic tumour residue in 2 patients. In 41 out of 70 patients, one or more complications were reported (59%). Thirty-four patients reported haemorrhage that needed transfusion (49%). Nine patients developed biliary complications of whom 8 needed one or more additional surgical interventions. Overall, 5 year survival was 83%. In the group of 73 patients who had partial hepatectomy 5 year survival was 93% and in the group of 18 patients who had initial transplantation 5 year survival was 82%.
Conclusions: Partial liver resection in children with hepatoblastoma is associated with high complication rates.

O-087

GEMCITABINE AND OXALIPLATIN FOR THE TREATMENT OF PEDIATRIC PATIENTS WITH HEPATOCELLULAR CARCINOMA

A.E. O'Neill[1], M.H. Malogolowkin[2], L. Brugieres[3], M. Casanova[4], J.I. Geller[5], I. Schmid[6], R. Venkatramani[7], P. Thompson[8], J. Feusner[9], A.A. Rangaswami[10]

[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA; [2]Pediatrics, Medical College of Wisconsin, Milwaukee, USA; [3]Pediatrics, Institut Gustave Roussy, Villejuif, France; [4]Pediatrics, IRCCS Fondazione Istituto Nazionale Tumori, Milano, Italy; [5]Pediatrics, University of Cincinnati, Cincinnati, USA; [6]Pediatrics, Dr. von Hauner Childrens Hospital, Munich, Germany; [7]Pediatrics, Children's Hospital of Los Angeles, Los Angeles, USA;

[8]Pediatrics, Texas Children's Cancer and Hematology Centers, Houston, USA; [9]Pediatrics, Children's Hospital & Research Center Oakland, Oakland, USA; [10]Pediatrics, Stanford University, Palo Alto, USA

Objectives: Pediatric patients with hepatocellular carcinoma (HCC) are often treated with hepatoblastoma-directed therapy despite distinct histologies and natural histories. Patients with unresectable or metastatic disease fare poorly with less than 20% overall survival indicating a need for new therapeutic approaches. Adult studies have demonstrated HCC responses to Gemcitabine and Oxaliplatin (GemOx) as either front-line or retrieval therapy. We compiled data from pediatric oncologists regarding their experience treating pediatric HCC patients with GemOx.
Methods: An international working group comprised of Children's Oncology Group (COG), Société Internationale d'Oncologie Pédiatrique (SIOP), Gesellschaft für Pädiatrische Onkologie und Hämatologie (GPOH), and Japanese Study Group for Pediatric Liver Tumors (JPLT) members met in Tubingen Germany in March 2014 to discuss prospective treatment strategies for pediatric HCC patients. We designed a secure electronic survey to collect de-identified patient information regarding histology, age, dose, response, and toxicity.
Results: Of 50 physicians polled, 20 responded. Eight physicians treated 24 patients (10 conventional, 14 fibrolamellar, FL) with GemOx. Patient age ranged from 4-24 years. All patients received Gemcitabine 1000mg/m2 and Oxaliplatin 100mg/m2 with the majority receiving q2 week dosing. GemOx was given first-line once and second-line two-thirds of the time. Using RECIST criteria, seven patients (29%) achieved an upfront partial response (PR) and seven patients (29%) achieved stable disease for a duration of 3-16 months (2 and 6 patients with FL, respectively). PR was sustained for 4-5 cycles; no patients became resectable. Ten patients progressed. Eleven patients experienced toxicities including grade 3-4 cytopenias, grade 3 nausea/vomiting and fever/neutropenia, and hepatopathy, neuropathy, or allergic reaction.
Conclusions: This is the most comprehensive report to date of GemOx use in pediatric patients with HCC. In the retrieval setting, response rates are more promising than those reported for adults (18%). These results support the potential trial of GemOx as first-line therapy in pediatric HCC.

O-088

UNDIFFERENTIATED EMBRYONAL SARCOMA OF THE LIVER – MULTICENTER GERMAN-POLISH EXPERIENCE OF THE CWS AND PPGGL GROUPS.

P. Czauderna[1], M. Murawski[1], T. Dantonello[2], I. Leuschner[3], J. Fuchs[4], G. Seitz[4], T. Klingebiel[5], E. Koscielniak[6]

[1]Surgery and Urology for Children and Adolescents, Medical University of Gdansk, Gdansk, Poland; [2] (CWS), Cooperative Weichteilsarkom Studiengruppe Group, Stuttgart, Germany; [3]Institue of Pathology, Cooperative Weichteilsarkom Studiengruppe Group, Kiel, Germany; [4]Department of Pediatric Surgery University of Tubingen, Cooperative Weichteilsarkom Studiengruppe Group, Tubingen, Germany; [5]University Hospital Frankfurt Klinik für Kinder- und Jugendmedizin, Cooperative Weichteilsarkom Studiengruppe Group, Frankfurt, Germany; [6]Department of Pediatric Oncology Olga Hospital, Cooperative Weichteilsarkom Studiengruppe Group, Stuttgart, Germany

Objectives: Liver sarcomas are rare, representing 6%-13% of primary hepatic tumors, among which undifferentiated embryonal sarcoma of the liver (UESL) prevails. The aim of our study was to assess the outcome of UESL in a multinational study.
Methods: Between 1994-2007, 25 patients with UESL were treated in CWS-96 and CWS-2002 trials in Germany and Poland. Median age at diagnosis was 7,5 years (4 months – 19 years). 12 patients were males, 13 - females. Lesion involved: single hepatic lobe in 22 cases (right – 15, left – 7), both lobes - 1 case and in 1 case information is missing. Tumor was multifocal in 1 case. The tumor size was 5-10 cm in 8 cases and greater than 10 cm in 17. Four children had distant metastasis on presentation (all disappeared following chemotherapy). Fifteen patients received preoperative chemotherapy.
Results: Good response to chemotherapy was observed in 2 cases, partial - in 9, progressive disease in 3, missing data - 1. Postoperative chemotherapy was administered in 20 children. Local radiotherapy was used in 3 children. Tumor resection was performed in 20 patients (10 - primary and 10 - delayed). Complete (R0) resection was achieved in 14 patients (12 are alive). Resection margins were positive (R1) in 5 patients (4 - alive). One child with macroscopically incomplete resection (R2) is alive. Five tumors never became operable: all of them died. The median FU was 153 months (83– 228). Seventeen patients (68%) are alive with no evidence of disease. Eight patients (32%) died (progression – 3, relapse – 3, therapy-related death – 2). Three patients relapsed. All, who were not operated on and/or relapsed, died.
Conclusions: Patients with UDS of the liver have good prognosis (68% ANED) when treated with multimodal therapy. Complete resection was traditionally considered the cornerstone of the treatment for UESL however in our experience even microscopically incomplete (R1) resection was associated with relatively good survival.

O-089

MDM4 IS A POTENTIAL NOVEL THERAPEUTIC TARGET IN HEPATOBLASTOMA

Y. Shi[1], I. Ma[1], R. Patel[1], C. Kettlun[2], J. Nuchtern[1], J. Yang[3], K. Bissig[4], D. Lopez-Terrada[5], S. Vasudevan[1]

[1]Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, USA; [2]Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, USA; [3]Department of Pediatrics, Baylor College of Medicine, Houston, USA; [4]Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, USA; [5]Department of Pathology, Baylor College of Medicine, Houston, USA

Objectives: Hepatoblastoma (HB) is the most common malignant liver tumor of childhood which continues to have poor outcomes in those with unresectable and/or metastatic disease. The majority of HB patients at diagnosis have a wild type p53 tumor suppressor gene and have endogenous mechanisms of p53 down-regulation. MDM4 and MDM2 are the major negative regulators of p53. Copy number gain or amplification of MDM4 has been observed in a subset of HB patients. We hypothesize that MDM4 is the primary regulator of p53 function in hepatoblastoma and that blocking MDM4 will cause tumor cell death due to uninhibited p53 tumor suppressor activity.
Methods: An MTT assay to measured cytotoxicity was performed on the HB cell linesHuh-6, HepG2, HepT1, and PDCL-1 (a patient-derived cell line) which were treated with varying concentrations of NSC207895 (MDM4 inhibitor) or Nutlin-3a (MDM2 inhibitor). CaspaseGlo3/7 luciferase assay was used to assess caspase-3 and -7 activity in HepG2 cells treated with NSC207895. Western blot was used to measure expression levels of p53, p21, BAX, PUMA, and (-actin in HepG2 and HepT1 cells treated with NSC207895.
Results: Huh-6, HepG2, and HepT1 were all tested with Nutlin-3a and did not show significant cell death (IC_{50}>25mM). MDM4 inhibition with NSC207895 caused significant cell death in Huh-6 (IC_{50} = 1.27(M), HepG2 (1.62(M), HepT1 (2.05(M), and PDCL-1 (0.66 (M). A 3.4-fold increase in caspase-3 and -7 activity was observed in HepG2 after 6 hours of exposure to NSC207895 ($p = 0.03$), indicating induction of apoptosis. By Western blot, expression of total-p53 and its downstream transcriptional targets, p21, BAX and PUMA, were increased in HepG2 and HepT1 cells 8 hours after exposure to NSC207895.
Conclusions: Our data supports the hypothesis that p53 activity is suppressed by MDM4 in hepatoblastoma and inhibition of MDM4 may be a viable therapeutic strategy.

O-090

DEVELOPMENT OF A NOVEL WEB-BASED CONSULTATION SERVICE FOR A PAEDIATRIC RARE TUMOR: THE SIOPEL CLINICIAN ONLINE CONSULTATION SERVICE

A. Rangaswami[1], E. Rinaldi[2], A. O'Neill[3], B. Haeberle[4], R. Maibach[5], D. Roebuck[6], D. Lopez-Terrada[7], E.I.S.O. Hiiyama[8], R. Meyers[9], P. Czauderna[10]

[1]Pediatric Hematology-oncology, Stanford University, Palo Alto, USA; [2]PMP, Cineca, Bologna, Italy; [3]Pediatric Oncology, Dana Farber Cancer Institue, Boston, USA; [4]Pediatric Surgery, Ludwig-Maximillians University, Munich, Germany; [5]Trial Activities, IBCSG, Bern, Switzerland; [6]Interventional Radiology, Great Ormond Street Hospital for Children, London, United Kingdom; [7]Department of Pathology & Immunology, Baylor College of Medicine, Houston, USA; [8]Natural Science Center for Basic Research and Development, Hiroshima University, Hiroshima, Japan; [9]Department of Surgery, University of Utah, Salt Lake City, USA; [10]Department of Surgery, Medical University of Gdansk, Gdansk, Poland

Objectives: Because liver tumors in children are quite rare, individual clinician experience is usually limited. Yet the treatment decisions which must be made can be complex and diagnostic dilemmas are common. This is especially true with relapsed/refractory patients. Optimal care requires coordination between disciplines. In an effort to improve care, clinicians representing the four major international trial groups, cooperated to develop a novel web-based consultation service.
Methods: Supported by a grant from ENCCA, representatives from SIOPEL, GPOH, COG, and JPLT developed a web-based service accessed through the SIOPEL home-page. Clinicians may submit a consultation request for assistance in diagnosis, radiographic or pathologic evaluation, and management of non-clinical-trial-eligible patients. The request is directed to a specific discipline or groups of disciplines (surgery, oncology, radiology, pathology) or to all disciplines. The request is reviewed by one of two moderators and then sent to a panel of recognized experts in each of these four disciplines, representing all cooperative groups. The panel provides evidence-based information regarding diagnosis and treatment options, with the website facilitating an opportunity for online discussion amongst the experts. These options are summarized and circulated back to the panelists and treating institution. The treating institution must attest to ultimate responsibility for making management decisions in order to gain access to the site. Total consultation time is seven days.
Results: This consultation service is in final development and is anticipated to be launched in July, 2014.
Conclusions: This service represents an opportunity to enhance the care of children with rare tumors and facilitates education of clinicians caring for such challenging patients. It may serve as a model for cooperative management of other paediatric rare malignancies.
The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under the project ENCCA, grant agreement n° 261474.

RENAL AND RARE TUMOURS

O-091

COMPREHENSIVE MOLECULAR CHARACTERIZATION OF CLEAR CELL SARCOMA OF THE KIDNEY (CCSK): A CHILDREN'S ONCOLOGY GROUP TARGET PROJECT

S. Gooskens[1], S. Gadd[2], D. Meerzaman[3], J. Khan[4], R. de Krijger[5], M. van den Heuvel-Eibrink[1], J. Guidry Auvil[6], D. Gerhard[6], D. Gerhard[6], M. Smith[7], E. Perlman[2]

[1]Department of Pediatric Hematology and Oncology, Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Department of Pathology, Northwestern University's Feinberg School of Medicine and Robert H. Lurie Cancer Center, Chicago, USA; [3]Center for Biomedical Informatics and Information Technology, National Cancer Institute / National Institutes of Health, Bethesda, USA; [4]Pediatric Oncology Branch, National Cancer Institute, Bethesda, USA; [5]Department of Pathology, Josephine Nefkens Institute Erasmus MC, Rotterdam, Netherlands; [6]Office of Cancer Genomics, National Cancer Institute, Bethesda, USA; [7]Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, USA

Objectives: Clear Cell Sarcoma of the Kidney (CCSK) is a rare childhood renal tumor that comprises approximately 5% of all primary renal tumors in children. The molecular background of CCSK is poorly understood. In the current study we aim to identify recurrent pathogenetic changes that result in the development or progression of CCSK.
Methods: Through the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) initiative a genome-wide analysis of 13 CCSK samples was performed, including the OMICs platforms gene expression profiling (Affymetrix 133+2.0), SNP array analysis (Affymetrix SNP array 6.0), whole genome sequencing (Complete Genomics) and RNA-Seq (Illumina Truseq).
Results: Gene expression analysis showed enrichment of multiple gene sets, of which most were involved in Sonic Hedgehog and Akt/PI3K pathways. No significant recurrent copy number changes were identified. Whole genome sequencing revealed an extremely low somatic mutation rate; non-recurrent variants were identified in 10 of 13 cases, verified by RNA-Seq. Apart from a t (10;17) (q22;p13) translocation identified in one case, no significant fusions or mutations were detected in other cases by RNA-Seq.
Conclusions: Although gene expression analysis continues to show Sonic Hedgehog and Akt/PI3K pathway activation, we report no recurrent copy number changes, no recurrent fusions and no recurrent somatic mutations to explain this. Hence, our results suggest that the genome of CCSK is rather stable.

O-092

HYPOMETHYLATION OF GLIPR1 IS A POTENTIAL MARKER OF BLASTEMA IN WILMSTUMOR

N.J. Farinha[1], P. Costa-Pinheiro[1], S. Monteiro-Reis[1], M. Afonso[2], H. Barroca[3], L. Antunes[4], R. Henrique[2], C. Jerónimo[1]

[1]Cancer Biology and Epigenetics Group, Research Center Portuguese Oncology Institute, Porto, Portugal; [2]Department of Pathology, Portuguese Oncology Institute, Porto, Portugal; [3]Department of Pathology, Centro Hospitalar de São João, Porto, Portugal; [4]Department of Epidemiology, Portuguese Oncology Institute, Porto, Portugal

Objectives: Wilms tumor (WT) is a tumor variably composed of an admixture of blastema, epithelium and mesenchyma. In pretreated children, residual blastema carries a poor prognosis. However, blastema is not easily discriminated from the other components. *Glioma pathogenesis related 1* (*GLIPR1*) gene was previously shown to be hypomethylated in WT and expressed in blastema, being correlated with clinical aggressiveness in other neoplasms. The objective of this study was to determine whether *GLIPR1* hypomethylation can differentiate blastema from other components of WT.
Methods: Forty-eight patients with WT from 2 institutions, admitted between 1998 and 2012, in which an homogenous sample for DNA extraction was available were enrolled. Four normal adult kidneys, 8 fetal kidneys, 3 dysplasias, and 16 renal non-WTs served as controls. The study was approved by the ethics committee. Upon pathology review, areas with more than 90% or with less than 10% blastema were selected and macrodissected. DNA was extracted and bisulfate treated for quantification of *GLIPR1* promoter methylation using real time methylation-specific PCR, with beta-actin as control for DNA input. Cases were considered hypomethylated when methylation levels were lower than those of normal adult kidneys. Non-parametric tests were used for statistical analysis.
Results: WT patients comprised 47 children (median age 42 months; range 6months – 10yrs) and one adult. Overall, 54 areas were selected in WT, 30 with more than 90% and 24 with less than 10% blastema. *GLIPR1* hypomethylation was observed in 52 (96%) WT samples, in all fetal kidneys and dysplasias. Although methylation levels significantly differed between WT and normal adult kidney ($p = 0.001$), no statistically significant difference was depicted between malignant and benign renal tumors ($p = 0.166$). The areas of blastema displayed significantly lower levels of *GLIPR1* methylation compared to non-blastema ($p = 0.017$).
Conclusions: In WT, *GLIPR1* hypomethylation levels may discriminate blastema from non-blastema, eventually providing a clinically useful biomarker if confirmed in further studies.

O-093

RENAL TUMORS WITH EXTENSIVE VASCULAR DISEASE: MANAGEMENT CHALLENGES IN A PEDIATRIC SERIES FROM THE HOSPITAL FOR SICK CHILDREN

G. Zamperlini-Netto[1], A. Zanette[1], E. Wehbi[2], S. Williams[1], R.M. Grant[1], L.R. Brandao[1]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Urology, The Hospital for Sick Children, Toronto, Canada

Objectives: Pediatric renal tumors have long been recognized, but their ideal management in the instances of vascular invasion remains controversial. We described the clinical behavior of patients diagnosed with renal tumors and extra renal vascular involvement at The Hospital for Sick Children in Toronto, Canada.
Methods: A retrospective analysis was conducted in patients diagnosed from 1990 to 2012. Data collected included: age, gender, symptoms at presentation, staging, pathology report, radiological evidence of intravascular thrombus [i.e. renal veins (RV), inferior vena cava (IVC) and right atrium (RA)], intraoperative findings, therapeutic protocol implemented and anticoagulation; for outcomes, tumor and/or thrombus recurrence, thromboembolic phenomena and survival.
Results: Of 289 patients with renal tumors identified, 273 were included: Wilms (225), Renal Cell Carcinoma (RCC, 28), Clear Cell Sarcoma of the Kidney (CCSK, 11), others (25). The median age of the group was 4.4 years (4 days - 18 years).
Extra renal vascular disease was identified in 22 patients, with a median age 6 years (1.2 years - 16 years), including Wilms tumors (16/225, 7%), RCC (3/28, 11%), CCSK (2/11, 18%) and PEComa of kidney (1/2, 50%). Vascular involvement comprised exclusive evidence of RV microscopic disease (2), radiological findings without intraoperative/pathology confirmation (5), macroscopic RV involvement (8) and macroscopic RV/IVC vascular disease (7).
Treatment escalation because of vascular disease included neoadjuvant chemotherapy (12; Wilms [11], RCC [1]), intraoperative thrombectomy (2; Wilms), and cavotomy (5; Wilms [3], RCC [1], CCSK [1]). No patient was placed under cardiopulmonary bypass.
Anticoagulation was administered in 2/22 patients for their tumor related thrombus, without complications. One patient had evidence of pulmonary embolism on a Chest CT.
Conclusions: Renal tumors with vascular invasion are a rare and challenging entity. Treatment included mostly cancer-related therapies and the role of vascular surgical approaches and/or systemic anticoagulation remains to be clarified.

O-094

LONG TERM OUTCOME IN ADOLESCENTS AND ADULTS TREATED FOR NEPHROBLASTOMA – A RETROSPECTIVE ANALYSIS OF THE SIOP 2001 GPOH TRIAL

N. Nourkami-Tutdibi[1], S.W. Warmann[2], R. Furtwängler[3], I. Leuschner[4], J.P. Schenk[5], C. Rübe[6], N. Graf[7]

[1]Pediatric Hematology and Oncology, University Children' s Hospital Pediatric Oncology, Homburg, Germany; [2]Pediatric Surgery and Urology, University Hospital Tuebingen, Tuebingen, Germany; [3]Pediatric Hematology and Oncology, University Childrens Hospital, Homburg, Germany; [4]Pediatric Pathology, University Hospital Kiel, Kiel, Germany; [5]Pediatric Radiology, University Hospital Heidelberg, Heidelberg, Germany; [6]Radiotherapy, University Hospital Homburg, Homburg, Germany; [7]Pediatric Hematology and Oncology, University Hospital Homburg, Homburg, Germany

Objectives: Wilms tumor (WT) in adults are very rare. Since 2002 the renal tumour study centre in Germany registered 50 cases of WT older than 15 years of age. They were uniformely treated according to SIOP pediatric WT protocols or the adapted adult WT guidelines. Our intention was to identify risk factors for relapse in adolescents and adults with WT.
Methods: We retrospectively analyzed patients older than 15 years treated for WT in German hospitals. For data collection the same forms were used as in children.
Results: Out of 50 patients, 12 were treated with neoadjuvant chemotherapy, all other underwent primary surgery. Initial tumor volume was documented for 25 cases with a mean tumor volume of 682ml (813-2259ml). 11 patients had metastasis at time of diagnosis. Central pathology review was done in 43 patients (86%). Local stage distribution after primary surgery compared to preoperative chemotherapy was 44% versus 50% in stage I, 13% versus 30% in stage II and 44% versus 20% in stage III. Overall survival (OS) in patients with primary surgery is 60% vs. 80% in metastatic versus non-metastatic patients at time of diagnosis. Multivariate analysis including age at diagnosis, sex, metastasis at time of diagnosis, time to treatment, initial treatment, histological subtype and local stage as confounders revealed local stage III to be independent risk factor for relapse (OR:18, $p < 0.025$).
Conclusions: Our data shows that local stage III is the main risk factor for relapse in adolescent and adult WT patients similar to WT patients below age of 15. With our data we emphasize to register this group of patients prospectively in a multicentre trial. Molecular genetic analysis need to be done in all of them to understand the aetiology of adult nephroblastoma and to find new treatment approaches.

O-095

THE SIGNIFICANCE OF RENAL DYSFUNCTION BEFORE SURGERY IN CHILDREN WITH UNILATERAL RENAL TUMOR

D. Cozzi[1], S. Ceccanti[1], S. Frediani[1], D. Morgante[1], I. Falconi[1], R. Iaconelli[1], F. Cozzi[1]

[1]Pediatric Surgery Unit, Sapienza University of Rome, Rome, Italy

Objectives: In adults with kidney tumor, baseline renal dysfunction (RD) is considered a significant risk factor for progressive renal function decline after nephrectomy. As in children

with unilateral renal tumor (URT) no data are available on renal function outcome of children with baseline RD, we evaluated long-term post-operative renal function in a cohort of children with URT and baseline RD.
Methods: We retrospectively identified 54 children with URT who underwent surgery at our institution between 1982 and 2011. As serum creatinine poorly reflects renal function, we estimated glomerular filtration rate (eGFR) by indexing serum creatinine measurements to age, sex, and race. Update bedside Schwartz equation or the MDRDS equation, as appropriate for age, were used to calculate eGFR. RD was defined as eGFR < 90 ml/min/1.73m^2.
Results: Of 52 children with sufficient data to evaluate baseline eGFR, 30 (57%) presented with baseline RD. During the second decade of life after surgery, 25 patients with baseline RD, despite the excision of 50 per cent of renal parenchyma, presented a significant increase in mean $\pm$ SD eGFR (64.41 ± 17.33 vs 91.69 ± 13.87 ml/min/1.73m^2; $p = 0.001$). Five children with baseline RD who underwent nephron-sparing surgery (NSS) presented during the second decade of life after surgery a mean $\pm$ SD eGFR similar to that of subjects with two healthy kidneys (66.7 ± 19.5 vs 123.4 ± 18.9 ml/min/1.73m^2; $p = 0.001$). Overall at follow-up, none of 12 patients who underwent NSS and 17 of 40 who underwent nephrectomy presented a persistent or newly acquired RD. Four of the 5 patients with post-nephrectomy new-onset RD presented baseline eGFR$<$100 ml/min/1.73m^2.
Conclusions: In children with URT, baseline RD appears to be a paraneoplastic clinical manifestation in subjects with reduced renal reserve capacity.
Renal tumor associate with baseline renal dysfunction may be a clinical surrogate marker for low nephron number endowment.

O-096

EMBRYONAL SARCOMA OF THE LIVER; A POPULATION BASED ANALYSIS USING THE SEER DATABASE

J. Smith[1], B. Crompton[2], M. Gruber-Olipitz[2], K. Ribeiro[3], L. Frazier[4]

[1]School of Medicine, Boston University, Boston, USA; [2]Pediatric Oncology, Dana-Farber Childrens Cancer Care, Boston, USA; [3]Faculdade de Ciencias Medicas, Santa Casa Medical School, Sao Paolo, Brazil; [4]Pediatric Oncology, Dana-Farber Childrens Cancer Center, Boston, USA

Objectives: Embryonal Sarcoma of the Liver (ESL) is a rare entity in adults; 90% of cases occur in children. Previous case series of this rare tumor have reported overall survival of localized disease as high as 70%. However, as recent as 2012 May et al. described 5 patients currently alive and disease free in their first remission (38 to 205 months from time of diagnosis). The incidence and survival of patients with ESL has not been studied using a retrospective population-based analysis. Our objective was to evaluate incidence, organized by patient demographics, as well as long-term survival of this malignancy using the United States National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry.
Methods: The SEER 18 database was searched for patients diagnosed with ESL between 1990 and 2010. Data analyzed included patient demographics, incidence, and survival.
Results: 60 cases between the ages of 0 and 19 years were identified, representing 7% of all liver tumors in children. Median age at diagnosis was 9 years (0-19 years). The tumor was more common in males than females (52% vs. 48%). Most tumors were undifferentiated grade IV tumors (81%). Although 52% of tumors were localized at diagnosis, 27% had regional, and 20% had distant disease. All patients had surgical resection; only 6 patients received radiotherapy (SEER does not collect info on chemotherapy). Cause-specific survival by stage was 88%, 79%, and 56% respectively. We report an overall 1-year, 5-year, and 10-year cause-specific survival for ESL of 91%, 80%, and 75%.
Conclusions: This population-based analysis of ESL allows for a more accurate assessment of survival outcomes than previously possible in case series. Our analysis demonstrates that the prognosis for ESL has improved over time. Prognosis is excellent for localized disease.

LYMPHOMA

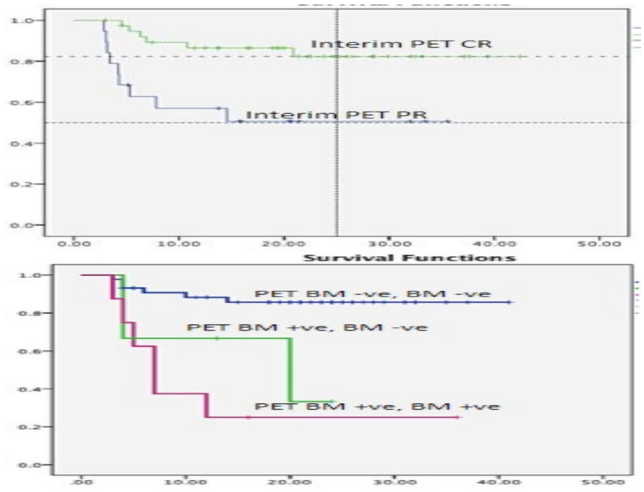
O-097

INCREMENTAL VALUE OF PET AND ROLE OF EARLY INTERIM PET ON RESPONSE PREDICTION AND OUTCOME OF PEDIATRIC NHL

N. Thacker[1], B. Arora[1], V. Rangarajan[2], S. Banavali[1], G. Narula[1], S. Shah[3], G. Chinnaswamy[4], S. Medhi[5], S. Gujral[6], T. Sheth[6], S. Laskar[7]

[1]Pediatric Oncology, Tata Memorial Hospital, Mumbai, India; [2]Nuclear Medicine, Tata Memorial Hospital, Mumbai, India; [3]Nuclear Medicine, Tata Memorial Hospital, Mumbai, India; [4]Pediatric Oncology, Tata Memorial Hospital, Mumbai, India; [5]Radiology, Tata Memorial Hospital, Mumbai, India; [6]Pathology, Tata Memorial Hospital, Mumbai, India; [7]Radiotherapy, Tata Memorial Hospital, Mumbai, India

Objectives: This study's objectives were to: To study the role of early interim PET in Pediatric NHL in terms of response prediction & final outcome and to study the incremental value of baseline PET over bone marrow for staging.
Methods: Newly diagnosed, chemo-naive cases of pediatric (0-18 yrs) NHL (non lymphoblastic), having an interim PET/CT scan were included in the study from January 2009 to December 2011. FDG-PET (PET-2) was done after 2 cycles of chemotherapy. All patients were treated on MCP 842 protocol (8 cycles). The relation of CR and PR in interim PET/CT scan with PFS and OS was analyzed using Kaplan-Meier survival analysis. Post completion of therapy, patients were followed up as per the institutional protocol.
Results: All 58 patients were included in study, of which 46 (79.3%) had advanced disease (stage III/IV). The median age of presentation was 8 yrs (3-18) with a median follow up of 21.4 months (3-43). All the BM positive patients (8/8) had uptake on PET, however 5 (8.6%) patients had marrow uptake on PET only, upstaging the disease. Patients with BM involvement on only PET had significantly lower PFS/OS as compared to PET negative marrow, and only marginally better PFS/OS as compared to conventional Stage IV. Interim PET showed CR in 39/58 (67.2%) of patients, PR in 17/58 (29.30%) of patients and progressive disease in 2/58 (3.4%). All the patients who were in CR in interim PET continued to be so at end of treatment. Response at interim PET could predict progression free survival (PFS) ($p < 0.000$) and overall survival ($p < 0.003$)



Conclusions: PET/CT scan in pediatric NHL picks up additional sites of marrow involvement leading to clinically relevant upstaging of disease with poor prognostic significance. Interim PET/CT significantly predicts PFS and OS in NHL making it a important for response assessment, prognostication and a risk adapted strategy in future.

O-098

PROGNOSTIC IMPACT OF CYTOGENETIC ABNORMALITIES IN CHILDREN AND ADOLESCENTS WITH MATURE B-CELL NON-HODGKIN LYMPHOMA: A REPORT FROM JAPANESE PEDIATRIC LEUKEMIA/LYMPHOMA STUDY GROUP (JPLSG)

M. Sekimizu[1], T. Mori[1], A. Kikuchi[1], T. Mitsui[1], S. Sunami[1], R. Kobayashi[1], N. Fujita[1], H. Inada[1], S. Kikuchi[1], T. Takimoto[1], A. Saito[1], T. Watanabe[1], J. Fujimoto[1], A. Nakazawa[1], K. Ohshima[1], K. Horibe[1], M. Tsurusawa[1]

[1]Lymphoma Committee, Japanese Pediatric Leukemia/Lymphoma Study Group, Nagoya, Japan

Objectives: There is only limited information about cytogenetic abnormalities and their prognostic importance in childhood mature B-cell non-Hodgkin lymphoma (B-NHL).
Methods: We performed a review of 79 abnormal karyotypes in childhood mature B-NHL treated on JPLSG B-NHL03.
Results: A total of 63% of cases were classified as Burkitt lymphoma (BL) or Burkitt-like lymphoma (BLL), 27% were classified as diffuse large B-cell lymphoma (DLBCL) and 10% were others. A total of 11% were stage I, 14% stage II, 24% stage III, 9% stage IV and 42% acute leukemia (Murphy staging). As compared with other 242 patients without abnormal karyotypes, there was a significant over-representation of advanced stage, especially patients with leukemia and with high LDH level. Almost all cytogenetic aberrations in whole population occurred at the same incidence as previously reported in childhood B-NHL (FAB/LMB96 study) except for rearranged MYC/8q24 (R8q24) (51%). The incidence of cytogenetic aberrations in BL/BLL was not distinct from those of reported except for R8q24 (68%). The pattern of chromosomal alterations in DLBCL was similar to those of reported. The prognostic value of cytogenetic abnormalities on event free survival (EFS) was studied by Cox model controlling for the clinical risk factors: der (9p) and del (17p) were independently associated with a significant inferior EFS (hazard ratio: 4.79 ($P = 0.033$) and 9.19 ($P = 0.002$), respectively). The adverse prognosis of del (17p) was observed only in BL/BLL. There is no tendency of EFS to decrease in the patients with +7q or del (13q) which were previously reported as prognostic factors in childhood mature B-NHL.
Conclusions: Cytogenetic risk factors in our study were different from reported in childhood mature B-NHL. Our results emphasize the significant biological difference in ethnicity and the development of cytogenetic risk-adapted therapy in childhood mature B-NHL.

O-099

THE CLINICOPATHOLOGICAL FINDINGS, TREATMENT AND OUTCOME OF JUVENILE MYCOSIS FUNGOIDES: CUTANEOUS T-CELL LYMPHOMA WITH FREQUENT FOLLICULAR INVOLVEMENT AND GOOD RESPONSE TO SKIN TARGETED THERAPY

E. Hodak[1], I. Amitay-Laish[2], M. Feinmesser[3], B. Davidovici[2], M. David[4], A. Zvulumov[5], F. Pavlotsky[6], I. Yaniv[7], G. Avrahami[8], D. Ben-Amitai[9]

[1]Dermatology, Beilinson Hospital Rabin Medical Center Sackler Faculty of Medicine Tel Aviv University, Petach-Tikva, Israel; [2]Dermatology, Beilinson Hospital Rabin Medical Center, Petach-Tikva, Israel; [3]Pathology, Beilinson Hospital Rabin Medical Center Sackler Faculty of Medicine Tel Aviv University, Petach-Tikva, Israel; [4]Dermatology, Beilinson Hospital Rabin Medical Center Sackler Facult of Medicine Tel Aviv University, Petach-Tikva, Israel; [5]Pediatric Dermatology, Schneider Children's Medical Center of Israel Faculty of Health Sciences Medical School of International Health Ben-Gurion University of the Negev Beer-Sheva, Petach-Tikva, Israel; [6]Dermatology, Sheba Medical Center Sackler Faculty of Medicine Tel Aviv University, Tel Hashomer, Israel; [7]Pediatric Hematology Oncology, Schneider Children's Medical Center of Israel Sackler Faculty of Medicine Tel Aviv University, Petach-Tikva, Israel; [8]Pediatric Hematology Oncology, Schneider Children's Medical Center of Israel Sackler Faculty of Medicine Tel Aviv University, Petah-Tikva, Israel; [9]Pediatric Dermatology, Schneider Children's Medical Center of Israel Sackler Faculty of Medicine Tel Aviv University, Petah-Tikva, Israel

Objectives: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma. About 75% of cases are diagnosed after age 50 years. [2] While studies from North America and Europe report a 0-5% rate of occurrence before age 20 years, several reports suggest that juvenile MF is much more common in Asian countries with prevalence of up to 25%. We aimed to evaluate the characteristics of juvenile MF in a large cohort.
Methods: Data were collected on all patients with MF aged ≤18 years at clinicopathological diagnosis who attended the Dermatology Department of Rabin Medical Center between1994-2012 and were followed prospectively.
Results: The sample included 50 patients (30 male; mean age 11.4 years at diagnosis); 18 (36%) had Fitzpatrick skin type ≥IV. All were diagnosed with early-stage disease (IA-IIA) except 1 (tumor-stage, IIB). Eight had only classical MF lesions and 42 had other variants, alone or in combination, mainly hypopigmented MF (n = 29) and delicate but clear clinicohistologic features of folliculotropic MF (FMF) (n = 18). Among the various skin-targeted therapies applied, psoralen+UVA (PUVA) (systemic/bath) proved very efficient for FMF. The vast majority of young patients present with early-stage disease and with unusual variants, especially hypopigmented MF. A novel finding of our study is the high percentage of FMF which affected one-third of our patients, was characterized by more superficial clinical features and histopathologically by fewer infiltrates than adult FMF and showed a good response to PUVA. During follow-up of 0.25-15 years (mean 4.5), 2 patients progressed from stage IA to IB or IIA.
Conclusions: Reported here is the largest series of juvenile MF and the first to focus on FMF. FMF is not uncommon in children/adolescents and is characterized by more superficial clinical features and fewer heavy infiltrates than adult FMF, with good response to PUVA. The prognostic significance of childhood FMF remains unclear.

O-100

MACROPHAGE POLARIZATION IN PEDIATRIC CLASSICAL HODGKIN LYMPHOMA CORRELATES WITH EPSTEIN-BARR VIRUS STATUS AND OUTCOME

M. Barros[1], P. Segges[2], G. Vera-Lozada[2], R. Hassan[2], G. Niedobitek[1]

[1]Institute for Pathology, Unfallkrankenhaus Berlin, Berlin, Germany; [2]Bone Marrow Transplantation Center, Brazilian National Cancer Institute, Rio de Janeiro, Brazil

Objectives: We have shown recently that in Epstein-Barr virus (EBV) -associated pediatric classical Hodgkin lymphoma (cHL) the tumor microenvironment (TUM) is characterized by a cytotoxic/Th1 profile and higher numbers of CD14+, CD68+ and CD163+ cells when compared to adult cHL. The objectives of this study were to evaluate the macrophage polarization (MP) in the TUM of pediatric cHL (3 to 18y, median: 14y) and its impact on the survival.
Methods: MP was analysed by double-immunohistochemistry combining CD68 or CD163 with pSTAT1 (M1-macrophages) and CD68 or CD163 with CMAF markers (M2-macrophages). Expression levels of STAT1 and LYZ genes were investigated by RT-qPCR. Results were analyzed in context of age, histological characteristics, EBV-status, clinical follow-up and our previous study of T-cell populations in these cases. 100 cHL cases were studied, including 69% nodular sclerosis (NS) and 23% mixed cellularity (MC) cases.
Results: There were 44.8% cases who were EBV-positive. Patients ≤14 years displayed higher numbers of CD168+pSTAT1+ cells (P = 0.01), when compared with the oldest age-group. Higher numbers of CD163+pSTAT1+ macrophages were observed in cases with cytotoxic/Th1 tumor microenvironment profile, as disclosed by the ratios FOXP3+/CD8+ cells > 1.5 and FOXP3+/TBET+ cells > 1.5 (P < 0.0005 and P = 0.04, respectively). EBV+ cases exhibited high numbers of CD68+pSTAT1+ (P = 0.02) macrophages. The level of *STAT1* and *LYZ* expression was associated the numbers of CD68+pSTAT1+ macrophages and EBV presence. Better overall-survival was observed in cases with high numbers of CD163+pSTAT1+ macrophages (P = 0.04). Worse progression-free survival (PFS) was observed in cases with high numbers of CD163+CMAF+ macrophages (P = 0.02). Gene expression was not associated with survival.
Conclusions: Our results suggest that in pediatric cHL macrophage polarization may depend on EBV status of HRS cell, and that a predominant M2 polarization is associated with worse PFS.

O-101

POST KIDNEY TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

S. Sorrentino[1], A. Garaventa[1], F. Ginevri[2], M. Cioni[2], M. Zecca[3], P. Comoli[3]

[1]Oncology, Istituto Giannina Gaslini, Genoa, Italy; [2]Nephrology, Istituto Giannina Gaslini, Genoa, Italy; [3]Oncoematologia Pediatrica, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Objectives: Post-transplant lymphoproliferative disease (PTLD) is a heterogeneous group of lymphoid disorders that may complicate transplantation. Due to the clinicopathologic heterogeneity and patient's peculiarities, there is not a unified treatment approach.
Methods: In this retrospective (1987-2013) monocentric study we have enrolled 15 patients (M/F 11/4) with PTLD after kidney transplantation.
Results: Median age at diagnosis was 11.5 years (4-29 years). Median time at PTLD was 72 months (1-156 months). In 3 cases it was an "early PTLD" at 1, 5 and 6 months after transplant, in the major part (12/15, 80%) it was a "late-onset PTLD" (21-156 months). PTLD was an "early lesion" in 2 cases; polymorphic in 3; monomorphic in 9 (B-cell lineage in 7 patients and T-cell lineage in 2); unknown in one. Treatment was surgical in 3 cases, anti-CD20 antibody in one, chemotherapy in 11, of whom 9 that derived from B-cell lineage received in association anti-CD20 antibody. The chemotherapy was administrated according to AIEOP protocols, without Methotrexate and reducing the doses. Nine patients received autologous EBV-specific cytotoxic T-lymphocyte at the end of treatment to consolidate the remission. The complete remission was achieved in 93% of patients. Three patients developed a second PTLD, in two cases with the same histological type, respectively 97 months after the first plasmacytic hyperplasia and 11 months after the first polymorphic hyperplasia; in the third with a monomorphic PTLD 24 months after an extramedullary plasmocytoma. The patient with plasmacytic hyperplasia developed, 45 months after the second form, a PTLD Hodgkin-like that treated with chemo and radiotherapy obtained remission. One patient died for an HIV-related infection and one for disease. Thirteen patients are alive disease free with a median follow-up of 59 months (3-197 months). The therapy was well tolerated. 80% of patients maintained a good function of allograft-kidney.
Conclusions: A multidisciplinary approach allows a good clinical course of this post-transplant complication.

O-102

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RELAPSED ALK + ANAPLASTIC LARGE CELL LYMPHOMA OF CHILDREN AND ADOLESCENTS: A STUDY ON BEHALF OF THE SFCE AND SFGM-TC

M. Strullu[1], J. Kanold[2], Y. Bertrand[3], J.H. Dalle[4], C. Paillard[5], A. Baruchel[6], A. Chevance[7], M.C. Le Deley[7], G. Michel[8], L. Brugiéres[9]

[1]Pediatric Oncology and Hematology, CHU de NANTES, Nantes, France; [2]Pediatric Oncology and Hematology, Hopital Estaing, Clermont Ferrand, France; [3]Pediatric Hematology, Insitut d'Hématologi ete d'Oncologie Pediatrique, Lyon, France; [4]Pediatric Hematology, Hopital Robert Debré, Paris, France; [5]Pediatric Oncology and Hematology, Hopital Hautepierre, Strasbourg, France; [6]Pediatric Hematology, Hopital Robert Debré, Paris, France; [7]Biostatistics and Epidemiology Unit, Gustave Roussy, Villejuif, France; [8]Pediatric Hematology, Hopital La Timone, Marseille, France; [9]Pediatric Oncology, Gustave Roussy, Villejuif, France

Objectives: Allogeneic hematopoietic stem cell transplantation (allo-SCT) is an option for the treatment of relapsedanaplastic large cell lymphoma (ALCL) in children. To date, few paediatric reports have assessed its efficiency and tolerance.
Methods: We analyzed the data of 34 patients under 18 years (median age 7.4y [1.1-17]) prospectively registered in the SFGM-TC (Soci*é*t*é* Française de Greffe de Moelle et de Th*é*rapie Cellulaire) database, who received an allo-SCT for the treatment of an ALCL ALK+ between 1993 and 2011. At transplant, 28 patients (82.4%) were in complete remission (CR) whereas 6 (17.6%) had a detectable disease. Conditioning regimens were mostly myelo-ablative (n = 31). Most donors were unrelated (n = 22) including 9 HLA-matched donors, 3 HLA-mismatched donors and 10 cord blood units.
Results: Median follow-up was 6.0 years [range 1.1-12.5]. The 5-year overall and progression-free survivals were respectively 70.0% (SE = 8.0%) and 58.1% (SE = 8.6%) on the whole series, and 94.7% (SE = 5.1%) and 73.7% (SE = 10.1%) in patients who received allo-SCT after a first relapse. Six patients relapsed after a median time of 141 days [35-235]. Durable CR was obtained in 4/6 patients after donor lymphocytes injection (n = 1) or Vinblastine-corticosteroid treatment (n = 3). Overall, the 5-year cumulative incidence of relapse and treatment-related mortality (TRM) was 17% (SE = 7%) and 24% (SE = 8%), respectively. Eventually, 10 patients died; 8 due to transplant toxicity and 2 of progressive disease. Five of the ten patients transplanted before 2004 died of TRM contrasting with three

of the 24 patients transplanted in 2004 or later (Hazard ratio of TRM = 5.2, 95% CI, 1.2-21.9, p-value = 0.02).
Conclusions: In children with high-risk relapse of ALK+ ALCL, allo-SCT is a valid therapeutic option. However, the high level of TRM raises the question of its place in the area of new-targeted agents. When allograft is required, reduced-intensity conditioning could help reducing toxicity in these heavily pre-treated patients.

RHABDOMYOSARCOMA

O-103

GENOME-WIDE EPIGENETIC AND COPY NUMBER ANALYSES IN RHABDOMYOSARCOMA

M. Seki[1], T. Shimamura[2], K. Yoshida[3], Y. Sato[3], N. Riki[1], M. Kato[1], G. Nagae[4], A. Oka[1], S. Miyano[2], H. Aburatani[4], Y. Hayashi[5], S. Ogawa[3], J. Takita[1]

[1]Department of Pediatrics, The University of Tokyo, Tokyo, Japan; [2]Laboratory of DNA Information Analysis, Human Genome Center Institute of Medical Science The University of Tokyo, Tokyo, Japan; [3]Department of Pathology and Tumor Biology, Graduate School of Medicine Kyoto University, Kyoto, Japan; [4]Genome Science Division, Research Center for Advanced Science and Technology The University of Tokyo, Tokyo, Japan; [5]Department of Hematology/Oncology, Gunma Children's Medical Center, Shibukawa, Japan

Objectives: Rhabdomyosarcoma (RMS) is a common pediatric soft tissue sarcoma and histologically classified into two major subtypes, alveolar (ARMS) and embryonal (ERMS). Most cases of ARMS have a characteristic fusion between the *PAX3/PAX7* and *FOXO1* genes, and the ERMS subtype commonly harbors loss of heterozygosity (LOH) at 11q15. However, epigenetic alterations underlying the pathogenesis of RMS are largely unknown. To explore the epigenetic basis of RMS, we performed genome-wide micro array based methylation and copy number analyses in 30 cases with ERMS and 17 cases with ARMS.
Methods: DNA methylation microarray analysis of 50 RMS cases was performed using Infinium HumanMethylation450 BeadChip (Illumina). In addition, copy number analysis was performed using GeneChip® 100K/500K arrays and Cytoscan® (Affymetrix). To determine DNA methylation profiles, we selected probes with variance ranked in the top 1% for unsupervised clustering analysis.
Results: Unsupervised hierarchical clustering identified 4 distinct subtypes. Interestingly, these 4 subtypes were correlated with clinical features and genomic alterations, including fusion status and copy number gains of chromosomes 2 and 8, and 11q LOH. Most cases with fusion negative ERMS were classified as clusters 3 and 4, whereas all fusion positive cases were classified as either clusters 1 or 2. Importantly, among these clusters, cluster 4 was significantly associated with favorable outcome (Fisher's exact test p value < 0.002).
Conclusions: In our analyses, we could separate RMS cases into 4 distinct methylation subtypes which are associated with clinicopathological findings. Our integrated epigenetic analyses enhance our understanding of the genetic and epigenetic mechanisms underlying pathogenesis of RMS.

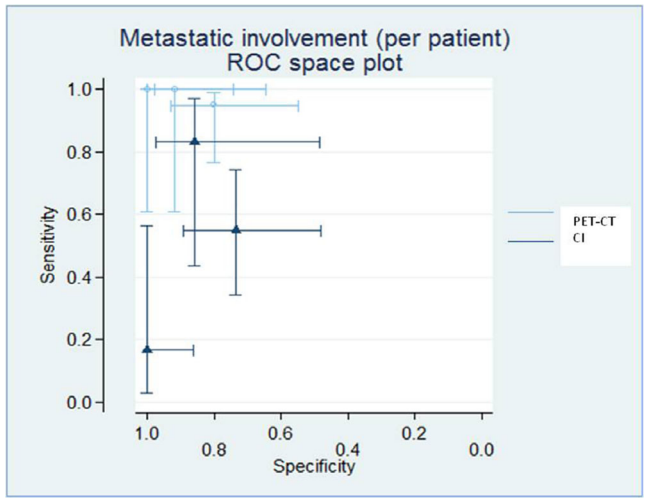
O-104

THE ROLE OF PET-CT IN THE MANAGEMENT OF CHILDHOOD RHABDOMYOSARCOMA: SYSTEMATIC REVIEW

G. Norman[1], D. Fayter[1], K. Light-Lewis[1], J. Chisholm[2], H. Mandeville[2], S. Gatz[2], D. Levine[2], M. Jenney[3], K. McHugh[4], B. Phillips[1]

[1]Centre for Reviews and Dissemination, University of York, York, United Kingdom; [2]Paediatric and Adolescent Oncology, Royal Marsden Foundation NHS Trust, London, United Kingdom; [3]Paediatric and Adolescent Oncology, Children's Hospital for Wales, Cardiff, United Kingdom; [4]Radiology, Great Ormond Street Hospital, London, United Kingdom

Objectives: Rhabdomyosarcoma (RMS) has an incidence of 4.6 per million children and adolescents. Management depends on risk stratification. Current staging includes computed tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy, and bone marrow biopsy. Advanced functional imaging has potential to improve staging accuracy and management strategies.
Methods: We conducted a systematic review (PROSPERO 2013:CRD42013006128) of the diagnostic accuracy and clinical effectiveness of functional imaging in histologically-proven paediatric RMS. Ten databases were searched to November 2013. Eligible studies compared positron emission tomography, with or without CT, or diffusion weighted (DWI) MRI to conventional imaging at any point in ≥10 RMS patients. Limited, heterogeneous data required narrative synthesis; sensitivity and specificity were plotted in receiver operating curve space.
Results: Eight studies (six PET-CT, two PET, with 272 RMS patients) were included. No studies of DWI-MRI met inclusion criteria. Pooled estimates were not calculated due to sparseness of data. Limited evidence indicated initial PET-CT results were predictive of survival. PET-CT was reported to change management of 7/40 patients in three studies. For nodal involvement PET-CT sensitivity ranged from 80% to 100% and specificity from 89 to 100%; for conventional imaging sensitivity was 67% to 86% and specificity 90% to 100%. For distant metastatic involvement PET-CT sensitivity ranged from 95% to 100% and specificity from 80% to 100% compared with sensitivity 17% to 83% and specificity 43% to 100% for conventional imaging. Very sparse data on particular metastatic sites and PET-CT response prediction for outcomes were reported.



Conclusions: PET/PET-CT may increase initial staging accuracy in paediatric RMS, specifically the detection of nodal involvement and distant metastatic spread. PET-CT should be further assessed in this population, ideally in a representative, unbiased and transparently selected patient cohort (i.e. those entering a randomised controlled trial of treatment).
Funding: Children's Cancer and Leukaemia Group (UK).

O-105

THE ROLE OF DOXORUBICIN IN THE TREATMENT OF RHABDOMYOSARCOMA: PRELIMINARY RESULTS FROM THE EPSSG RMS2005 RANDOMIZED TRIAL

G. Bisogno[1], G.L. De Salvo[2], C. Bergeron[3], M. Carli[1], A. Ferrari[4], M. Jenney[5], H. Mercks[6], A. Kelsey[7], S. Gallego[8], J. Chisholm[9], D. Orbach[10], H. Martelli[11], O. Oberlin[12], M. Stevens[13]

[1]Department of Pediatrics, University Hospital of Padova, Padova, Italy; [2]Biostatistics Unit, E, Padova, Italy; [3]Department of Pediatrics, Centre Leon Berard, Lyon, France; [4]Pediatric Unit, Istituto Nazionale Tumori, Milano, Italy; [5]Pediatric Unit, Children Hospital for Wales, Cardiff, United Kingdom; [6]Department of Pediatric Oncology, Emma Children Hospital Academic Medical Centre, Amsterdam, Netherlands; [7]Department of Diagnostic Paediatric Histopathology, Royal Manchester Children's Hospital, Manchester, United Kingdom; [8]Pediatric Oncology, Hospital Universitario Vall d'Hebron, Barcelona, Spain; [9]Pediatric Oncology, Royal Marsden Hospital, Sutton, United Kingdom; [10]Pediatric Oncology, Institute Curie, Paris, France; [11]Service di Chirurgie Pediatrique, Hopital de Bicetre, Le Kremlin-Bicetre, France; [12]Pediatric Oncology, Institute Goustave Roussy, Villejuif, France; [13]Pediatric Oncology, Institute of Child Life and Health, Bristol, United Kingdom

Objectives: Doxorubicin is an effective drug against rhabdomyosarcoma (RMS), but its value when incorporated into an established multidrug regimen remains controversial. Previously, evidence for lack of benefit may have related to its use at low dose intensity. The E*p*SSG RMS2005 study incorporated a randomization to explore the benefit of early dose intensification with doxorubicin in high risk non-metastatic patients.
Methods: From June 2005 to October 2013, 481 patients (age >6 months, <21 years) were randomized between 9 cycles standard IVA (n = 241) (ifosfamide 3g/m^2 day 1,2; vincristine 1.5mg/m^2 day 1, actinomycin-D 1.5mg/m^2 day 1) and IVADo (n = 240), an experimental arm consisting of 4 cycles IVA with doxorubicin 30mg/m^2 on day 1,2 followed by 5 cycles of IVA. Tumor response was evaluated after the 3rd cycle and local treatment (surgery and/or radiotherapy) was delivered after the 4th cycle. The statistical plan was to randomize 500 patients in order to detect, with 80% power, a 35% relative reduction in events in the experimental arm (HR = 0.65).
Results: An interim analysis was performed including 448 patients (223 IVA, 225 IVADo) with adequate follow up data. 134 patients had at least 1 event (65 IVA, 69 IVADo). At median follow-up 37 (14-56) months, 3-year event free survival was 67.2% (95% CI: 59.7–73.6) for IVA and 64.8% (95% CI: 57.3–71.2) for IVADo. 3-year overall survival was 83.0% (95% CI: 76.2–88.0) and 79.1% (95% CI: 72.3–84.5) respectively. Toxicity was greater with IVADo. Futility analysis led to a recommendation from the DMC to stop the randomization earlier than planned.
Conclusions: The addition of dose intense doxorubicin to standard chemotherapy failed to show an improvement in the outcome of patients with high-risk non metastatic RMS. The

EpSSG RMS2005 trial continues to evaluate the role of maintenance therapy (cyclophosphamide/vinorelbine).
Supported by Città della Speranza Foundation

O-106

ALVEOLAR RHABDOMYOSARCOMA WITH NODAL INVOLVEMENT, A GROUP WITH UNFAVOURABLE OUTCOME: EXPERIENCE OF THE EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA GROUP (EPSSG)

S. Gallego[1], G. Bisogno[2], C. Bergeron[3], M. Carli[2], A. Ferrari[4], M. Jenney[5], H. Martelli[6], M. Gaze[7], O. Oberlin[8], J. Chisholm[9], J.H.M. Merks[10], D. Orbach[8], A. Kelsey[11], G.L. De Salvo[12], M. Stevens[13]

[1]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Barcelona, Spain; [2]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Padova, Italy; [3]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Lyon, France; [4]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Milan, Italy; [5]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Cardiff, United Kingdom; [6]Paediatric Surgery, European Paediatric Soft Tissue Sarcoma Group, Bicetre, France; [7]Paediatric Radiotherapy, European Paediatric Soft Tissue Sarcoma Group, London, United Kingdom; [8]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Paris, France; [9]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, London, United Kingdom; [10]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Amsterdam, Netherlands; [11]Paediatric Pathology, European Paediatric Soft Tissue Sarcoma Group, Manchester, United Kingdom; [12]Biostatistics, European Paediatric Soft Tissue Sarcoma Group, Padova, Italy; [13]Paediatric Oncology, European Paediatric Soft Tissue Sarcoma Group, Bristol, United Kingdom

Objectives: Alveolar rhabdomyosarcoma (aRMS) with nodal involvement (N1) accounts for up to 10% of all RMS. Results from most previous European co-operative studies suggested very poor survival (3-5 year EFS 25-39%), comparable to that of stage IV disease, although outcome was better in one more recent study (SIOP MMT95: 3yr EFS 57%). In the EpSSG RMS2005 protocol, aRMS/N1 received intensified initial chemotherapy (IVADo: ifosfamide, vincristine, dactinomycin, doxorubicin) and additional maintenance chemotherapy with systematic local treatment to primary and nodal sites.
Methods: Ninety-eight patients with aRMS/N1 (8.2% of all (n = 1198) patients) were enrolled in EpSSG RMS2005 from October 2005 to October 2013. After primary surgery/biopsy, all received 4 cycles IVADo, 5 cycles IVA and 6-months maintenance therapy with cyclophosphamide and vinorelbine. Local treatment scheduled after IVADo included radiotherapy to primary site and/or nodes with or without secondary surgical resection of the primary and/or involved nodes.
Results: The incidence of adverse prognostic factors was high: 50% patients were >10 years age; 90% had gross residual disease (IRS Group III) after initial surgery/biopsy; 63% primary tumours were locally invasive (T2); 76% had primary size >5 cm and 82% occurred at unfavourable sites. At median follow-up of 49 months, 3-year EFS was 56.2% (95%CI: 44.2%-66.2%). Outcome data were available in 81 patients. Eight (10%) demonstrated refractory disease with early progression and died; 28 (34%) relapsed (22 after completion of therapy) with median time to relapse 11.5 (11-18) months: 27/28 of these died.
Conclusions: Patients with aRMS/N1 may benefit from intensification of therapy although 10% fail to respond to initial chemotherapy and prospects for salvage of those who relapse are poor. Additional strategies are needed to further improve outcome for this high risk group and enrolment in phase I/II studies is justified for those who do not achieve early local control or who relapse.

O-107

PROTON THERAPY FOR NON-METASTATIC RHABDOMYOSARCOMA: EARLY CLINICAL OUTCOMES

D. Indelicato[1], R. Rotondo[1], J. Bradley[1], T. Vern-Gross[1], C. Morris[1], S. Bradfield[2], E. Sandler[2], N. Mendenhall[1]

[1]Radiation Oncology, University of Florida, Jacksonville, USA; [2]Pediatric Oncology, University of Florida, Jacksonville, USA

Objectives: This study reports early toxicity and disease control in children with non-metastatic rhabdomyosarcoma (RMS) treated with proton therapy (PT).
Methods: From February 2007 through November 2013, 66 patients with a median age of 4.1 years (range, 0.6-15.3 years) were treated with PT for non-metastatic RMS. The most common primary sites were parameningeal (28), orbital (14), and bladder/prostate (13). The median tumor size was 5 cm (range, 2-15 cm). Thirty-six patients were Intergroup Rhabdomyosarcoma Study (IRS) stage 3 and 62 patients were IRS Group III. Patients received chemotherapy per the EPSSG RMS 2005 (n = 40) or contemporary COG (n = 26) protocols. The median interval between the start of chemotherapy and radiotherapy was 15 weeks (range, 3-60). The median follow-up is 1.5 years. Various patient and treatment factors were examined to identify predictors for disease control outcomes.
Results: The actuarial 2 year overall survival, progression free survival, local control, and freedom from distant metastases was 89%, 85%, 88%, and 94%, respectively. On multivariate analysis, tumor size > 5 cm, parameningeal site, and duration of induction chemotherapy >15 weeks were each associated with significantly lower rates for local control and progression free survival ($p < 0.05$ for both). Of note, children with >5 cm parameningeal tumors had inferior rates of local control compared to all other tumors (54% vs 95%, $p < 0.002$). Permanent toxicity was limited to 9 patients with cataracts, 1 patient requiring a unilateral hearing aid, and 4 patients requiring hormone replacement therapy.
Conclusions: To date, this is the largest cohort of children with RMS treated with PT. Early data suggests that highly conformal radiation does not compromise early tumor control or increase early toxicity in a group of young patients with unfavorable risk characteristics. Consistent with previous reports, we do not recommend delaying radiation beyond week 13 in patients with non-metastatic disease.

O-108

LONG-TERM EVALUATION OF ORBITAL RHABDOMYOSARCOMA IN CHILDREN: THE INSTITUT CURIE EXPERIENCE

H. Boutroux[1], C. Levy[2], V. Mosseri[3], L. Desjardins[4], C. Plancher[3], S. Helfre[5], P. Freneaux[6], C. Cellier[7], J. Michon[1], D. Orbach[1]

[1]Pediatric Adolescent and Young Adult Oncology Department, Institute Curie, Paris, France; [2]Ophtalmology Department, Institute Curie, Paris, France; [3]Department of Biostatistics, Institute Curie, Paris, France; [4]Ophtalmology Department, Institute Curie, Paris, France; [5]Radiotherapy Department, Institute Curie, Paris, France; [6]Department of Pathology, Institute Curie, Paris, France; [7]Department of Radiology, Institute Curie, Paris, France

Objectives: Orbital rhabdomyosarcoma (ORMS) is associated with an excellent survival rate greater than 85%, and is considered to be a favorable site for this tumor. Treatment is based on combination chemotherapy together with best local therapy, sometimes surgery but more often radiation therapy. Local therapy is associated with frequent and potentially severe late sequelae and pediatric oncology groups have therefore tried for many years to reduce these sequelae without jeopardizing the outcome of ORMS in response to an adapted treatment strategy. A retrospective single-center analysis was set up in order to more clearly define the long-term status of ORMS survivors.
Methods: Among the 95 patients with localized ORMS treated at the Institut Curie between 1975 and 2010, 82 survivors were analyzed in this study.
Results: Median age at diagnosis was 6 years [range: 8 months – 19 years], and median follow-up was 8.5 years [range: 7 months -24 years]. The 5-year globe conservation rate was 90.4%. Ophthalmic dysfunction was present in 79% of patients. Impaired visual acuity (VA), defined by VA<20/20 on the affected eye, was present in 62% of patients; 38% of them had severe visual disability with VA<20/200. Late effects on orbitofacial structure were present in 39.8% of patients. Ocular or palpebral sequelae were present in 79% of survivors, mainly cataract (42%), ocular surface lesions such as keratoconjunctivitis (40%) and eyelid abnormalities (29%). General late effects were rare.
Conclusions: These data suggest that ocular and orbital late effects are frequent after treatment of ORMS, indicating the need for systematic long-term ophthalmologic follow-up of these patients. Radiation therapy is an important part of the total burden of therapy.

RETINOBLASTOMA

O-109

THE DLX2 HOMEOBOX GENE REGULATES THE P107 TUMOUR SUPPRESSOR IN MOUSE RETINA DEVELOPMENT: IMPLICATIONS FOR MOUSE AND HUMAN RETINOBLASTOMA

J. Zagozewski[1], H. Aghazadeh[2], J. Bush[3], D. Eisenstat[4]

[1]Medical Genetics, University of Alberta, Edmonton, Canada; [2]Biological Sciences, University of Alberta, Edmonton, Canada; [3]Pathology, University of Manitoba, Winnipeg, Canada; [4]Pediatrics and Medical Genetics, University of Alberta, Edmonton, Canada

Objectives: Retinoblastoma is the most common malignant eye tumour of childhood. In humans, sporadic or germline mutations of the retinoblastoma gene Rb-1 are implicated in almost all cases. However, mutations of Rb-1 and either of its pocket protein family members, p107 or p130, are necessary to induce tumours in mouse models of the disease. The developmental regulation of p107 is relatively unknown. Dlx homeobox genes encode homedomain-containing transcription factors expressed in ganglion cells, amacrine and horizontal cells of the embryonic and adult retina.
Methods: Chromatin immunoprecipitation (ChIP) was performed on embryonic mouse retina tissues (E18.5) using a polyclonal antibody to DLX2. Electrophoretic mobility shift assays (EMSA) were used to confirm specific protein:DNA interactions. Reporter gene assays were performed using luciferase reporter constructs containing the p107 promoter. p107 gene expression was assessed in the Dlx1/Dlx2 double knockout mouse (DKO). DLX2 expression was assessed in mouse models of retinoblastoma and human retinoblastoma samples.
Results: ChIP demonstrated that DLX2 occupies several regions of the p107 gene promoter in vivo. EMSA confirmed specific DLX2 transcription factor:p107 promoter DNA complexes in

vitro. Co-expression of Dlx2 activated p107-luciferase promoter gene expression in vitro. p107 expression was reduced in the Dlx1/Dlx2 DKO mouse retina at E18.5. DLX2 was expressed in the nuclei of Chx10:Rb-p107 conditional DKO retinoblastoma as well as in almost all human retinoblastoma tissues we studied.
Conclusions: The homeodomain transcription factor DLX2 directly activates expression of the tumour suppressor p107, a member of the Rb pocket protein family essential for cell cycle regulation. Expression of DLX2 in both mouse and human retinoblastoma supports that these developmental tumours are partially differentiated and contributes to our knowledge regarding the cell of origin. Future studies will determine whether modulation of DLX2 expression regulates cell proliferation and differentiation of retinoblastoma.

O-110

IMPACT OF RB1 MUTATION PRENATAL DIAGNOSIS ON CHILDREN AT RISK FOR RETINOBLASTOMA

B. Gallie[1], H. Dimaras[1], H.S.L. Chan[2], E. Héon[1], J. Sutherland[1], M. Day[1], M. Day[1]

[1]Ophthalmology and Vision Science, The Hospital for Sick Children, Toronto, Canada; [2]Division Hematology Oncology Dept Paediatrics, The Hospital for Sick Children, Toronto, Canada

Objectives: Canadian Guidelines for Retinoblastoma Care[1] recommend testing infants for their affected parent's *RB1* mutation prenatally or at birth; infants carrying the *RB1* mutation may be delivered late pre-term [HD1] or near-term (36, 37 weeks gestation) to optimize opportunities for minimal impact treatment of small tumors. We evaluate effects of gestational age at first eye examination on outcomes of children carrying an *RB1* mutation.
Methods: We retrospectively studied infants carrying their family's *RB1* mutation, born between 1 June 1996 and 31 May 2013 and treated at SickKids. Information collected included: affected parent; sex; gestational age at birth, *RB1* testing and first eye exam; pregnancy or perinatal complications; type of sample tested and *RB1* mutation; locations of first and subsequent tumors; International Intraocular Retinoblastoma Classification and Tumour Node Metastasis staging; treatments delivered; last followup date; and overall and visual outcomes.
Results: Twenty infants carried their parent's *RB1* mutation, detected prenatally in 12 and after birth in 8. Nine were tested prenatally and electively delivered at 36-37 weeks gestation and 3 were spontaneously premature. All infants not tested prenatally were born at term. All newborn infants had weekly eye examinations. Vision-threatening tumors were present at birth in 25% (3/12) of infants delivered early or born prematurely and 75% (6/8) of full-term infants; posterior tumors appeared age 1 to 6 months in 9 infants. All patients eventually developed bilateral retinoblastoma. Good vision was maintained in all children born early; treatments included focal therapy (all) and later chemotherapy (5), stereotactic radiation and enucleation of one eye due to chemotherapy intolerance (1). Full-term infants received focal therapy (8), chemotherapy (5), and enucleation of one eye (2); bilateral macular tumors blinded one child.
Conclusion
Prenatal molecular detection and early delivery facilitated optimal outcomes.
1. National Retinoblastoma Strategy Canadian Guidelines for Care. Canadian Journal of Ophthalmology. 2009;44:S1-88.

O-111

A PROSPECTIVE SINGLE INSTITUTION TRIAL USING TOPOTECAN BASED CHEMOTHERAPY FOR THE TREATMENT OF BILATERAL INTRAOCULAR RETINOBLASTOMA

R. Brennan[1], M.W. Wilson[2], S. Mao[3], J. Wu[3], I. Qaddoumi[1], C. Rodriguez-Galindo[4]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Ophthalmology, University of Tennessee Health Science Center, Memphis, USA; [3]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA; [4]Oncology, Dana Farber Cancer Institute, Boston, USA

Objectives: To evaluate efficacy of systemic chemo-reduction using topotecan for advanced intraocular retinoblastoma.
Methods: 27 newly diagnosed bilateral retinoblastoma patients (14 males, median age 7.9 months), worse eye Reese- Ellsworth (RE) group IV-V, received 11 cycles of chemotherapy: topotecan and vincristine (TV) x 2 followed by three alternating courses of carboplatin and vincristine x 2 and TV x 1. Intensive focal therapy was applied after the first 2 cycles. Event free survival (EFS) was defined as avoidance of external beam radiation (EBRT) and enucleation.
Results: Of 54 eyes, 42 were RE IV-V and 37 were International Classification (IC) C-E. 24 patients (89%) completed all prescribed chemotherapy; one was removed due to persistent viral infection and two had progressive disease requiring EBRT. All eyes received focal therapy. Seven patients received subconjunctival carboplatin during therapy, and six received plaque brachytherapy during follow-up. Eleven eyes were enucleated: one at diagnosis, nine with progressive disease including three eyes treated with EBRT, and one which developed neovascular glaucoma. At 8 years, cumulative incidence of EBRT was 2.4% (SE ± 2.4) and EFS for patients was 66.7% (SE ± 38.5). Ocular survival for RE group IV-V eyes was 76.2% (SE ± 26.3) and 70% (SE+ 27.0) for IC group D-E eyes. All patients experienced thrombocytopenia (41 episodes in 275 courses, 15%). There were 29 episodes of febrile neutropenia (10%). Fifteen patients had a documented source of infection (40% viral etiology). Grade 3 diarrhea was present in 9/27 patients, and one patient reacted to carboplatin. All patients are alive with median follow up was 7.4 years.
Conclusions: Topotecan combined with vincristine, carboplatin and aggressive focal therapies is an effective regimen for the treatment of advanced retinoblastoma (RE IV-V) that avoids radiation and results in globe salvage with measurable vision. Toxicities were anticipated and managed with appropriate supportive care.

O-112

TREATMENT OF RECURRENT OR PROGRESSIVE INTRAOCULAR RETINOBLASTOMA: PRELIMINARY RESULTS OF A NATIONAL PHASE II STUDY OF THE SWISS PEDIATRIC ONCOLOGY GROUP

M. Beck Popovic[1], S. Binaghi[2], M.C. Gaillard[3], M. Diezi[4], E. Garcia[4], S. Houghton[3], M.T. Galley[1], M. Cornu[1], S. Pampallona[5], F. Munier[3]

[1]Pediatric Hematology Oncology Unit, CHUV-University Hospital, Lausanne, Switzerland; [2]Interventional Radiology, CHUV-University Hospital, Lausanne, Switzerland; [3]Jules Gonin Eye Hospital, University Hospital, Lausanne, Switzerland; [4]Pediatric Hematology-Oncology Unit, CHUV-University Hospital, Lausanne, Switzerland; [5]Statistics for Medicine, forMed, Evolene, Switzerland

Objectives: To determine the effectiveness and safety of injections of Melphalan via the ophthalmic artery (SOAC), or into the vitreous cavity (IVC), or of periocular Topotecan (POT), as salvage therapies for recurrent/progressive retinoblastoma (Rb) according to the site of recurrence/progression. To evaluate the eye preservation rate after 3 courses of SOAC, 3 courses of IVC, 2 courses of POT (no enucleation and/or radiotherapy).
Methods: National single arm phase II prospective study including patients (pts) with recurrent/progressive Rb between 6 months and 15 years of age after failure to prior treatment (chemoreduction/focal therapy, plaque therapy, external beam radiation), with RetCam images and ultrasound biomicroscopy for identification of tumor-free meridian mandatory for IVC. Each patient was enrolled and evaluated only for one treatment arm. Response was evaluated after each treatment course for retinal tumors and/or vitreous seeds. Treatment was stopped at any time in case of progression, toxicity or parental refusal.
Results: Thirty-one pts were registered, 14 (4 with unilateral and 10 with bilateral disease) were eligible after failure to prior chemotherapy only (12) or chemotherapy/radiotherapy (2). Salvage treatment consisted of SOAC in 7, IVC in 5 and POT in 2 pts. Response was favorable in 3/7 SOAC, 5/5 IVC and 2/2 POT administrations. There was no enucleation or radiotherapy after a median follow-up of 7 months (1-16). Six out of 14 pts needed further treatment, 5 in the same eye (SOAC 1, IVC 1, combined SOAC/IVC 3), 1 in the contralateral eye (combined). Ocular hemorrhage in 2/14 eyes after SOAC was the worst adverse event observed, treated successfully with anti-VEGF.
Conclusions: In heavily pretreated Rb patients SOAC, IVC and POT are efficient in treating recurrent/progressive disease and preventing enucleation and/or radiotherapy. However, almost half of the treated eyes need further treatment for disease control. Treatment combinations should be considered in future.

O-113

EFFICACY OF SECOND COURSE OPHTHALMIC ARTERY CHEMOSURGERY FOR RETINOBLASTOMA THAT RECURS FOLLOWING PRIOR OPHTHALMIC ARTERY CHEMOSURGERY

L.J. Dunkel[1], Y.P. Gobin[2], B.P. Marr[3], I. Tendler[4], S.E. Brodie[5], D.H. Abramson[3], J.H. Francis[6]

[1]Pediatrics, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [2]Neurosurgery, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [3]Ophthalmology, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [4]Pediatrics, Memorial Sloan Kettering Cancer Center, New York, USA; [5]Ophthalmology, Memorial Sloan Kettering Cancer Center and Mount Sinai, New York, USA; [6]Ophthalmology, Memorial Sloan Kettering Cancer Center, New York, USA

Objectives: Melphalan-based ophthalmic artery chemosurgery (OAC) has been highly effective for intra-ocular retinoblastoma, but some patients who achieve remission develop recurrence following completion of therapy. We aimed to evaluate the efficacy of second course OAC for such patients.
Methods: Single-arm, retrospective study of 32 eyes that underwent OAC at our centers between May 2006 and July 2013 and achieved remission, but suffered intra-ocular retinoblastoma recurrence at least 2 months off-therapy. Outcome measurements included Kaplan-Meier estimates of ocular progression-free survival (PFS) and ocular survival, and the Mantel-Cox test was used to compare curves.
Results: The eyes previously received a mean of 3.1 first course OAC infusions and developed off-therapy disease recurrence at a median of 4.4 months following completion of initial OAC.

Median follow-up is 34 months following initiation of second course OAC. The Kaplan-Meier estimates of 2-year ocular PFS and ocular survival following second course OAC were 47.0% (95% confidence interval 27.8-64.0%) and 80.2% (95% confidence interval 58.5-91.3%), respectively. Presence of vitreous seeds (seen in 53% of eyes requiring second-course OAC) was significantly associated with inferior 2-year ocular PFS (33.6% [95% confidence interval 12.9-56.0%] versus 65.8% [95% confidence interval 32.0-85.8%]; $p = 0.01$) and ocular survival ($p = 0.01$). Factors not associated with ocular PFS included pre-OAC treatment history, age at initial OAC, early (<4.4 months) versus later recurrence, addition of new drug during second course OAC, and number of infusions during second course OAC.
Conclusions: Eyes with recurrent intra-ocular retinoblastoma following first course OAC treatment may be cured with second course OAC. However, a significant portion of the eyes may require additional therapy (third or fourth course OAC or other treatment modalities such as intra-vitreal chemotherapy), particularly if vitreous seeds are present at the time of initial OAC failure.

O-114

AGE AND SITE-SPECIFIC RISKS OF SECOND MALIGNANT NEOPLASMS IN RETINOBLASTOMA SURVIVORS: A POPULATION-BASED STUDY

R. Naves[1], R. Amorim[1], B. Truong[2], A. Green[3], P. Friedrich[3], K. Ribeiro[1], C. Rodriguez-Galindo[3]

[1]Department of Social Medicine, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil; [2]Pediatric Oncology, Harvard Medical School, Boston, USA; [3]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA

Objectives: Retinoblastoma (RB) survivors have an increased risk of developing second malignant neoplasms (SMN). The aim of our study was to assess the site-specific, and age-specific risk of SMN among retinoblastoma survivors using population-based data.
Methods: We retrieved data from Surveillance Epidemiology and End Results (SEER) database (9 registries,1973-2010). All children ages 0-19 diagnosed with RB (ICCC group V) were included in the study. Standardized incidence ratios (SIR) and corresponding 95% confidence intervals (95% CI) were calculated using SEERStat 8.1.2.
Results: Our cohort comprised 820 children with RB (mean age at diagnosis 1.8 years). 589 children (72.6%) had unilateral and 222 (27.4%) had bilateral RB. Thirty-one patients developed SMN (SIR = 9.8, 95% CI 6.6-13.9). Children with bilateral RB had a higher risk of developing a head and neck second malignancy (HN-SMN) (n = 12; SIR = 93.7, 95%CI 48.4-163.8) than in other sites (n = 14; SIR = 23.2, 95%CI 12.7- 38.9). The observed increased risk of a HN-SMN was present even for those children with bilateral RB who did not receive RT (SIR = 71.1, 95%CI 14.7-207.8), while a more modest risk of developing SMN at other sites was observed (SIR = 22.2, 95%CI 7.2-51.8). Children with bilateral RB diagnosed < 1 year had higher risk of HN-SMN (RT: SIR = 168.8, 95%CI 72.9-332.6; Without RT: SIR = 75.3, 95%CI 9.1-271.9) than those diagnosed > 1 year, corrected for use of RT (RT: SIR = 30.0, 95%CI 0.8-167.4; Without RT: SIR = 64.0, 95%CI 1.6-356.7).
Conclusions: The risk of SMN among RB survivors is higher for patients diagnosed before one year of age. Children with bilateral RB are at an increased risk of SMN in the HN regardless of the use of RT. The need to use non-irradiating diagnostic studies of the HN should be emphasized.

CNS TUMOURS

O-115

INTEGRATED GENOMICS ELUCIDATES RELATIVE SPATIAL HOMOGENEITY OF PEDIATRIC BRAIN TUMORS

M. Remke[1], F. Jorgensen[1], A.S. Morrissy[1], V. Ramaswamy[1], R. Packer[2], U. Schueller[3], E. Bouffet[4], S.M. Pfister[5], N. Jabado[6], M. Taylor[7]

[1]Developmental & Stem Cell Biology, Hospital for Sick Children, Toronto, Canada; [2]Center for Neuroscience and Behavioral Medicine, Children's National Medical Center, Washington, USA; [3]Department of Neuropathology, Ludwig-Maximilians-University, Munich, Germany; [4]Division of Pediatric Hematology/Oncology, Hospital for Sick Children, Toronto, Canada; [5]Department of Pediatric Neurooncology, German Cancer Research Center, Heidelberg, Germany; [6]Departments of Pediatrics and Human Genetics, McGill University and the McGill University Health Center Research Institute, Montreal, Canada; [7]Department of Neurosurgery, Hospital for Sick Children, Toronto, Canada

Objectives: Comprehensive, genome-wide profiling and next-generation sequencing based studies have dramatically improved our understanding of pediatric brain tumor biology over the past decades. However, the vast majority of theses studies are based on the assumption that single biopsies are representative for the entire primary tumor. Intratumor heterogeneity comprises a common phenomenon previously described in renal cell carcinoma, breast cancer, and glioblastoma multiforme. Highly disparate genetic profiles of spatially separated tumor areas within the same tumor may preclude development of personalized, molecularly targeted therapies based on single tumor biopsies.
Methods: To address this issue, we conducted multiregion whole exome sequencing, high-resolution DNA copy number analysis (Cytoscan HD) and DNA methylation profiling (Infinium HumanMethylation450 BeadChip) on over 25 distinct pediatric and adult brain tumors with a median of six spatially distant biopsies per tumor (range 4-9). Histological entities included ATRT (n = 2), DIPG (n = 2), ependymoma (n = 1), glioblastoma (n = 10), medulloblastoma (n = 10), and medulloepithelioma (n = 1). We assessed the degree of intratumor heterogeneity and subgroup affiliation using integrated genomics and unsupervised hierarchical clustering algorithms.
Results: Epigenetic signatures were highly similar from individual multiregion biopsies within a single tumor. However, we identified up to 250,000 CpG dinucleotides that were differentially methylated when comparing the intertumor heterogeneity of DNA methylation patterns even within disease subgroups. Further, pediatric brain tumors displayed highly similar focal and broad DNA copy number alterations unlike their adult counterparts. Multiregion sequencing further reinforced the relatively higher degree of intratumor homogeneity in pediatric brain tumors. Lastly, we showed that subgroup affiliation was stable in all multiregion biopsies from the same medulloblastoma.
Conclusions: Our results demonstrate that single biopsies are representative of the tumor genomics landscape and that subgroup affiliation of pediatric brain tumors is more stable than in their adult counterparts.

O-116

SPINAL MYXOPAPILLARY EPENDYMOMA EXHIBIT A 'WARBURG' PHENOTYPE

S.C. Mack[1], M.D. Taylor[1], G.E.N.E. Global Ependymoma Network of Excellence[1]

[1]Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada

Objectives: Myxopapillary spinal ependymomas are a distinct histological variant arising predominantly in the conus medullaris, cauda equina, or filum terminale. Despite a generally favorable prognosis, metastases, subarachnoid dissemination, and late recurrences have been reported. Currently, maximal safe resection is the only effective treatment for myxopapillary ependymoma. We characterized the genomic and transcriptional landscape of spinal ependymomas in an effort to delineate the genetic basis of this disease and identify new targets for therapy.
Methods: Gene expression profiling was performed on 35 spinal ependymomas using Affymetrix Gene 1.1ST microarrays, and on 16 spinal ependymomas using RNA seq. Copy number profiling was also performed on an overlapping cohort of 38 spinal ependymomas using Affymetrix SNP6.0 microarrays. Western blot analysis was used to confirm gene expression values. Functional validation experiments were performed on tumour lysate consisting of assays measuring pyruvate kinase M activity (PKM), hexokinase activity (HK), and lactate production.
Results: On a transcriptional level, we demonstrate that Grade II and myxopapillary spinal ependymomas are molecularly distinct. These findings are supported by subgroup-specific copy number alterations occurring in each histological variant. Pathway analysis revealed that myxopapillary ependymoma are characterized by metabolic networks, namely up-regulation of HIF-1a and its transcriptional targets. These findings were validated by western blot analysis demonstrating increased protein expression of HIF-1a, HK2, PDK1, and phosphorylation of PDHE1a. Functional assays were performed on myxopapillary tumour lysates to demonstrate decreased PKM activity, increased HK activity, and elevated lactate production.
Conclusions: Our findings suggest that myxopapillary ependymoma may be driven by a Warburg metabolic phenotype, mediated by the HIF1a transcriptional network. The key enzymes promoting the Warburg phenotype: HK2, PKM2, and PDK are targetable by next-generation small molecule inhibitors/activators that inhibit glycolysis, and which should be tested in pre-clinical studies as therapy for myxopapillary ependymoma.

O-117

NEW INTRAOPERATIVE MONITORING OF CORTICOBULBAR MOTOR EVOKED POTENTIALS IN CHILDREN

O. Bozinov[1], J. Sarnthein[1]

[1]Neurosurgery, University Hospital of Zurich, Zurich, Switzerland

Objectives: The motor function of cranial nerves (CN) can be continuously monitored by transcranial corticobulbar motor evoked potentials (CoMEPs) during neurosurgical interventions. While there are several publications of these new CoMEPs in adults, the feasibility and safety of CoMEPs in children has not yet been documented.
Methods: We included 13 consecutive procedures involving 12 patients (median age 2.5 y, range 1-15 y, 7 male) that were operated by the first author in 2013 and in whom CoMEPs were monitored. While most authors use a 50% reduction of CoMEP response amplitudes as a warning criterion, our approach was to keep the response amplitude constant by increasing the stimulation intensity and to establish a warning criterion based on the "threshold-level" method. For the facial nerve, a threshold increase greater than 20 mA for eliciting CoMEPs in the most reliable facial nerve target muscle was considered a prediction of reduced postoperative facial nerve function, and subsequently a warning was issued to the surgeon.
Results: Monitoring of CoMEPs was feasible in all 13 surgeries in at least one facial nerve target muscle. The mentalis muscle yielded the best result (89% of trials), followed by

orbicularis oris (85%) and orbicularis oculi muscles (80%). The median stimulation threshold was initially 69 mA (range 40-100 mA) for CoMEPs and 60 mA (15-95 mA) for MEP of the thenar muscles. The initial CoMEP threshold exceeded the MEP threshold in 5/13 patients (median difference 5 mA). CoMEP deterioration showed specificity for HB deterioration of 88% CI [47-100%].
Conclusions: Intraoperative CoMEP monitoring is feasible and safe also in young children. We found no evidence that procedures and thresholds should differ from CoMEP in adults. CoMEP monitoring is a valid indicator of CN function in neurosurgery. It should be used as an adjunct to direct electrical CN stimulation and continuous EMG monitoring of CN target muscles.

O-118

REPORT FOR THE SIOP-CPT-2000 STUDY AND THE CURRENT SIOP-CPT REGISTRY

U.R. Kordes[1], S. Hartung[1], M. Hasselblatt[2], V. Ruland[2], T. Pietsch[3], R.D. Kortmann[4], M. Warmuth-Metz[5], M. Garami[6], H. Traunecker[7], J.E.A. Wolff[8]

[1]Pediatric Hematology and Oncology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [2]University Medical Center, Institute for Neuropathology, Münster, Germany; [3]University Medical Center, Institute for Neuropathology Brain Tumor Reference Center, Bonn, Germany; [4]University Medical Center, Radiooncology Reference Center, Leipzig, Germany; [5]University Medical Center, Neuroradiology Reference Center, Würzburg, Germany; [6]Semmelweis University, 2nd Department of Pediatrics, Budapest, Hungary; [7]The Children's Hospital for Wales Heath Park, Paediatric Oncology, Cardiff, United Kingdom; [8]Cleveland Clinic Children's Hospital, Department of Pediatric Hematology Oncology, Ohio, USA

Objectives: Analysis of clinico-pathological variables of patients with choroid plexus tumors (CPT) of all age groups and WHO grades recruited into an international registry and treatment outcomes according to risk-adapted treatment stratification.
Methods: The SIOP-CPT-2000 study (01/2000 - 03/2010) and the SIOP-CPT registry (04/2010 - 04/2014) have recruited 221 patients with reference reviewed CPT. A risk-adapted treatment algorithm stratified into an observational group for all non-metastatic classical plexus papilloma (CPP) and atypical plexus papilloma (APP), and a treatment group for all metastatic CPT, incompletely resected APP and all choroid plexus carcinoma (CPC). SIOP-CPT-2000 patients older than 3 years diagnosed with CPC received primary focal irradiation.
Results: Median age at diagnosis was 2.7/0.64/2.11 years for CPP/APP/CPC with equal gender distribution. Primary location for all CPT was the lateral ventricles without right/left preference. With increasing age, CPP localized more frequently to the IVth ventricle. CPC did not occur exclusively within the IIIrd ventricle. Primary metastasis were recognized in 10/14 / 20% of all CPP/APP/CPC. Germline mutational analysis identified 8 patients with Li-Fraumeni syndrome. The median follow-up time for 130 SIOP-CPT-2000 study patient was 5.5 years. The 5-year overall survival / 5-year event-free survival was 100/97% for CPP (n = 48), 96/85% for APP (n = 37) and 50/38% for CPC (n = 45). Extended follow up showed no difference between a carboplatin based regimen compared to a cyclophosphamide based regimen. The cumulative incidence for secondary neoplasm was comparable to infant brain tumor populations with different histologies. Nuclear accumulation of p53 showed no prognostic impact.
Conclusions: Adjuvant treatment improved outcome of high grade choroid plexus tumors. Carboplatin as well as cyclophosphamide based regimens are equally effective. WHO grade is the most significant prognostic marker.
A*cknowledgement
Funded by the German Childhood Cancer Foundation (DKKS)

O-119

IS RE-VACCINATION UPON A NEW EVENT IN PATIENTS WITH HIGH-GRADE GLIOMA USEFUL?

S. Van Gool[1], S. De Vleeschouwer[2]

[1]Microbiology and Immunology, KU Leuven, Leuven, Belgium; [2]Neurosciences, KU Leuven, Leuven, Belgium

Objectives: Multimodal strategies are developed to treat patients with high grade glioma (HGG). Active specific immunotherapy rapidly emerges as a new treatment modality. We provide immunotherapy for adults with primary diagnosis of GBM (HGG-2006) and for children/adults with relapsed HGG (HGG-IMMUNO-2003). In this retrospective analysis, we questioned whether second immunotherapy upon a new event was useful in patients who already got immunotherapy for their disease.
Methods: 35 patients were treated with two vaccination treatments, 12 adults (26-69y) with primary diagnosis of GBM and 23 patients (7-55y) with relapsed HGG at time of first immunotherapy. At both times, leukapheresis was performed and DCs were loaded with lysate of the newly resected tumor tissue.
Results: HGG-2006 enrolled patients treated with two immunotherapies had a median OS of 41.8m versus 14.8m in HGG-2006 patients (n = 68) treated with one immunotherapy program. The age distribution of the former was younger than of the latter group. Similarly, HGG-IMMUNO-2003 patients treated with two immunotherapies had a median OS of 32m versus 11m in HGG-IMMUNO-2003 patients (n = 163) with one immunotherapy program. The age of the former patient group was younger, and their HGG-IMMUNO-RPA risk profile was better. The time interval between the first and second leukapheresis was longer in the HGG-2006 than the HGG-IMMUNO-2003 patients. All second immunotherapy approaches were similar. There were less injections during second immunotherapy as compared to the first immunotherapy. The number of injections was similar to the numbers given to HGG-IMMUNO-2003 patients who got first vaccination at time of relapse. The OS calculated from the second leukapheresis in re-vaccinated patients was similar as the OS observed in HGG-IMMUNO-2003 patients treated for the first time at relapse. Second immunotherapy was feasible, and no extra vaccine-related toxicities were observed.
Conclusions: These retrospective results show that second immunotherapy is worth to be considered along the disease course of patients with HGG.

O-120

ADULT SURVIVORS OF CHILDHOOD CNS TUMOURS: THEIR SELF-PERCEIVED MOST PROMINENT ILLNESS- AND TREATMENT-RELATED LATE EFFECTS, DIFFICULTY OF SEQUELAE, AND SURVEILLANCE NEEDS

L. Hörnquist[1], B. Lannering[2], G. Gustafsson[1], K.K. Boman[1]

[1]Department of Women's and Children's Health - Childhood Cancer Research Unit, Karolinska Institutet, Stockholm, Sweden; [2]Department of Clinical Sciences - Pediatric Oncology, University of Gothenburg, Gothenburg, Sweden

Objectives: As part of the longitudinal Swedish childhood CNS tumour LIFE study, this study aimed at identifying self-perceived most prominent late-effects (SPLEs) among very long-term survivors (VLTSs), and the extent to which sequelae were experienced as disabling. SPLEs were analysed in relation to self-perceived needs of -, and current involvement in clinical follow-up.
Methods: The study targeted an entire cohort of 706 Swedish 24-46 years old (mean = 32) VLTSs diagnosed 1982-2001. SPLEs data were collected using a study-specific questionnaire in the second wave of data collection, while single predictor factor data emanate from prior wave 6 years earlier. SPLEs were in this study addressed in open-ended question format, and ratings of their difficulty using 5-point Likert-scale response format. Data were analysed quantitatively and qualitatively.
Results: Three hundred thirty, 65.7%, of 507 data-providing survivors, reported prevalence of one to several SPLEs. Sixteen identified categories of problems, experienced by ≥20 survivors, covered a range of SPLEs of medical, neurological, neurosensory, or neuropsychological origin. Most prevalent sequelae involved one or several of *vision*, *balance*, *endocrinopathy*, *fatigue*, *hearing*, *pain*, *memory*, and *seizures/epilepsy*. SPLEs were experienced as harmless by 7.4%; somewhat, clearly, very difficult by 33.4%, 28.5%, and 24.8% respectively; and completely disabling by 5.9%. Occurrence and severity varied with diagnosis age, gender, sub-diagnosis, and whether past cancer treatment included radiation therapy or not. Of 132 survivors with considerable to entirely disabling SPLEs. and who experienced need of surveillance/follow-up, 21% lacked access to such. As expected, health status 6 years earlier predicted SPLEs later in life.
Conclusions: A majority of CNS tumour VLTSs experience late effects that intrude upon functioning and quality of survival. Open-ended enquiry reveals subjectively experienced prominent difficulties, and informs about their perceived manageability. Today, as many as 1of 5 studied CNS tumour VLTSs may lack required specialised surveillance in life-long follow-up.

NEW DRUGS

O-121

AALL07P1: BORTEZOMIB WITH REINDUCTION CHEMOTHERAPY FOR FIRST RELAPSE PEDIATRIC ALL. A CHILDREN'S ONCOLOGY GROUP STUDY

T. Horton[1], X. Lu[2], M. O'Brien[3], M. Borowitz[4], M. Devidas[5], E. Raetz[6], P. Brown[7], H.U.I. Zeng[8], S. Hunger[9], J. Whitlock[10]

[1]Texas Childrens Cancer and hematology center, Baylor College Of Medicine, Houston, USA; [2]COG Operations Center, Childrens Oncology Group, Arcadia, USA; [3]Pediatric Oncology, Cincinnati Childrens Hospital, Cincinnati, USA; [4]Pathology, Johns Hopkins University, Baltimore, USA; [5]COG Data Center, Children's Oncology Group, Gainesville, USA; [6]Pediatric Oncology, Primary Children's Hospital, Salt Lake City, USA; [7]Pediatric Oncology, Johns Hopkins University, Baltimore, USA; [8]COG data center, Children's Oncology Group, Gainesville, USA; [9]Pediatric Oncology, Childrens Hospital of Colorado, Aurora, USA; [10]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada

Objectives: Bortezomib (bortez) is a reversible inhibitor of the 26S proteasome. Promising results were reported adding bortez to reinduction chemotherapy in patients (pts) with ALL in 2nd or later relapse (Messinger, Blood 2012). The primary objective of this study was to compare CR2 rates at the end of block 1 to historical control CR2 rates. Biology objectives included assessment of NF-(B and proteasome activity.
Methods: This phase 2 study of bortez with reinduction chemotherapy in 1st relapse pediatric ALL enrolled pts with either pre-B ALL, T-cell ALL or T cell lymphoblastic lymphoma (T-

LL). This report summarizes results from 99 evaluable pre-B ALL pts ≤21 yrs old, either <18m (stratum 1) or 18-36m (stratum 2) from diagnosis, and 22 evaluable T-cell ALL patients. Initial therapy consisted of bortez (1.3 mg/m^2, days 1, 4, 8, and 11) with reinduction chemotherapy (vincristine, prednisone, PEG-asparaginase, doxorubicin). CR2 rates were determined at the end of the first 5-week therapy block. We compared CR2 to the historical control study AALL01P2.
Results: 121 evaluable ALL pts were assessed. Toxicities included18 Grade 3- 4 hypotension, 8 Grade 3-4 typhlitis, 5 Grade 3-4 pancreatitis, 5 Grade 3 sensory/motor peripheral neuropathy, and 4 Grade 3-4 enterocolitis. There were 3 deaths due to infection. Although Grade 3-4 infections were not infrequent (54 infections in 44 patients in block 1 and 13 infections in block 2) there were no reports of respiratory distress syndrome or Grade 4 peripheral neuropathy. 63 of the 99 pre-B patients (27/45 (60%) in Stratum 1 and 36/54 (67%) in stratum 2) attained CR2 at the end of block I. 15/22 (68%) patients with T-cell ALL also achieved CR2. The study met its primary response objective.
Conclusions: The addition of bortezomib to ALL reinduction therapy appears quite effective and is worthy of further study in pediatric ALL. Clinical trial information: NCT00873093.

O-122

THERAPEUTIC EFFECTS OF ROMIDEPSIN, A HISTONE DEACETYLASE INHIBITOR (HDACI), ALONE AND IN COMBINATION WITH NATURAL KILLER CELLS AGAINST PEDIATRIC BURKITT LYMPHOMA

Y. Chu[1], A. Yahr[1], J. Ayello[1], C. vandeven[1], M. Cairo[1]

[1]Pediatrics, New York Medical College, Valhalla, USA

Objectives: The outcome for children with Burkitt Lymphoma (BL) has improved significantly but for patients who relapse or progress, the prognosis is dismal due to chemo-radiotherapy resistance (Cairo, *J Clin Oncol*, 2012). Our group has successfully engineered expanded peripheral blood Natural Killer cells (exPBNK) cells with an anti-CD20 chimeric antigen receptor (CAR$^+$ exPBNK) to target relapsed/resistant CD20$^+$ BL (Chu & Cairo, *ASH*, 2013). Romidepsin, a histone deacetylase inhibitor, enhances NKG2D ligand expression on tumor cells (Chu & Cairo, *EMBT*, 2013). We investigated the anti-tumor effect and mechanisms of Romidepsin against BL; and the combination effect of Romidepsin with CAR$^+$ exPBNK cells against CD20$^+$ BL cells in NSG mice.
Methods: CD20$^+$ BL cells were treated with 10ng/ml Romidepsin, provided by Celgene. Cell viability, MICA/B expression, cell cycle, and signal pathway changes were analyzed by flow cytometry. Raji-Luc or Raji-2R-Luc cells were injected into NSG mice. CAR$^+$ exPBNK, Romidepsin or combination was given to each mouse once a week for 3 weeks. The cumulative luciferase signals and tumor size were measured with the IVIS-200 system and caliber.
Results: Romidepsin induced strong cell death in rituximab rsensitive Raji (p
We further found MICA/B expression was significantly enhanced in Romidepsin treated BL cell lines (p$^+$ exPBNK cells combined with Romidpesin significantly increased the survival of Raji-Luc xenografted NSG mice compared to the controls ($p < 0.01$).
Conclusions: Romidepsin has dual-therapeutic effectsin BL by inducing cell death, cell cycle arrest, and enhancing CAR$^+$ exPBNK cytotoxicity against CD20$^+$ BL.

O-123

CLOFARABINE IN COMBINATION WITH HIGH-DOSE CYTARABINE AND LIPOSOMAL DAUNORUBICIN IN PEDIATRIC AML: RESULTS OF A PHASE 1 COMBINATION STUDY BY THE ITCC CONSORTIUM

C.M. Zwaan[1], M. Dworzak[2], T. Klingebiel[3], C. Rössig[4], G. Leverger[5], J. Stary[6], E.S. de Bont[7], C.M. Niemeyer[8], G.J. Kaspers[9], Y. Bertrand[10], S. Ramnarain[1], E.A. Ghazaly[11], D. Reinhardt[12]

[1]Pediatric Hematology/Oncology, Erasmus MC -Sophia Children's Hospital, Rotterdam, Netherlands; [2]Pediatrics, St. Anna Children's Hospital Medical University of Vienna, Vienna, Austria; [3]Children and Adolescents, University Hospital Frankfurt Goethe University, Frankfurt, Germany; [4]Pediatric Hematology and Oncology, University Children's Hospital Muenster, Muenster, Germany; [5]Pediatric Haematology and Oncology Unit, Hospital Armand Trousseau, Paris, France; [6]Pediatric Haematology and Oncology, Charles University Prague University Hospital Motol, Prague, Czech Republic; [7]Pediatric Oncology/ Hematology, University Medical Center Groningen, Groningen, Netherlands; [8]Pediatric Hematology and Oncology, University Medical Center Freiburg, Freiburg, Germany; [9]Pediatric Hematology and Oncology, VU University Medical Center, Amsterdam, Netherlands; [10]Hematology and Oncology, Les Hospices Civils de Lyon, Lyon, France; [11]Center for Haemato-Oncology, Barts Cancer Institute Queen Mary University of London, London, United Kingdom; [12]Pediatric Hematology/Oncology, Medical School Hannover, Hannover, Germany

Objectives: Relapsed/refractory pediatric AML has a poor prognosis despite salvage therapy including stem-cell transplantation. Chemotherapy using FLAG plus liposomal daunorubicine (FLAG-DNX) is currently considered the standard in 1strelapse in Europe. FLAG is based on potentiation of cytarabine (Ara-C) by fludarabine (Flu) by increasing Ara-CTP levels. Clofarabine (CLO) is a novel purine nucleoside analog, designed to have improved efficacy.
Methods: We initiated an ongoing phase 1B dose-escalation study using a '3 × 3 design' to define the optimal dose of CLO, replacing FLU in FLAG-DNX. Dosages consisted of Ara-C 2gr/m^2/day (day 1-5), with escalation of DNX from 40, 60 to 80 mg/m^2/day (day 1, 3 and 5), and CLO from 20, 30 to 40 mg/m^2/day (day 1-5) in 5 dose-levels, without GCSF priming. At day 6 intrathecal Ara-C was administered. Serum and CSF were collected for pharmacokinetics (PK). CLO plasma and CSF concentrations were analyzed using LC-MS/MS.
Results: We report safety and PK data on all dose levels after accrual of 33 AML patients. Patients were treated at 5 dose-levels (DL). Updated results and DLTs will be presented at the meeting. PK samples were available from 19 patients. At day 1 the median AUC was 28 ng/ml. mg.hr (range 6-401), with a mean T1/2 of 1.5 hrs. Day 1 and day 5 results were similar. CSF levels were not measurable in most patients and were 0.1-0.2 ng/ml.mg in the 3 patients with detectable levels.
Conclusions: The RP2D of CLO in a CLARA/DNX course in relapsed/refractory pediatric AML is 40 mg/m^2, excluding patients with evidence of prior subclinical aspergillus. There is no evidence for PK interaction between CLO and the other drugs. We are currently testing the safety of an augmented dose of DNX (80 mg/m2) in 1strelapse AML patients (n = 4). Reponses are centrally reviewed and will be disclosed at the meeting.

O-124

BLINATUMOMAB IN PEDIATRIC PATIENTS WITH RELAPSED/REFRACTORY (R/R) B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (BCP-ALL): A PHASE 1/2 STUDY

J. Whitlock[1], A. von Stackelberg [2], R. Handgretinger[3], F. Locatelli[4], C. Rizzari[5], T. Trippett[6], A. Borkhardt[7], M. O'Brien[8], S. Rheingold[9], L. Gore[10]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Pediatric Oncology/Hematology, Charité Campus Virchow, Berlin, Germany; [3]Pediatric Oncology, University of Tübingen, Tübingen, Germany; [4]Oncohematology, Ospedale Pediatrico Bambino Gesu University of Pavia, Rome, Italy; [5]Pediatrics, San Gerardo Hospital University of Milano-Bicocca, Monza, Italy; [6]Pediatric Hematology/Oncology, Memorial Sloan-Kettering Cancer Center, New York, USA; [7]Pediatric Oncology, University of Düsseldorf, Düsseldorf, Germany; [8]Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [9]Pediatrics, Children's Hospital of Philadelphia, Philadelphia, USA; [10]Pediatrics, Children's Hospital Colorado, Aurora, USA

Purpose/Objective: Blinatumomab, a bispecific T-cell engaging (BiTE®) antibody, has demonstrated activity in adults with r/r ALL. In the phase 1 part of this phase 1/2 study, the optimal blinatumomab dose was evaluated in children with r/r BCP-ALL.
Materials and Methods: Eligible patients.
Results: 41 patients received a median (range) of 2 (1 to 5) cycles. 83% of patients had refractory disease or relapses after hematopoietic stem cell transplantation (HSCT), 17% had relapses without prior HSCT. Dose-limiting adverse events (AEs) were grade 4 cytokine release syndrome (CRS) with gastrointestinal hemorrhage (15 μg/m^2/day), 2 instances of CRS (grades 4 and 5; 30 (g/m^2/day), and grade 5 respiratory failure (15→30 μg/m^2/day). The MTD was 15 μg/m^2/day. To mitigate CRS, stepwise dosing of 5 μg/m^2/day for 7 days then 15 μg/m^2/day was subsequently evaluated (18 patients). At this dose, 1 patient developed CRS (grade 3). Across all doses, the most common AEs regardless of causality included pyrexia (71%), headache (37%), and hypertension (32%). One patient permanently discontinued treatment due to a grade 3 seizure. Within the first 2 cycles, the overall remission rate was 37%; 30% achieved minimal residual disease (MRD) negativity. 5 and 9 patients achieved response by days 15 and 29, respectively. 8/15 responders received HSCT during CR (MRD-negative = 7; MRD-positive = 1); 7/15 did not (MRD-negative = 5; MRD-positive = 2).
Conclusions: In phase 1 of this study, 15 (g/m^2/day was established as the MTD. CRS was dose-limiting but could be ameliorated with stepwise dosing (5→15 (g/m^2/day). 53% of responders underwent HSCT following blinatumomab treatment.

O-125

PHASE I STUDY OF THE CDK4/6 INHIBITOR LEE011 IN PATIENTS WITH MALIGNANT RHABDOID TUMORS OR NEUROBLASTOMA

B. Geoerger[1], F. Bourdeaut[2], S.G. DuBois[3], J.I. Geller[4], A. Marabelle[5], A.D. Pearson[6], R. Kan[7], A. Matano[8], S.G. Bhansali[9], S. Parasuraman[7], S.N. Chi[10]

[1]Département de Pédiatrie, Institut Gustave Roussy, Villejuif, France; [2]Département de Pédiatrie & INSERM U830, Institut Curie, Paris, France; [3]Pediatric Hematology/Oncology, University of California-San Francisco, San Francisco, USA; [4]Division of Hematology/ Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [5]Institute for Pediatric Hemato-Oncology, Leon Berard Comprehensive Cancer Center, Lyon, France; [6]Children and Young People's Unit, Royal Marsden Hospital and the Institute of Cancer Research, London, United Kingdom; [7]Oncology Translational Medicine, Novartis Institutes for BioMedical Research, Cambridge, USA; [8]Oncology Translational Medicine, Novartis Pharma AG, Basel, Switzerland; [9]Clinical Pharmacology, Novartis Pharmaceuticals, East Hanover, USA; [10]Pediatric Neuro-Oncology Program, Dana-Farber Cancer Institute, Boston, USA

Objectives: The majority of malignant rhabdoid tumors (MRTs) have *SMARCB1* mutations and are dependent on cyclin D1 (*CCND1*) for genesis and survival. Genetic aberrations in *CCND1* and *CDK4* are frequent in neuroblastoma cell lines. LEE011, an orally bioavailable, selective inhibitor of CDK4/6, demonstrated tumor growth inhibition in MRT and neuroblastoma models. This multicenter, Phase I, dose-escalation study evaluated LEE011 in patients with MRT, neuroblastoma, or other cancers with documented cyclin D–CDK4/6–INK4a–Rb pathway aberrations.
Methods: Patients (aged 1–21 years) receive once-daily LEE011 for 21 days of 28-day cycles in a dose-escalation fashion using a Bayesian Logistic Regression Model with overdose control. Primary objective: maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) determination. Secondary objectives: safety, pharmacokinetics, efficacy. This study was approved by local institutional review boards/ethics committees and patients/guardians signed written informed consent.
Results: As of February 27, 2014, 20 patients (10 MRT [eight primary central nervous system (CNS) and two extra-CNS], nine neuroblastoma, and one *CDK4*-amplified alveolar rhabdomyosarcoma) have received LEE011: five at 280 mg/m^2; nine at 350 mg/m^2; six at 470 mg/m^2. Median age: 4.5 (range: 1–20) years. Two dose-limiting toxicities were reported: one Grade (G) 3 fatigue at 280 mg/m^2; one G4 thrombocytopenia at 470 mg/m^2. Study drug-related AEs (n = 17) (all grade [>20%], G3/4 [all]) included neutropenia (65%, 59%), leukopenia (53%, 24%), thrombocytopenia (29%, 24%), anemia (24%, 0), lymphopenia (24%, 12%), vomiting (24%, 0), fatigue (18%, 6%), and decreased appetite (12%, 6%). Preliminary pharmacokinetic data suggest exposure is similar to that in adults at 280 and 350 mg/m^2 and slightly higher at 470 mg/m^2. LEE011 demonstrates rapid absorption (1–4 hours; median $T_{max} = 2$ hours). Currently, best response is stable disease.
Conclusions: LEE011 demonstrated an acceptable safety profile and dose-dependent pharmacokinetics. Enrollment continues to identify the MTD/RDE with expansion arms for patients with MRT or neuroblastoma at the RDE.

O-126

A PHASE I STUDY OF RACOTUMOMAB IN NEUROBLASTOMA AND OTHER REFRACTORY MALIGNANCIES

W. Cacciavillano[1], C. Sampor[1], M. Guthmann[2], M. Gabri[3], E. Lagomarsino[4], M.T.G. de Davila[5], S. Eandi[1], L. Fainboim[6], D. Alonso[3], G. Chantada[1]

[1]Hematología y Oncología, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [2]Dirección Médica, Laboratorio ELEA, Buenos Aires, Argentina; [3]Laboratorio de Oncología Molecular, Universidad Nacional de Quilmes, Buenos Aires, Argentina; [4]Farmacia, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [5]Servicio de Patología, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [6]Laboratorio de Inmunogenética, Hospital de Clínicas. Universidad de Buenos Aires, Buenos Aires, Argentina

Objectives: The objective was to evaluate the toxicity and maximum tolerated dose, and secondarily immunological response, of an anti-idiotype vaccine targeting N-glycolylated gangliosides including N-glycolyl GM3 (NGcGM3): racotumomab, formerly known 1E10, as a candidate for immunotherapy.
Methods: A Phase I study enrolling children with relapsed or resistant neuroblastoma and other neuroectodermic tumors was carried out, due to the expression of NGcGM3 in those tumors. Dose was escalated into 3 levels (0.15 – 0.25 – 0.4 mg) of racotumomab administered intradermally. Each drug level included 3 patients receiving a total of 3 doses, every 14 days; with clinical, radiologic and laboratory evaluations at 30 and 60 days after the last dose was administered. A confirmation cohort was added to the higher dose level. Antibody response was assessed upon study entry and at 4-week intervals for at least 3 immunological determinations for each patient.
Results: Fourteen patients were enrolled (10 with neuroblastoma, 1 with retinoblastoma, 1 with Wilms tumor and 2 with brainstem glioma). 3 patients were included in each dose-level and 4 in the confirmation cohort. One patient died of tumor progression before completing the 3 applications. The remaining patients completed the applications scheduled. Racotumomab was well tolerated. The most common local side effects included grade 1 erythema, induration, and local mild pain at the injection site. Racotumomab elicited an antibody IgM and/or IgG response directed to NGcGM3 in 9 patients, and IgM against racotumomab in 11 of 13 evaluable patients. The maximum tolerated dose was not reached and no dose-limiting toxicity was seen. No antitumor activity was evident in any patient.
Conclusions: Racotumomab vaccination showed a favorable toxicity profile up to a dose of 0.4 mg, and most patients elicited an immune response. Its activity as immunotherapy for neuroblastoma will be tested in further clinical trials.

LEUKEMIA, MDS AND BONE MARROW TRANSPLANTATION

O-127

ETV6 MUTATIONS AND DELETIONS IN PEDIATRIC ACUTE MYELOID LEUKEMIA

E. Beuling[1], J.D.E. de Rooij[1], A. Obulkasim[1], A. Baruchel[2], J. Trka[3], D. Reinhardt[4], E. Sonneveld[5], R. Pieters[1], M. Fornerod[1], M.M. van den Heuvel-Eibrink[1], C.M. Zwaan[1]

[1]Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Hematology, Hopital Saint-Louis, Paris, France; [3]Pediatric Hematology/Oncology, Medical School Charles University, Prague, Czech Republic; [4]AML-BFM Study Group Pediatric Hematology/Oncology, Medical School Hannover, Hannover, Germany; [5]DCOG, Dutch Childhood Oncology Group, The Hague, Netherlands

Objectives: The ETS-Variant gene 6 (*ETV6*) encodes a transcription factor that acts as transcriptional repressor required for hematopoiesis of all lineages. In pediatric and adult acute lymphoblastic leukemia (ALL), and adult acute myeloid leukemia (AML) *ETV6* mutations and deletions that lead to silencing of the *ETV6* gene have been described. However, the prevalence of such alterations in pediatric AML has not been fully addressed.
Methods: *ETV6* mutations and deletions are recurrent mutations in exons 2-8 were determined with direct sequencing and for deletions by multiplex ligation-dependent probe amplification; outcome parameters were analyzed.
Results: In a cohort of 275 pediatric patients with AML with available gene-expression data (median age 9.6 years, median white blood cell count (WBC) 46.7 $\times$ 10^9/L, and 5-yr pOS 62 $\pm$ 3%), we found 6 patients (2.2%) with mutations affecting the predicted amino acid sequence of *ETV6*. Three cases showed a heterozygous insertion resulting in a frame shift and shorter predicted amino acid length, while 3 had point mutations leading to an amino acid change. In addition, *ETV6* deletions were found in 4/257 (1.6%) patients. The median age of patients with an *ETV6* gene alteration was 11.3 years (4.0-15.3) and median WBC 15.1 $\times$ 10^9/L. The 5-yr pOS was 17 $\pm$ 15%, 6/10 patients encountered a relapse and 1/10 died in complete remission, demonstrating poor clinical outcome. Other cytogenetic aberrations were *RUNX1/RUNX1T1* (n = 3), *PML/RARA* (n = 1), *MLL/AF6* (n = 1) and one *NPM1*-mutant. Previously, functional *ETV6*-silencing in T-ALL demonstrated up-regulation of genes, such as *CLDN5* and *BIRC7*, and high expression of *BIRC7* has been associated with poor prognosis in acute leukemia. In patients with an *ETV6* mutation (n = 6) or deletion (n = 4) 13 and 38 genes, respectively, were significantly up-regulated, including *CLDN5* and *BIRC7*.
Conclusions: We conclude that *ETV6* mutations and deletions are rare but recurrent in pediatric AML and may associate with poor prognosis.

O-128

PRODUCTION AFFECTING CYTOKINE GENE VARIANTS AS BIOMARKERS OF POST ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION COMPLICATIONS

G. Tripathi[1], P. Khan[2], R.M. Faridi[2], V. Lewis[3], J. Storek[4], N. Berka[5], F.M. Khan[5]

[1]Pathology and Laboratory Medicine, University of Calgary, Calgary, Canada; [2]Pathology and Laboratory Medicine, University of calgary, Calgary, Canada; [3]Pediatrics, University of calgary, Calgary, Canada; [4]Blood and Bone Marrow Transplant Program, Tom Baker Cancer Centre, Calgary, Canada; [5]Pathology and Laboratory Medicine, Calgary Laboratory Services, Calgary, Canada

Objectives: Complications of hematopoietic cell transplantation (HCT), mainly graft-vs-host disease (GVHD) and infections are substantial and are the leading causes of morbidity and mortality. Cytokines act as chief mediators/regulators of immune responses. Genetic control of cytokine production is evidenced by polymorphisms in cytokine gene regulatory regions resulting in low, moderate, or high cytokine production. Here, we investigated the impact of cytokine gene variants on allogeneic HCT outcomes.
Methods: A total of 240 adult and 55 pediatric allo-HCT donors and 50 healthy individuals were analyzed for 22 single nucleotide variants located in the regulatory and/or exonic regions of 13 cytokine or cytokine receptor genes. Genotyping was performed by sequence-specific primer based assay. PBMNCs from healthy individuals were stimulated with CMV lysate, CMV peptide and SEB to enumerate CMV specific immune response.
Results: Allo-HCT donors carrying low producing IL-10 genotypes have high incidence of both acute GVHD grades II-IV (p = 0.001, HR = 2.3), and chronic GVHD (p = 0.01, HR = 1.7). 28% vs 76% of HCT recipients developed significant GVHD when they received graft from donors carrying high vs. low IL-10 producing genotypes respectively (p = 0.01, OR = 8.167). Further, allogeneic HCT performed with donors carrying low producing IL-1R genotype showed high rates of CMV reactivation (p = 0.01, HR = 2.3), recurrent CMV infection (p = 0.001, HR = 3.9) and low counts of CMV-specific T cells.
Conclusions: Genetic predisposition to low IL-10 production and that to low production of IL-1R are strong predictors of GVHD and post HCT CMV complications respectively. These results implicate the importance of assessment of cytokine gene variants in developing new algorithm for improved allogeneic HCT donor selection.

O-129

OUTCOME OF CHILDHOOD ACUTE PROMYELOCYTIC LEUKEMIA (APML) TREATED WITH SEQUENTIAL ARSENIC TRIOXIDE (ATO) AND ALL TRANS RETINOIC ACID (ATRA) BASED THERAPY:A RETROSPECTIVE STUDY FROM A TERTIARY CARE CENTRE

S.P. Panda[1], N.D. Pradhan[1], N. Shah[1], M. Prasad[1], T. Vora[1], G. Narula[1], G. Chinnaswamy[1], P.G. Subramanyam[2], A. Chougule[3], P. Amre[4], B. Arora[1], P. Kurkure[1], S.D. Banavali[1]

[1]Paediatric Oncology, Tata Memorial Hospital, Mumbai, India; [2]Hematopathology, Tata Memorial Hospital, Mumbai, India; [3]Medical Oncology, Tata Memorial Hospital, Mumbai, India; [4]Cancer Cytogenetic Laboratory, Tata Memorial Hospital, Mumbai, India

Objectives: To study the clinical profile and outcome of children treated with a novel protocol using sequential ATO and ATRA based chemotherapeutic regimen in APML.
Methods: Children <15 years of age with APML diagnosed between March-2009 and February-2014 were retrospectively analyzed. Patients received induction with ATO (8 weeks) along with oral prednisolone, etoposide and thioguanine (PET); consolidation with ATRA and anthracycline; followed by 4 monthly cycles of maintenance with ATO+PET/four 3monthly cycles of ATRA (Total treatment duration 18months).
Results: Forty four patients were registered during this period (Median age-9years, range 2-14years, M:F-3:1). Presenting symptoms were fever (75%), mucosal bleeding (32%), cutaneous bleeding (32%) and CNS bleed (18%). 42% patients had WBC counts >10,000/mm^3 and 33% had >25,000/mm^3. As per Sanz risk stratification, 16% had low, 34% intermediate and 50% high risk disease.7patients were not evaluable (3 died before starting induction, 4 still on induction). Out of 37 evaluable patients who received induction, 4 expired (2 CNS bleed,1 pulmonary bleed, 1 infection). Rest all (89.2%) achieved CR. During induction, 5 developed differentiation syndrome, 1 pulmonary bleed, 2 fungal pneumonia, 2 asymptomatic QT prolongation. Except for initial phase of induction, no patient required admission or blood/platelet support. Post consolidation, all except one achieved complete cytogenetic and molecular remission. At median follow up of 22.2 months (range:3-59months), 1 high risk patient relapsed,1 patient in CR died at home of uncertain cause. The EFS is 86.5% (HR:94.4%, IR:69.2%, LR:100%) with DFS of 94.6% (HR:94.4%, IR:92.3%, LR:100%).
Conclusions: Sequential use of both ATO and ATRA showed a favorable outcome with minimal toxicity in pediatric APML with minimal supportive care need. This novel protocol is able to achieve a very high rate of EFS in high risk patients. Bleeding rather than relapse continues to be important cause of treatment failure in APML.

O-130

GSTA1 HAPLOTYPES INFLUENCE CLEARANCE OF INTRAVENOUS BUSULFAN AND OCCURRENCE OF SINUSOIDAL OBSTRUCTIVE SYNDROME IN CHILDREN UNDERGOING HSCT ON BEHALF OF THE PDWP OF THE EBMTGROUP

M. Ansari[1], M.A. Rezgui[2], C.R.S. Uppugunduri[1], Y. Théoret[3], Y. Chalandon[2], L.L. Dupuis[4], T. Schechter-Finkelstein[5], I.H. Bartelink[6], J.J. Boelens[7], J.H. Dalle[8], S. Azarnoush[8], P. Sedlacek[9], V. Lewis[10], S. Mezziani[2], M.F. Vachon[2], M. Duval[2], M. Champagne[11], C. Peters[12], H. Bittencourt[2], M. Krajinovic[2]

[1]Department of Pediatrics Onco-Hematology Unit CANSEARCH Research Laboratory, University Hospitals of Geneva, Geneva, Switzerland; [2]Department of Pediatrics CHU Sainte-Justine, Charles-Bruneau Cancer Center, Montreal, Canada; [3]Clinical Pharmacology Unit Department of Pediatrics, Charles-Bruneau Cancer Center, Montreal, Canada; [4]Department of Pharmacy Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [5]Department of Paediatrics Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [6]Clinical Pharmacy Department of Bioengineering and Therapeutic Sciences, University Medical Center Utrecht, Utrecht, Netherlands; [7]Pediatric Blood and Marrow Transplantation Program, University Medical Center Utrecht, Utrecht, Netherlands; [8]Pediatric Hematology Department, Robert Debré Hospital Assistance Publique-Hôpitaux de Paris INSERM 1149 Paris Diderot University, Paris, France; [9]Department of Pediatric Hematology and Oncology, Teaching Hospital Motol and 2nd Medical School Charles University, Prague, Czech Republic; [10]Departments of Oncology Paediatrics, Alberta Children's Hospital, Calgary, Canada; [11]Department of Hematology, Hospital Verdun, Montreal, Canada; [12]Department of Pediatrics Stem Cell Transplantation Unit, St. Anna Children Hospital, Vienna, Austria

Objectives: Intravenous Busulfan (BU) based conditioning regimens are widely used in children undergoing hematopoietic stem cell transplantation (HSCT). Assessment and prediction of inter-individual differences in BU pharmacokinetics (PKs) are important since BU has narrow therapeutic window. BU is mainly metabolized by glutathione S-transferase alpha1 (GSTA1). We recently reported the relationship between *GSTA1* haplotypes with first-dose BU PKs, and the relationship with HSCT outcomes in 69 children receiving myeloablative conditioning regimen in UHCSJ. To validate these observations further we have extended our analysis to include 135 children diagnosed with malignant and non-malignant conditions recruited at 5 different centres.
Methods: All patients received IV BU in 16 doses, with first dose decided based on age. BU plasma levels were measured by HPLC or LC-MS/MS methods and majority of the patients were dose-adjusted to have a steady state concentration of 600-900 ng/ml. Genotyping of *GSTA1* promoter variants at -69, -513, -631 and -1142 loci and inferred haplotypes were analyzed, for their association with BU PKs and occurrence of sinusoidal obstructive syndrome (SOS).
Results: In accordance with its suggested functional role *GSTA1*A2* haplotype was associated with lower BU levels and higher BU clearance ($P \leq 0.02$), with apparent influence in female patients. Higher incidence of SOS was observed in *GSTA1*B* haplotypes carriers ($P = 0.02$), and this association was also potentiated in female patients ($P = 0.003$).
Conclusions: These results confirm our prior observations and support the possibility to tailor the first BU dose according to *GSTA1* haplotype status. We also demonstrate the possibility of segregation of patients at higher risk for SOS development based on *GSTA1* haplotype status.

O-131

APPLICATION OF BONE MARROW (BM) AND PERIPHERAL BLOOD (PB) FOR MINIMAL RESIDUAL DISEASE (MRD) MONITORING IN INFANTS WITH MLL-REARRANGED ALL ENROLLED INTO MLL-BABY PROTOCOL

G. Tsaur[1], A. Popov[1], T. Riger[1], T. Nasedkina[2], A. Solodovnikov[3], A. Kustanovich[4], O. Aleinikova[5], O. Streneva[1], E. Shorikov[1], L. Saveliev[6], L. Fechina[1]

[1]Pediatric Oncology and Hematology Center, Regional Children's Hospital/Research Institute of Medical Cell Technologies, Yekaterinburg, Russia; [2]Biochip Laboratory, Engelgardt Institute of Molecular Biology Russian Academy of Science, Moscow, Russia; [3]Pediatric Oncology and Hematology Center, Research Institute of Medical Cell Technologies, Yekaterinburg, Russia; [4]Genetic Biotechnology Laboratory, Belarusian Research Center for Pediatric Oncology Hematology and Immunology, Minsk, Belarus; [5]Director, Belarusian Research Center for Pediatric Oncology Hematology and Immunology, Minsk, Belarus; [6]Chair of Laboratory Medicine, Ural State Medical University, Yekaterinburg, Russia

Objectives: To estimate prognostic significance of MRD in BM and PB by qualitative detection of different *MLL* fusion gene transcripts (FGt) in infants with ALLtreated by MLL-Baby protocol.
Methods: Fifty three infants (20 males and 33 females) and with defined *MLL* rearrangements were included in the current study. Median age was 5.3 months (range 0.03-11.80). MRD detection was performed from BM and PB samples by real-time PCR and nested RT-PCR with sensitivity non-less than 1E-04. MRD-negativity was defined as absence of FGt in the both assays. Median of follow-up period in the observed group was 5.2 years. TPs for MRD assessment were as follows: day 15 of remission induction (time point (TP) 1), at the end of remission induction (TP2), after each course of ATRA administration (TP3-TP9).
Results: We estimated 142 paired BM/PB samples. Among them 79 samples were double positive, 41 were double negative. Thus concordance between MRD results in BM and PB samples achieved 84.5%. All discrepant results (22 samples, 15.5%) were BM-positive/PB-negative. MRD-positivity at TP4 in BM led to unfavorable outcome. EFS was significantly lower in MRD-positive group in comparison to MRD-negative one ($9.9 \pm 6.1\%$ vs $75.9 \pm 8.0\%$, $p = 0.001$). MRD-positivity at this TP in BM was the only significant factor in the diagnostic model where initial risk factors (age at diagnosis, initial WBC count, immunophenotype, CNS disease, presence of *MLL-AF4*) were combined to response criteria (number of blast cells at day 8) (Table). We could not find any TP when MRD data obtained from PB samples had prognostic values.

Parameters	Patients	Events	Univariate analysis Hazard ratio (95% CI)	p	Multivariate analysis Hazard ratio (95% CI)	p
Age (mo)						
≥6 mo	22	8	Reference	0.059	Reference	0.513
<6 mo.	31	19	2.179 (0.949-5.005)		1.393 (0.515-3.765)	
Immunophenotype						
BI-ALL	36	16	0.746 (0.346-1.610)	0.623	1.611 (0.405-6.416)	0.499
BII-ALL	8	7	2.136 (0.899-5.077)	0,079	1.225 (0.274-5.469)	0.790
BIII-ALL	9	4	0.703 (0.242-2.041)	0.514	1 (-)	-
MLL-AF4						
Absence	28	16	Reference	0.685	Reference	0.529
Presence	25	11	0.853 (0.396-1.840)		0.752 (0.311-1.821)	
Initial WBC count						
$< 100*10^9$/L	29	11	Reference	***0.019***	Reference	0.995
$\geq 100*10^9$/L	24	16	2.443 (1.129-5.285)		0.996 (0.338-2.934)	
Initial CNS disease						
Absence	33	12	Reference	***0.004***	Reference	0.071
Presence	19	15	2.995 (1.382-6.493)		2.187 (0.936-5.114)	
Absolute blast cell on day 8 of dexamethasone administration						
<1000	46	21	Reference	0.096	Reference	0.993
≥1000	7	6	2.131 (0.856-5.304)		0.996 (0.364-2.722)	
MRD-positivity at TP4 in BM						
Absence	31	7	Reference	***0.001***	Reference	***0.001***
Presence	22	20	7.181 (3.002-17.177)		7.326 (2.378-22.565)	

Conclusions: Despite high qualitative concordance rate between BM and PB samples we could not show prognostic significance of MRD monitoring by FGt detection in PB. Univariate and multivariate analysis revealed that MRD-positivity at TP4 in BM was significant and independent prognostic factor of unfavorable outcome.

O-132

GENETIC AND METABOLIC DETERMINANTS OF METHOTREXATE INDUCED MUCOSITIS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

M. den Hoed[1], E. Lopez-Lopez[2], M.L. te Winkel[1], W. Tissing[3], J.D.E. de Rooij[1], A. Gutierrez-Camino[2], A. Garcia-Orad[2], E. den Boer[4], R. Pieters[5], S.M.F. Pluijm[1], R. de Jonge[4], M.M. van den Heuvel-Eibrink[1]

[1]*Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands;* [2]*Department of Genetics, Physical Anthropology and Animal Physiology University of the Basque Country, Leioa, Spain;* [3]*Pediatric Oncology, Beatrix Children's Hospital University Medical Centre Groningen, Groningen, Netherlands;* [4]*Department of Clinical Chemistry, Erasmus University Medical Center, Rotterdam, Netherlands;* [5]*Pediatric Oncology, Princess Maxima Center Utrecht, Utrecht, Netherlands*

Objectives: Methotrexate (MTX) is an important and effective chemotherapeutic drug in the treatment of pediatric acute lymphoblastic leukemia (ALL). However MTX can induce toxicity, which can lead to amendments of treatment and subsequent impaired survival. The aim of this study was to identify metabolic and genetic determinants of MTX toxicity.
Methods: In this prospective study, 134 Dutch pediatric ALL patients were treated with four high dosages MTX (HD-MTX: 5 g/m^2) every other week according to the DCOG-ALL10 protocol. Toxicity of previous courses was prospectively scored before each HD-MTX course and a National Cancer Institute (NCI) grade $\geq$3 was considered clinically relevant toxicity. Plasma MTX levels were measured at 24 and 48 hours after each HD-MTX infusion. Erythrocyte folate, plasma folate and plasma homocysteine levels were determined at the start of protocol M. Seventeen single nucleotide polymorphisms (SNPs) in 7 candidate genes in the MTX pathway were analyzed.
Results: Mucositis occurred in 20% of the patients, skin toxicity in 7%, diarrhea in 3%, and neurotoxicity in 3%. Hospital admissions were necessary in 8% of the patients in between MTX courses. Mucositis was not associated with plasma MTX, plasma folate or plasma homocysteine levels. Patients with mucositis had higher baseline levels of erythrocyte folate (median 1.2 (mol/L vs. 1.4 (mol/L, $p < 0.008$). Wildtype rs7317112 in the *ABCC4* gene was the only SNP associated with a higher frequency of mucositis (AA (39%) vs. AG/GG (15%), $p = 0.016$).
Conclusions: Only a higher baseline erythrocyte folate and the wild-type variant of rs7317112 SNP in *ABCC4* were determinants of mucositis in pediatric ALL during MTX-HD treatment. In contrast, plasma MTX and plasma folate were unrelated to toxicity.

PULMONARY MANIFESTATIONS OF PAEDIATRIC SOLID TUMOURS

O-133

PROGNOSIS IMPACT OF REMAINING LUNG NODULES AFTER METASTASECTOMY IN OSTEOSARCOMA PATIENTS: ARE THEY RESPONSIBLE FOR RECURRENCE?

C. Cellier[1], M. Le Deley[2], L. Brugiéres[3], H. Pacquement[4], M. Tabone[5], M. Jimenez[6], M. Larroquet[7], E. Fadel[8], S. Sarnacki[9], S. Irtan[9]

[1]*Radiology, Curie Institute, Paris, France;* [2]*Biostatistic, Gustave Roussy Institute, Villejuif, France;* [3]*Paediatric Oncology, Gustave Roussy Institute, Villejuif, France;* [4]*Paediatric Oncology, Curie Institute, Paris, France;* [5]*Paediatric Oncology, Trousseau Hospital, Paris, France;* [6]*Paediatric Oncology, Unicancer, Paris, France;* [7]*Paediatric Surgery, Trousseau Hospital, Paris, France;* [8]*Thoracic Surgery, Marie Lannelongue Hospital, Le Plessis-Robinson, France;* [9]*Paediatric Surgery, Hopital Necker Enfants Malades, Paris, France*

Objectives
Aim of the study: Survival of patients having a pulmonary metastatic osteosarcoma is improved by the complete removal of all metastases. Due to the dramatic increase of CT-scan quality over the years allowing the detection of millimetric nodules unable to be found at surgery, we aimed to determine if the remaining nodules has an impact on recurrence.
Methods: We retrospectively compared all lung CT scans performed from diagnosis to first relapse to the surgical and pathological reports in 24 patients treated for an osteosarcoma with a high-dose methotrexate based chemotherapy (OS2006 protocol) and operated on for lung nodules from 2007 to 2012.
Main results: Three patients were excluded, 2 because of countless nodules and one because of tuberous sclerosis at pathology. Among the 21 patients finally included, 12 were classified as metastatic at diagnosis and 9 had doubtful nodules. With a median follow-up of 35 months from diagnosis [range, 10-61], 5 patients relapsed and 3 experienced a progression. Among 210 nodules (median 6 per patient [1-52]) described at diagnosis, 165 remained after neoadjuvant chemotherapy and 37 new nodules were detected. Among these 202 nodules, 130 (64%) were found at surgery and 111 proved to be lung metastases either viable ($n = 54$) or necrotic ($n = 57$) at pathological analysis. 48 additional nodules were removed (18 viable and 22 necrotic metastases). Among the 72 nodules not found at surgery, 37 were still present at the end of treatment (EOT) of which only 2 (5%) were involved in a relapse (9 nodules described) and 2 (5%) in a progression (13 nodules described).
Conclusion: The lung nodules not found at surgery and still remaining on the CT scan at EOT did not seem to be responsible for recurrence in pulmonary metastatic osteosarcoma patients.

O-134

CLAMSHELL THORACOTOMY: A PLAUSIBLE ALTERNATIVE FOR BILATERAL PULMONARY METASTASECTOMY IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA

J. Palacios[1], J. Shalkow[1], D. Hernandez[1], A. Leon[1], J. Echavez[1], J. Vazquez[2]

[1]*Surgical Oncology, National Institute of Pediatrics, Mexico City, Mexico;* [2]*Pediatric Surgical Oncology, ABC Medical Center, Mexico City, Mexico*

Objectives: Osteosarcoma is the most common malignant bone tumor in children and adolescents. Up to 70% of patients will eventually develop metastatic disease. Lung is the most frequent site. Techniques described for bilateral metastasectomy include staged posterolateral thoracotomy and median sternotomy.
We present our experience for bilateral pulmonary metastasectomy in pediatric patients with osteosarcoma, using the "clamshell" thoracotomy. We describe indications, advantages and disadvantages.
Methods: During a 25-years review, out of 297 cases of osteosarcoma, 69 cases of bilateral lung metastasectomy were identified. 43 underwent staged posterolateral thoracotomy, 10 had a median sternotomy, and 16 cases underwent "clamshell" thoracotomy.
Results: There were seven males and nine females, with a median age of 11 years. Most common primary site was distal femur; most common tumor type was osteoblastic. 69% of patients had limb-salvage. Most frequent time of presentation of pulmonary metastases was during follow up (50%). We preserved the sternum (synchronous bilateral anterior thoracotomy) in five out of the 16 cases. Five patients required reoperation for local recurrence. Surgical time ranged from 2 to 6 hours. Average blood loss was 250 ml. Chest tubes were removed on postoperative day two. Hospital length of stay was 5 days. Thoracotomy identified more lesions than CT in 70% of cases. There was no perioperative mortality, and surgical complications were minimal (three cases of postoperative pneumothorax requiring 24 extra hours of pleural drainage). All lesions were removed with histological confirmation. Chemotherapy was initiated 7 to 10 days postoperatively.
Conclusions: Clamshell thoracotomy is a safe and feasible alternative for bilateral metastasectomy in pediatric patients with osteosarcoma. Procedure is well tolerated, with minimal postoperative pain, allowing adequate simultaneous exploration of both lungs, including posterior-basal segments, decreasing the time of recovery needed for chemotherapy. Re-do thoracotomies via this approach are easily performed. Anterior chest-wall lesions are technically difficult.

O-135

SURGERY PLAYS A KEY ROLE IN THE TREATMENT OF PULMONARY RELAPSES FROM WILMS TUMORS: DATA FROM SIOP 93-01/GPOH AND SIOP 2001/GPOH

J. Fuchs[1], N. Nourkami[2], J.P. Schenk[3], N. Graf[2], S. Warmann[1]

[1]*Pediatric Surgery and Pediatric Urology, University Children's Hospital, Tübingen, Germany;* [2]*Pediatric Oncology and Hematology, University Hospital Saarland, Homburg, Germany;* [3]*Radiology, University Hospital, Heidelberg, Germany*

Objectives: To evaluate the outcome of children suffering from pulmonary Wilms tumor relapses registered within the multicenter trials SIOP 93-01/GPOH and SIOP 2001/GPOH of the Society of Pediatric Oncology and Hematology (GPOH).
Methods: Data of children with pulmonary Wilms tumor relapses were retrospectively analysed with regard to patients' characteristics, as well as oncological and surgical outcome.
Results: In both study trials there were 87 children with nephroblastoma relapses in the lung. Histology revealed intermediate risk in 62 and high risk in 25 patients. Relapses were singular (<6) in 59 and multiple (>6) in 25 patients (no data in 3). Location was unilateral in 54 and bilateral in 28 cases (no data in 5). Primary lung metastases were initially present in 28 patients, whereas in 59 patients there were no primary lung metastases. All but 4 patients had received neoadjuvant chemotherapy during first line treatment, Tumor nephrectomy was performed as first line local treatment of primary tumors in 84 patients, partial nephrectomy in 4 patients. Median time to pulmonary relapse was 5 months (0-75). Local treatment of pulmonary relapses (surgery, irradiation or both) was performed in 70 patients, in 64 of them, surgery was part of the local treatment. Overall survival was 56/87 patients (64.4%).
Conclusions: The vast majority of children with pulmonary relapses undergo surgery for local treatment. Survival is relevantly inferior compared to children without relapses. A aggressive approach seems justified in order to treat affected patients.

O-136

SURVIVAL WITH LUNG METASTASES IN PEDIATRIC SOLID TUMORS - A SYSTEMATIC REVIEW

G. Borrell-Mather[1], D. Mullassery[1], W. Jawaid[1], P. Losty[1]

[1]*Department of Paediatric Surgery, Institute of Child Health, Liverpool, United Kingdom*

Objectives: Metastatic lung lesions from pediatric solid tumors are treated using multimodal therapy and survival is reported to be improving. We performed a systematic review of the literature to robustly analyse survival outcomes for these children with disseminated disease linked with their primary tumor sub-group (s) and the role of surgical metastectomy.
Methods: Studies were identified using Medline (1950-), Embase (1980-) and Cochrane database (s) using the key relevant search terms. Literature reviews, case reports (<3 patients)

and adult studies (age >18 years) were excluded. Data were extracted independently following paper selection by at least 2 study authors. Overall survival (OS) and event-free survival (EFS) was assessed for the different primary tumors.
Results: The original search retrieved 2,080 articles. Following application of exclusion criteria and removing duplicate data - 34 studies (1,643 patients) were included for final review. Published studies covered the era (s) 1967 - 2013. The most common primary tumor disseminating to lung was osteosarcoma (n = 535) followed by Wilm's tumour (n = 435). Overall patient survival was 36% (CI 26% - 48%), 55% (CI 39%-71%), 32% (CI 22%-44%) for osteosarcoma, Wilms' tumor and Ewing sarcoma respectively. Surgical metastasectomy was performed in 1153/1643 (71%) patients linked to cancer therapy programmes to achieve 'cure'. Insufficient high quality data was available to address and answer the real therapeutic benefit (s) of surgical metastasectomy vs chemotherapy or radiotherapy in patients with pulmonary metastases.
Conclusions: Surgical lung metastectomy is well-established oncological practice. This review found no individual case series or subgroup (s) of pediatric cases which were exclusively managed without considering the potential role for operative metastectomy. The true value of surgery in management of patients with advanced pulmonary metastases cannot be fully established currently. Examination of the published world literature has allowed us though to summarise and benchmark outcomes for subgroups of patients / tumour types with pulmonary metastases.

SARCOMA

O-137

LOCAL CONTROL FOR DIFFUSE INTRABDOMINAL AND PELVIC RHABDOMYOSARCOMA: RESULTS OF A PHASE 1-2 STUDY OF CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC)

A. Hayes Jordan[1], H.L. Green[2], P. Anderson[3], W. Huh[2]
[1]Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, USA; [2]Pediatrics, University of Texas MD Anderson Cancer Center, Houston, USA; [3]Pediatric Hematology/Oncology, Levine Children's Hospital/Levine Cancer Institute, Charlotte, USA

Objectives: Diffuse and recurrent intrabdominal and pelvic rhabdomyosarcoma are rare forms of RMS. Instead of a localized mass, RMS can be multiple and present as sarcomatosis, in the abdominal/pelvic cavity. This presentation can be secondary to tumor rupture or 'de novo'. The incidence sarcomatosis in rhabdomyosarcoma is unknown, but of approximately 250 RMS cases per year in the USA, 10-15 are abdominal/pelvic, non genito-urinary cases.
Methods: We performed cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) with curative intent, as part of neoadjuvant and adjuvant chemotherapy, as a phase 1 and then a phase 2 trial. RMS patients were a subset of a larger cohort of patients with other sarcoma histologies. Patients included had RMS that was multifocal in the abdominal cavity and/or recurrent post radiation. All patients had imaging characteristics consistent with surgically resectable disease. Cisplatin was used at 100mg/M2 and 150mg/M2 continuously for 90 minutes intra-operatively after surgical resection.
Results: There were 8 patients aged 2 to 16 years, who underwent 9 cytoreductive surgery and HIPEC procedures. Three of eight, 37%, of patients had successful local control of their abdominal disease for greater than one year. Two of eight, 25%, of patients are alive without disease, at 21 and 34 months. Five of eight, 62%, had a complete resection prior to HIPEC. All patients with an incomplete resection recurred at less than 3 months from surgery. Dose limiting toxicity was grade 3 or higher elevation in creatinine. One patient required chronic dialysis. There were 2/9, 22%, major postoperative complications including high grade bowel obstruction and wound infection with skin separation.
Conclusions: At a dose of 100mg/M2 Cisplatin, HIPEC is safe in children with RMS sarcomatosis. Complete or partial response was seen in 37% of patients with RMS and sarcomatosis. Alternative intraperitoneal chemotherapy is needed for cisplatin insensitive patients.

O-138

EVALUATING THE NECESSITY FOR SURGERY AS LOCAL THERAPY IN RHABDOMYOSARCOMA OF THE BLADDER AND PROSTATE: 14 YEAR EXPERIENCE AT A TERTIARY CARE CENTRE

A. Mitra[1], S. Agarwala[1], S. Bakhshi[2], M. Jana[3], S. Pathy[4], S. Thulkar[3], M. Srinivas[1], M. Bajpai[1], D.K. Gupta[1], V. Bhatnagar[1]

[1]Pediatric Surgery, All India Institute of Medical Sciences, Delhi, India; [2]Medical Oncology, BRAIRCH All India Institute of Medical Sciences, Delhi, India; [3]Radiology, BRAIRCH All India Institute of Medical Sciences, Delhi, India; [4]Radiotherapy, BRAIRCH All India Institute of Medical Sciences, Delhi, India

Objectives: To assess whether surgical resection is essential for good outcomes in children with rhabdomyosarcoma (RMS) of the bladder and/or prostate (BP).
Methods: The records of children treated for RMS-BP from 1999 through 2013 were analysed. Outcomes in terms of 2-year overall survival (OS) and event free survival (EFS) were analysed according to the age, presence of metastases and local therapy given (resection vs no resection). Events included death, recurrence and progression. Multimodal chemotherapy (Vincristine+Actinomycin+Cyclophosphamide), external beam radiotherapy (RT) was used in all children.
Results: Of the 41 children with RMS-BP included for analysis, 20 (48.8%) were older than 24 months at presentation, of whom 9 (45%) had events including 3 deaths (15%) giving an OS of 53.6% (95CI 0.61,0.95) and EFS of 53.7% (95CI 0.43,0.95). The EFS was significantly better (p = 0.038) than those < 24 months of age. Tenof the 41 (24.4%) had metastasis. Five (50%) had events including two deaths giving an OS of 26.8% (95CI 0.44,0.95) and EFS of 26.8% (95CI 0.17,0.76). The OS (p = 0.896) and EFS (p = 0.148) were not significantly different for those without metastasis. Thirty-four of the 41 (83%) received neoadjuvant chemotherapy and all received adjuvant chemotherapy and RT. Only 9 (22%) had surgical resection (6 upfront) as a part of the local therapy. Of these 9, there were no deaths, 2 events and 5 (55.5%) achieved complete remission (CR) giving an EFS of 75% (95CI 0.52,17.1). Among the 32 (74%) who were not operated upon, 16 (50%) had events including 8 (25%) deathsand 9 (28%) achieved CR giving an OS of 78% (95CI 0.22,7.19) and an EFS of 50% (95CI 0.05,0.94).
Conclusions: Though 28% achieved CR without resection, the chances of achieving it were three times greater in those undergoing surgery (upfront or after neodajuvant chemotherapy). The OS (p = 0.102) and EFS (p = 0.301) were not different in the two groups. These results lead us to question the need for aggressive surgical excision for patients with RMS-BP.

O-139

HIGH DOSE RATE BRACHYTHERAPY IN SUCCESSFUL TREATMENT OF CHILDHOOD LOWER URINARY TRACT MALIGNANCIES

J. Stenman[1], M. Jalnäs[1], P.J. Svensson[1], N. Pal[2], C. Mercke[3]

[1]Department of Paediatric Surgery, Karolinska University Hospital, Stockholm, Sweden; [2]Department of Paediatric Oncology, Karolinska University Hospital, Stockholm, Sweden; [3]Department of Oncology Radiumhemmet, Karolinska University Hospital, Stockholm, Sweden

Objectives: Iridium-192-based low dose rate brachytherapy (BT) has been shown to reduce long term morbidity after treatment for bladder-prostate rhabdomyosarcoma (BP-RMS).[1,2] Aiming at minimized long term morbidity from radical surgery we developed and introduced high dose rate brachytherapy (HDR-BT) using Iridium-192 in multi-modal treatment of childhood lower urinary tract malignancies.
Methods: 6 children, (4 males), aged 1-10 years, diagnosed with BP-RMS (n = 5) and malignant triton tumour in the bladder (MTT, n = 1) were treated with HDR-BT at the Karolinska University Hospital 2004-2013. All patients were pre-treated according to CWS protocols. Surgery was limited to placement of BT-catheters in 4 out of 6 patients that had a tumour diameter less than 5 cm after induction chemotherapy. Blind ending brachytherapy catheters were placed at intervals of 10 mm to cover the clinical target volume with a margin of 5-10 mm in all directions. A dose-planning CT-scan was performed during the same anaesthesia and HDR-BT was given twice daily during the first five postoperative days (HDR Micro-Selectron, Nucletron, The Netherlands). The dose per fraction was 3.0-3.3 Gy to a total dose of 18-39 Gy. Most treatments were performed under mild sedation.
Results: All 5 children treated for primary tumours (4 BP-RMS, 1 MTT) are alive with no evidence of disease after 12-120 months. The child receiving HDR-BT as part of salvage treatment for recurrent BP-RMS died. All patients alive have retained their bladder function. Detailed urological follow-up including voiding patterns, upper urinary tract ultrasonography, kidney function and erectile function is ongoing.
Conclusions: We report the use of HDR-BT on a widely available instrument platform to reduce the need for radical surgery and potential long-term morbidity. The clinical results are promising and warrant further investigation.
1 Martelli H et al. J Ped Surg. 2009
2 Jenney M et al. Pediatr Blood Cancer 2014

O-140

REDUCING LONGITUDINAL BONY RESECTION MARGINS IN LIMB-SPARING SURGERY FOR EXTREMITY OSTEOSARCOMA DOES NOT IMPACT ONCOLOGIC OUTCOMES

A.H.P. Loh[1,7], H. Wu[2], A. Bahrami[3], F. Navid[4,8], M.W. Bishop[4], M.B. McCarville[5], J. Wu[2], N.C. Daw[6], M.D. Neel[1], B.N. Rao[1]

[1]Department of Surgery, St Jude Children's Research Hospital, Memphis, USA; [2]Department of Biostatistics, St Jude Children's Research Hospital, Memphis, USA; [3]Department of Pathology, St Jude Children's Research Hospital, Memphis, USA; [4]Department of Oncology, St Jude Children's Research Hospital, Memphis, USA; [5]Department of Radiological Sciences, St Jude Children's Research Hospital, Memphis, USA; [6]Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, USA; [7]Department of Paediatric Surgery, KK Women's and Children's Hospital, Singapore; [8]Department of Pediatrics, University of Tennessee Health Science Center, Memphis, USA

Objectives: Bony resection margins in limb-sparing surgery for osteosarcoma should be sufficiently wide while maximizing preservation of native bone. However the optimal distance of this margin is not well established. This study investigated the effect of decreasing bony

resection margins, and the association of other surgicopathological factors, with oncologic outcomes in these patients.
Methods: Retrospective review of children and adolescents with newly diagnosed osteosarcoma enrolled on 4 consecutive institutional trials (1986–2012), where the preoperatively-planned longitudinal bony resection margins for limb-sparing surgeries were serially decreased from 5 to 1.5 cm. The association between bony resection margins and other surgicopathological factors with local recurrence-free survival (LRFS), event-free survival (EFS), and overall survival (OS) was determined.
Results: One hundred eighty-one limb-sparing surgeries were performed on 173 patients. Planned and actual resection margins did not correlate with LRFS, EFS, and OS; that is, serial reduction of planned bony resection margins from 5 to 1.5 cm did not adversely affect survival outcomes. At median 5.8 years' follow-up, there were 18 (9.9%) local recurrences, 41 (22.6%) distant recurrences, and 6 (3.3%) concurrent local and distant recurrences. Fifty-one (29.5%) patients died from their disease. On multivariable Cox regression analysis, metastatic disease at diagnosis was independently associated with decreased LRFS, EFS, and OS ($P = 0.002$, 0.005 and <0.0001, respectively). Post-chemotherapy tumor necrosis $\leq 90\%$ was independently associated with decreased OS and EFS ($P = 0.022$ and 0.001, respectively). Earlier years of treatment and pathologic fractures were independently associated with decreased OS only ($P = 0.018$, and 0.008, respectively), and previous cancer history and male gender were associated with decreased EFS only ($P = 0.043$ and 0.023, respectively).
Conclusions: In limb-sparing surgery for osteosarcoma in children and adolescents, reducing longitudinal bony resection margins to 1.5 cm does not increase the risk of local recurrence or adverse survival outcomes. Established prognostic factors continue to be relevant in this group of patients.

O-141

LYMPH NODE SAMPLING IN PEDIATRIC EXTREMITY SOFT TISSUE SARCOMAS: RISK-ADJUSTED SURVIVAL OUTCOMES

E.A. Perez[1], J. Tashiro[1], J.E. Sola[1]

[1]Division of Pediatric Surgery Department of Surgery, Miller School of Medicine University of Miami, Miami, USA

Objectives: Extremity rhabdomyosarcoma (RMS) and some subtypes of non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) commonly involve regional lymph nodes. We sought to determine the effect of lymph node sampling (LNS) on survival for pediatric extremity soft tissue sarcomas (STS).
Methods: The SEER registry (1973-2010) was analyzed for all patients <20 years of age with extremity STS. Multivariate and propensity-score matched analyses were performed to obtain risk-adjusted assessments of survival.
Results: Overall, 1,554 patients were identified with an overall age-adjusted incidence of 0.31 per 100,000 persons and a significant annual increase of 0.95% ($p < 0.05$) over the study period. Patients were most commonly male (53%), age $\geq$10 years (72%), and white (78%). Most were diagnosed with localized disease (64%), lower extremity (63%), originating from muscle (24% NRSTS/19% RMS) or fibrous tissues (18%), and with undifferentiated/anaplastic grade IV (34%). Most RMS were alveolar type (69%). The majority of patients had surgery (89%) but only 40% had radiotherapy. LNS was performed in 46% of RMS and 11% of NRSTS patients. Overall, 20-year disease specific survival was 69%, and 46% for RMS, but higher for age 5-9 years (77%), localized disease (80%), arm (76%), and NRSTS adipose (96%), fibrous (92%), and vascular (80%) types (all $p < 0.05$). There was no survival advantage for LNS by stage, grade, histology type, or site for RMS or NRSTS. Multivariate analysis revealed poorly differentiated ($OR = 2.916$), undifferentiated/anaplastic grade ($OR = 3.236$), and nerve tissue type ($OR = 8.211$) as significant independent prognostic indicators of mortality, while localized ($OR = 0.133$) and regional disease ($OR = 0.215$) as significant independent prognostic indicators of decreased mortality (all, $p < 0.01$). Propensity score matched analyses revealed that LNS was associated with improved overall survival for RMS (73% vs 51%, $p = 0.006$) but not for synovial sarcoma.
Conclusions: Analysis of SEER with propensity score matching demonstrates a survival advantage with LNS for pediatric extremity RMS.

SURGICAL TECHNIQUES

O-142

RETROPERITONEOSCOPIC ADRENALECTOMY FOR ADRENAL TUMOR IN CHILDREN

S. Tran[1], Q. Tran[1]

[1]Surgery, National Hospital of Pediatrics, Hanoi, Vietnam

Objectives: To report the authors' results of retroperitoneoscopic adrenalectomy (RA) for adrenal tumor in children.
Methods: Medical records of all patients undergoing RA for adrenal tumor at our center from December, 2009 to December, 2013 were reviewed. Only relatively small adrenal tumors with well defined border, without encasement of the great vessels and without lymph node involvement on CT scan were selected for RA. A lateral retroperitoneal approach was used in all cases.
Results: 19 patients were identified, 8 females and 11 males, with a median age of 5 years (range: 1 to 14 years). Tumors were on the left side in 4 cases, on the right – in 15, with a median size of 4.5 cm (range: 3.0 to 9.0 cm). Three ports were used in 15 cases and just 4 cases required additional fourth port. RA was successful in 18 cases (94.7%) with minimal blood loss. The median operative time was 110 minutes (range: 70 to 220 minutes). Conversion to open surgery was needed in a case of 9 cm pheochromocytoma due to bleeding. There was no perioperative death or major complication. Most patients resumed oral feeding in the same day after the operation. Pathology study showed ganglioneuroma in 6 cases (31.6%), pheochromocytoma in 5 cases (26.3%) ganglineuroblastoma in 4 cases (21.0%) and neurobastoma with favorable histology in 4 cases (21.0%). At a median follow up of 31 months, all patients were alive and disease free.
Conclusions: RA for pediatric adrenal tumor is feasible and safe in carefully selected cases. This technique can give good results not only for benign tumors but also for some malignant tumors, including neuroblastomas with favorable histology.

O-143

THORACOSCOPIC ASSISTED RESECTION OF PEDIATRIC CHEST WALL TUMORS

G. Ahmed[1], M. Elshafiey[2]

[1]Surgery, Children's Cancer Hospital Egypt, Cairo, Egypt; [2]Surgery, NCI Cairo Children's Cancer Hospital Egypt, Cairo, Egypt

Objectives: was to evaluate the role of thoracoscopy in facilitating resection of pediatric chest wall Tumors without rib spreading, and how it could decrease number of resected ribs without compromising the margin.
Methods: This was a retrospective study which included 14 cases (rib Ewing sarcoma 12 cases, rabdomyosarcoma chest wall one case and rib chondorosarcoma one case) treated by surgical resection.
Results: The average age was 9.1 years. Neoadjuvant chemotherapy was given in all cases of Ewing sarcoma. The procedure started by thoracoscopic assessment in 10 cases. It could identify all margins in 7 cases so we made the incision directly around the lesion and resection was done without rib spreading. Thoracoscopic assessment failed to identify one or more of the margins in 3 cases (tumor arise from the 2nd rib in one case, 2 cases the tumor was attached to the diaphragm), thoracoscopy was not attempted in 4 cases due to large tumor diameter or massive adhesions. Resection included 1,2,3 and 4 ribs in (5,3,4 and 2 cases) respectively. Primary closure was feasible in 7 cases and rib transposition was done in one case. Reconstruction by prolene mesh covered by muscle flap was done in 6 cases. Margins were negative in all except one case.
Conclusions: Pediatric chest wall tumors are rare. Thoracoscopic assisted resection helps to accurately choose the site of incision, and in some cases avoids rib spreading and decreases the number of ribs resected.

O-144

LARAROSCOPIC RETROPERITONEAL LYMPH NODE DISSECTION FOR PARATESTICULAR RHABDOMYOSARCOMA IN CHILDREN

A. Mudegoudra[1], R. Nerli[1], S. Patil[1]

[1]Urology, Department of Urology, KLES Kidney Foundation, KLE University's JN Medical College, Belgaum, India

Objectives: Paratesticular rhabdomyosarcomas usually present with an enlarging painless scrotal mass. A majority of patients will have clinical stage 1 disease. The most common sites of metastases are the retroperitoneum and lungs. Patients with retroperitoneal metastases should undergo a modified unilateral nerve-sparing RPLND (Retroperitoneal lymph node dissection). The increased use of minimally invasive surgery has spread to RPLND. We report on our experience with Laparoscopic-RPLND in adolescents.
Methods: Children with Paratesticular rhabdomyosarcomas presenting to us formed the study group. Children underwent detailed evaluation and imaging. The surgical procedure of laparoscopic RPLND involved placement of three ports, one 10 mm periumbilical camera port and two 5 mm ports (one midline below the xiphoid and one midline above the pubis). The colon was medialised by incising along the white line of Toldt from the spleen up to the sigmoid colon exposing the common iliac vessels bifurcation, the testicular vessels and the ureter. First, the spermatic cord was dissected out and taken down to the point of the previous orchiectomy. The ureter was dissected out from the nearby vessels to avoid ureteral injury. The peri-aortic tissue was then split to begin the dissection of the peri-aortic lymph nodes. Dissection was carried out from the renal vessels down to the bifurcation of the aorta. The common iliac, pericaval and interaortocaval lymph nodes were dissected out.
Results: During the study period Jan 2013 to Dec 2013, three children with a mean age of 10.3 years underwent laparoscopic RPLND. The mean operative time was 363.3 mins and the mean blood loss was 40 cc. There were no major intra/postoperative complications. The mean hospital stay was 50 hrs.
Conclusions: The increased use of minimally invasive surgery has spread to RPLND. Laparoscopic RPLND for high-risk pediatric patients with PTRMS is a safe diagnostic and therapeutic procedure with the benefit of rapid convalescence, enabling early commencement of adjuvant chemotherapy.

O-145

ENDOSURGERY IN THE DIAGNOSIS OF ONCOLOGY IN CHILDREN

D. Rybakova[1], P. Kerimov[1], M. Kazantcev[1], M. Rubansky[1]

[1]children Oncology, Federal State Budgetary Institution «N.N. Blokhin Russian Cancer Research Center» under the Russian Academy of Medical Sciences, Moscow, Russia

Objectives: To summarize and analyze the experience of use in the diagnosis of endosurgery neoplastic diseases in children.
Methods: From 2007 to 2012, performed 161 diagnostic operations in 153 patients. Of them diagnostic thoracoscopy – 44, diagnostic laparoscopy - 63, thoracoscopic lung resections for the differential diagnosis of cancer with an infectious process – 53 operations and one-stage laparoscopy and thoracoscopy - 1 operation. The age of patients ranged from 2 months to 19 years (median 12.6 years)
Average time during laparoscopic operations was - 62min., thoracoscopic - 54 min. The mean blood loss during laparoscopy 61ml at thoracoscopy - 104ml. Intraoperative complications appeared in 5 cases out of 161 operations. In 3 cases there was bleeding from the tumor, the superior vena cava injury and wound duodenum 1 case. In 4 of 5 cases required conversions. In one case, bleeding from the tumor site was eliminated without resorting to conversion. In 8 cases identified postoperative complications.
Surgical complications in 4 registrars patients: 2 cases eventration omentum through an incision in periomphalic region, two cases pneumothorax; nonsurgical complications also occurred in 4 patients: two children, pneumonia, and one case of acute bronchitis and chickenpox.
Results: During two surgeries material for histological examination was not obtained, which required in one case re endosurgery operation and suddenly open surgery. In other cases, the material obtained for morphological examination. Use of narcotic analgesics (fentanyl, promedol) was needed during surgery and during the postoperative period first day. All patients received prophylactic antibiotic therapy. Average number of hospital days was - 4 ± 2 days.
Conclusions: Thoracoscopy and laparoscopy allows you to perform a biopsy of tumors of the chest and abdominal cavity, retroperitoneal and pelvic cavity, and given the minimal invasiveness, short postoperative period and rapid recovery after such an operation may start special treatment as soon as possible after surgery.

O-146

SAFETY AND DIAGNOSTIC ACCURACY OF TISSUE BIOPSIES IN CHILDREN WITH CANCER

R. Interiano[1,2], A.H. Loh[1,3], N. Hinkle[1,2], F.N. Wahid[1], A. Malkan[1], S. Mao[4], J. Wu[4], A.S. Pappo[5], R. Gold[6], A.M. Davidoff[1,2]

[1]Department of Surgery, St Jude Children's Research Hospital, Memphis, USA; [2]Department of Surgery, University of Tennessee Health Science Center, Memphis, USA; [3]Department of Paediatric Surgery, KK Women's and Children's Hospital, Singapore; [4]Department of Biostatistics, St Jude Children's Research Hospital, Memphis, USA; [5]Department of Oncology, St. Jude Children's Research Hospital, Memphis, USA; [6]Department of Radiological Sciences, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Tissue biopsies are frequently used in pediatric cancer and may be increasingly employed for research purposes, yet information on their associated risks and diagnostic yield is lacking. This study sought to evaluate the safety and diagnostic accuracy of tissue biopsies in children with cancer.
Methods: With IRB approval, all surgical or percutaneous biopsies performed in children with a suspected or established diagnosis of cancer from January 2003 to December 2012 were retrospectively reviewed. Patient, disease, and procedural factors were correlated with diagnostic accuracy and incidence of complications using logistic regression analysis.
Results: One thousand seventy-three biopsies were performed in 808 patients. Median age at procedure was 12.7 (range: 0–33.7) years, and median body mass index (BMI) was 19.0 (range: 10.1–61.1). Of 1023 biopsies that had at least 30-days' postoperative follow-up, 69 (6.7%) had complications. Using Common Terminology Criteria for Adverse Events, 35 were minor (Grade 1–2) and 34 were major (Grade 3-4) adverse events. No deaths occurred that were procedural-related. The most common major adverse events were blood transfusions of >10cc/kg (24 cases) and infections requiring intravenous antibiotics or debridement (6 cases). Nine hundred sixty-two (90%) biopsies provided definitive histologic diagnoses, and 111 (10%) yielded unconfirmatory or non-diagnostic results; 150 were biopsies of a previously-biopsied site. Using multivariable analysis, thoracic sites ($P < 0.0001$), decreased age at procedure ($P = 0.052$), increased BMI ($P = 0.005$), and decreased hematocrit ($P = 0.0005$) were associated with an increased risk of complications. Musculoskeletal sites ($P = 0.0077$), incisional biopsies ($P = 0.0025$), increased white blood cell count ($P = 0.0181$), a non-malignant histology result ($P < 0.0001$), a malignant primary diagnosis ($P = 0.0232$), and method of performing biopsy ($P < 0.0001$) were associated with a non-diagnostic histologic result.
Conclusions: Tumor biopsies in children with cancer are associated with a low incidence of complications and a high rate of diagnostic accuracy. Predictive factors identified for these adverse outcomes may aid preoperative counseling and risk assessment.

O-147

BILATERAL ANTERIOR STERNOTHORACOTOMY (CLAMSHELL INCISION) IS A SUITABLE ALTERNATIVE FOR BILATERAL LUNG SARCOMA METASTASIS RESECTION IN CHILDREN

J.-M. Joseph[1], R. Guatta[1], M. Diezi[2], K. Pinnagoda[1], O. Abbo[1]

[1]Pediatric Surgery, CHUV - University of Lausanne, Lausanne, Switzerland; [2]Pediatric Oncology, CHUV - University of Lausanne, Lausanne, Switzerland

Objectives: The aim of our study was to assess the postoperative course of bilateral anterior sternothoracotomy (BAT) in children with sarcoma lung metastases, in a curative care perspective.
Methods: We reviewed the records of 7 patients under 18 years old, who underwent surgical procedures for sarcoma metastasis to the lung between 2000 and 2012. We compared the postoperative course of the BAT group to that of patients who underwent unilateral posterolateral thoracotomies (PLT) for the same etiology.
Results: Of 17 surgical procedures, there were 7 BAT and 10 unilateral PLT. Mean ages at the time of the procedures were 12.9 +/- 5.4 years old for BAT, and 17.4+/-1.9 years old for PLT. Mean operative time was 173 +/- 37minutes in the BAT group, and 145 +/- 39 minutes in the PLT group ($p = 0.19$). Patients received epidural analgesia in all cases for a mean time of 3.8 +/- 1.3 days in the BAT group, and 3.21 +/-4 days in the PLT group ($p = 0.36$). Chest tubes were removed after 3.6+/-1.3 days in the BAT group, and 3 +/- 1.2 days in the PLT group ($p = 0.69$). Total hospital stay was 7.7 +/- 6.6 days in the BAT group, and 7 +/- 1.2 days in the PLT group ($p = 0.72$).
Conclusions: In our experience, BAT seems suitable and shows similar outcomes to PLT for sarcoma metastasis resection. The BAT procedure allows the manual exploration of both lungs during a single surgical intervention, and so to reduce the delay of further therapies.

PBC-SESSION: BEST OF IPSO

O-148

IMPROVEMENTS IN THE TREATMENT OF PATIENTS SUFFERING FROM EMBRYONAL BLADDER-PROSTATE-RHABDOMYOSARCOMA – A COMPARISON BETWEEN THE CWS-96 AND CWS 2002-P TRIALS

G. Seitz[1], J. Fuchs[1], T.M. Dantonello[2], M. Sparber-Sauer[2], I. Leuschner[3], J. Godzinski[4], T. Klingebiel[5], E. Koscielniak[2]

[1]Department of Pediatric Surgery and Pediatric Urology, University Children's Hospital, Tübingen, Germany; [2]Department of Pediatric Hematology / Oncology, Olgahospital Klinikum Stuttgart, Stuttgart, Germany; [3]Department of Paidopathology, University Hospital, Kiel, Germany; [4]Department of Pediatric Surgery, Marciniak Hospital, Wroclaw, Poland; [5]Department of Pediatric Hematology / Oncology, University Children's Hospital, Frankfurt/ Main, Germany

Objectives: Modern treatment of bladder/prostate rhabdomyosarcoma (BPRMS) is aimed to improve survival, to reduce therapy intensity as well as to increase bladder preservation rates. The aim of the study was to compare treatment results of patients suffering from BPRMS treated within the CWS-2002P trial with the precursor trial CWS-96.
Methods: A total number of 119 children with non-metastasized embryonal BPRMS treated within CWS-96 ($n = 69$) and -2002P ($n = 50$) trials were analyzed. Fourteen patients were excluded (CWS-2002P: $n = 8$, CWS-96: $n = 6$). Patients received 3 cycles of neoadjuvant chemotherapy (CWS-96: VAIA/CEVAIE, CWS-2002P: VAIA/I^2VA). At week 9, reassessment was carried out. Depending on tumor size, age, and response, local therapy consisting of radiotherapy and/or surgery was initiated. After local control, adjuvant systemic therapy was continued.
Results: Patients 'age ranged from 0 to 16 years in both trials. Median follow up was 59 (CWS-2002P) and 64 months (CWS-96). The 5-year-OS and -ES for the whole group were higher in CWS-2002P than in CWS-96 (5-y-OS CWS-2002P: $84.5\% \pm 6$; CWS-96: $76.3\% \pm 5.6$; 5-y-ES CWS-2002P: $79.9\% \pm 6.4$; CWS-96: $69.8\% \pm 6.2$). One third of the patients received radiotherapy in both trials. Successful local control was feasible using radiotherapy and/or surgery and the outcomes for different local control approaches were comparable. The bladder preservation rates were matchable (67% (CWS-2002P) / 73% (CWS-96)).
Conclusions: Despite reduction of chemotherapy burden, the outcome of patients suffering from BPRMS treated within the CWS-2002P trial regarding OS and ES was obviously better than in the precursor trial CWS-96. Although there was no difference in individual local control rates, the improved outcome is caused by the fact that the number of prognostic unfavourable incomplete resections with salvage radiotherapy was significantly lower in CWS-2002P than in CWS-96. Novel concepts will be required in the future to improve bladder preservation rates.

O-149

WILMS TUMOUR NOT RESPONDING TO PREOPERATIVE CHEMOTHERAPY

J. Godzinski[1], H. Heij[2], J. Fuchs[3], D. von Schweinitz[4], G. Cecchetto[5], G. Audry[6], B. Sandstedt[7], B. Sznajder[8], N. Graf[9]

[1]Dept. of Paediatric Surgery and Chair of Emergency Medicine, Medical University and Marciniak Hospital, Wroclaw, Poland; [2]Dept. of Paediatric Surgery, AMC & VUMC, Amsterdam, Netherlands; [3]Dept. of Paediatric Surgery, University of Tuebingen, Tuebingen, Germany; [4]Dept. of Paediatric Surgery, University of Munich, Munich, Germany; [5]Dept. of Paediatric Surgery, University of Padova, Padova, Italy; [6]Dept. of Paediatric Surgery, Hospital Trousseau, Paris, France; [7]Childhood Cancer Research Unit and Dept. of Pathology, Karolinska Institutet & Danderyds Hospital, Stockholm, Sweden; [8]Statistics, NKI, Amsterdam, Netherlands; [9]Dept. of Paediatric Oncology and Hematology, University of Homburg, Homburg, Germany

Objectives: In majority of patients with nephroblastoma (WT), preoperative chemotherapy decreases tumour volume. Risk of the intraoperative tumour rupture and stage of the disease become lower. In some, however, tumour volume does not decrease or even increases. Aim of this review was to describe surgical, clinical and pathological characteristics of WT not responding to preoperative chemotherapy.
Methods: Of 1774 patients (SIOP9301), 220 (12%) with unilateral or metastatic WT evidenced stable (31) or increasing volume (189) of their tumours under preoperative chemotherapy (106/males, 114/females, age range 6-187 months, median = 33); 209 had localised tumours, 11 – metastatic. Abdominal stages were I/108 (49%), II/57 (26%), III/39 (18%), IV/3 (1%) missing 13 (6%). Pathology was of low risk in 14 (6%), intermediate risk in 161 (73%) and high risk in 45 (20%). The stage III rate, the intraoperative tumour rupture rate and the pathology groups in non-responders and the remaining patients were compared.
Results: The stage III rates in non-responders (18%) and remaining patients (11%) were not different ($p = 0.105$), intraoperative tumour ruptures were more frequent in non-responders (8% vs. 2%, $p = 0.00006$). Pathology of low and intermediate risk was less frequent in non-responders (respectively: 6% vs. 11%, $p = 0.0387$ and 73% vs. 85%, $p = 0.00001$). The stromal predominant subtype, however, was more frequent in non-responders (15% vs. 8%, $p = 0.0005$), whereas the rates of blastemal predominant subtype were not different (10% vs. 7% $p = 0.193$). High risk pathology was more frequent in non-responders (20% vs. 3%, $p = 0.00000$). Outcomes: 78% of non-responders with localized tumour and 8/11 metastatic cases are in 1st CR; 87% of non-responders and 9/11 metastatic patients are alive (60 months).
Conclusions: Patients with WT non-responding to preoperative chemotherapy have higher rates of high risk pathology variants and the stromal predominant subtype of intermediate risk and are at elevated risk of tumour rupture. Outcome remains acceptable.

O-150

WILMS TUMOUR WITH INTRAVASCULAR EXTENSION - TIME TO REFLECT AND RESECT. A REPORT FROM SIOP 2001

L. Adamson[1], R. Squire[1], B. Sznajder[2], H. van Tinteren[2], J. Godzinski[3], N. Graf[4], M. Powis[1]

[1]Department of Paediatric Surgery, Leeds General Infirmary, Leeds, United Kingdom; [2]Statistical Center, Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Pediatric Surgery, Marciniak Hospital, Wroclaw, Poland; [4]Paediatric Haematology and Oncology, Saarland University Hospital, Homburg, Germany

Objectives: Preoperative chemotherapy is recommended for children with Wilms tumour with intravascular extension. Extended chemotherapy may improve resectability, but increase tumour adherence to vascular endothelium, precluding complete resection. To evaluate the optimal length of preoperative treatment we report a review of patients with tumour thrombus treated in the SIOP 2001 study.
Methods: Patients with Wilms tumour (WT) and thrombus were identified from the SIOP 2001 study. Preoperative chemotherapy with Vincristine/Actinomycin D was recommended for all patients. Overall (OS) and event free (EFS) survival, tumour regression, completeness of resection, use of cardiopulmonary bypass (CPB) and cavectomy were analysed for those patients receiving standard preoperative chemotherapy (4 courses over 4 weeks) versus extended treatment (more than 4 courses).
Results: Of 4,500 registered patients 166 had thrombus. Pre-treatment tumour extent was cardiac in 31, caval in 120 and renal vein in 15. 97% received chemotherapy; details were available for 139 of which 65 received standard treatment (StC); 65 extended treatment (EC). Tumour regression was observed in 20% StC and 25% EC; complete resection achieved in 70% and 73% respectively; cavectomy was required in 20% and 28% (n.s.). Survival was significantly higher in those receiving StC than EC (OS 95% vs 82%, $p = 0.025$; EFS 88% vs 72%, $p = 0.047$), though there were more high-risk tumours in the EC group (18% vs 5% StC). Of 30 patients with intracardiac extension, 9 received StC and 12 EC. Slightly more tumour regression into the vena cava was observed in the EC group (58% vs 50%); with reduced CPB (33% StC 17% EC); but without improved survival.
Conclusions: Extended preoperative chemotherapy confers no added benefit in those with intracaval thrombus. For those with intracardiac extension, the current data is inadequate to guide the value of extended treatment, but improved tumour regression into the cava may permit resection without bypass.

O-151

ADRENOCORTICAL CARCINOMA IN CHILDREN: A REVIEW OF THE NATIONAL CANCER DATABASE

Y. Rojas[1], Y. Shi[1], W. Zhang[2], E. Beierle[3], J. Doski[4], M. Goldfarb[5], K. Gow[6], A. Golden[6], M. Langer[7], S. Vasudevan[1], J. Nuchtern[1]

[1]Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, USA; [2]Outcomes & Impact Services, Texas Children's Hospital, Houston, USA; [3]Department of Surgery, University of Alabama, Birmingham, USA; [4]Department of Surgery, University of Texas Health Science Center- San Antonio, San Antonio, USA; [5]Department of Surgery, University of Southern California, Los Angeles, USA; [6]Department of Surgery, University of Washington, Seattle, USA; [7]Department of Surgery, Tufts University, Portland, USA

Objectives: Adrenocortical carcinoma (ACC) rarely occur in children. Prior studies suggest that ACC in children may represent a different pathologic entity when compared to adults. The purpose of this study was to compare the survival trends of children with that of adults with ACC.
Methods: Utilizing data from the National Cancer Data Base (NCDB), we analyzed all patients, adults (≥18 years of age) and children (< 18 years of age), with ACC from 1998 to 2011. Kaplan-Meier and logistic regression models were used to analyze trends and factors associated with improved survival.
Results: A total of 2,886 patients with a primary ACC were identified (2,765 adults, 121 children). Factors that significantly ($p < 0.05$) affected survival include ethnicity, tumor grade, regional lymph node status, extent of surgery at primary site, surgical margins, and age. Patients with ACC <18 years of age had a significantly superior 5-year overall-survival (OS), 64% (95% CI 53-74%), compared to those > 18 years of age, 32% (95% CI 30-34%; $p < 0.0001$). Improved 5-year OS in the younger age group remained significant when stratified by tumor size >5 cm and positive lymph node status ($p < 0.0001$, $p = 0.002$, respectively). In patients where complete resection was achieved, younger patients had better 5-year OS than older patients (82% [95%CI 66-91%] vs 48% [95% CI 44-51%]).
Conclusions: ACC patients < 18 years of age had a better 5-year OS compared to older adults, a finding that persisted in a subgroup with complete resection. These data support that ACC in children behaves as a different pathologic entity from that observed in adults.

GERM CELL TUMOURS / RARE TUMOURS

O-152

PREDICTORS OF OUTCOME IN PEDIATRIC HEPATOCELLULAR CARCINOMA: A REVIEW OF THE NATIONAL CANCER DATA BASE

Y. Shi[1], Y. Rojas[1], W. Zhang[2], E. Beierle[3], J. Doski[4], A. Goldin[5], M. Goldfarb[6], K. Gow[5], M. Langer[7], J. Nuchtern[1], S. Vasudevan[1]

[1]Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, USA; [2]Outcomes & Impact Service, Texas Children's Hospital, Houston, USA; [3]Department of Surgery, University of Alabama, Birmingham, USA; [4]Department of Surgery, University of Texas Health Science Center - San Antonio, San Antonio, USA; [5]Department of Surgery, University of Washington, Seattle, USA; [6]Department of Surgery, University of Southern California, Los Angeles, USA; [7]Department of Surgery, Tufts, Portland, USA

Objectives: To examine demographic characteristics and factors associated with survival in children with hepatocellular carcinoma (HCC).
Methods: The National Cancer Data Base was queried for pediatric patients (<18 years) with HCC of all subtypes diagnosed between 1998 and 2011. We examined demographic, diagnostic, and treatment variables to identify factors associated with survival using log-rank comparisons of Kaplan-Meier survival curves. We also compared the variables of pediatric and adult patients with HCC.
Results: Of 110,438 total patients with HCC, 309 (0.280%) were less than 18 years old. Pediatric patients had an average age of 14.7 years, and better 5-year overall survival (OS) than adult patients (30.9% vs. 14.8%; $p = <0.001$). In the pediatric cohort, the children with fibrolamellar HCC comprised 32.7% of the cases, were older than 7 years, and had better OS than patients with non-fibrolamellar HCC (46.5% vs. 21.3%; $p = < 0.001$). White children had better OS than black children and those of other racial groups (36.5% vs. 16.7% vs. 8.11%; $p < 0.001$). Additionally, improved OS was observed in children with negative lymph nodes (69.2% vs. 25.70%; $p < 0.020$), in those who underwent some type of lymph node sampling or resection (58.3% vs. 17.8%; $p < 0.001$), and in those with negative margins after resection (57.2% vs. 23.8%; $p = 0.002$). There were 148 resections: 47 wedge/segmentectomies, 44 anatomic hepatectomies, 18 extended hepatectomies, and 39 transplants. The OS for each type of procedure was 73.1%, 51.0%, 25.0%, and 34.0%, respectively. In children, neither size of primary tumor nor treatment with chemotherapy was associated with improved OS.
Conclusions: Histologic subtype, race, lymph node resection and status, and complete resection of primary tumor were the most significant predictors of survival for pediatric HCC.

O-153

PROGNOSTIC IMPLICATIONS OF MULIFOCALITY IN HEPATOBLASTOMA

S. Qureshi[1], S. Kembhavi[2], M. Bhagat[1], T. Vora[3], G. Chinnaswamy[3], S. Laskar[4], N. Khanna[4], M. Ramadwar[5], P. Kurkure[3]

[1]Pediatric Surgical Oncology, TaTa Memorial Hospital, Mumbai, India; [2]Radiology, TaTa Memorial Hospital, Mumbai, India; [3]Medical Oncology, TaTa Memorial Hospital, Mumbai, India; [4]Radiation Oncology, TaTa Memorial Hospital, Mumbai, India; [5]Pathology, TaTa Memorial Hospital, Mumbai, India

Objectives: To evaluate the impact of multifocalilty in hepatoblastoma outcome.
Methods: The analysis included 52 patients treated between March 2006 and February 2014. Tumors characteristics like the lobe affected, unifocal or multifocal disease, extrahepatic extension, involvement of portal vein or the hepatic veins and presence of metastases were recorded. Serum alfa-fetoprotien levels were measured in all patients. The tumors were assigned PRETEXT group and risk categories as per SIOPEL system in retrospect. All patients, except one, received induction chemotherapy (cisplatin, doxorubicin or cisplatin, vincristine and 5-fluoruracil). Right or left hepatectomy were performed in 27 patients, extended resection in 13 and non-anatomical resection in 9 patients. Left lateral sectorectomy, median hepatectomy and enucleation were performed in one each. Parenchymal cut margins were negative in 48 patients.
Results: The median age was 15 months (range, 11-138 months) with 36 males and 16 females. There was no postoperative mortality and complications occurred in 5 patients (biliary fistula = 3, wound infection = 1 and intestinal obstruction = 1). The projected 5-year overall and relapse-free survival were 88% and 70% respectively. Disease relapsed in 11 patients (7 within 18 months) at local site (7) or in the lungs (4). Multifocality was significant prognostic factor for both overall and event free survival ($p < 0.05$).
Conclusions: Multifocal hepatoblastoma are associated with increased risk of disease relapse and death.

O-154

SINGLE CENTRE REVIEW OF HEPATOBLASTOMA OVER 20 YEARS IN NEW ZEALAND

J. McCall[1], P. Johnston[1], J. Skeen[2], R. Cockcroft[2], R. Corbett[3], J. Arudchelvam[4], A. Bartlett[1], P. Morreau[5]

[1]NZ Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand; [2]Paediatric Oncology, Starship Children's Hospital, Auckland, New Zealand; [3]Paediatric Oncology, Christchurch Hospital, Christchurch, New Zealand; [4]NZ Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand; [5]Paediatric Surgery, Starship Children's Hospital, Auckland, New Zealand

Objectives: Hepatoblastoma (HB) is a rare childhood malignancy for which surgical resection remains the only chance of cure. The aim of this study was to review the outcome of all children that underwent surgical resection or liver transplantation (LT) for HB at a single centre in New Zealand.
Methods: The patients were identified retrospectively from 1992 to 2014. Data included patient demographics, associated conditions, PRETEXT staging with CT scanning, histology, treatment and outcome.
Results: 22 children aged from 1.8 to 74 months (median 15.8) with a male to female ratio of 12:10 were identified. 13 were European (59%), 4 Asian and 1 indigenous Maori. Two patients had Familial adenomatous polyposis and one patient each had neurofibromatosis and Beckwith- Wiederman Syndrome. The majority were PRETEXT II (32% n = 7) with 2 in I, 5 in III and 5 in IV. Staging was not available in 3 patients. Six (27%) had lung metastasis at diagnosis, one of whom had tumour involving diaphragm and IVC. All except one patient with a small tumour were treated with neoadjuvant chemotherapy according to SIOPEL protocol. 18 patients underwent R0 hepatic resection and 4 patient LT. The most common histological type was epithelial (61%) followed by mixed type (39%). One patient developed intrahepatic recurrence post resection and was treated with LT.
Conclusions: At a mean follow up of 104 months (3-253) five patients developed recurrence. Two with pulmonary and one with cerebral metastases that were resected with no evidence of recurrence after 25 and 204 months respectively, the other 3 died. 19 patients remain alive and well with 1 and 5 year overall and event free survival of 91/86% and 91/85% respectively. This is one of the largest single centre reports of HB with survival rates exceeding multicentre reviews.

O-155

MALIGNANT HEMOPERITONEUM IN CHILDREN: A SINGLE INSTITUTION EXPERIENCE

J. Palacios[1], J. Shalkow[1], I. Guzman[1], A. Leon[1], J. Vazquez[2]

[1]Surgical Oncology, National Institute of Pediatrics, Mexico City, Mexico; [2]Pediatric Surgical Oncology, ABC Medical Center, Mexico City, Mexico

Objectives: We present our experience with malignant hemoperitoneum in children. Tumors may produce hemoperitoneum after spontaneous or chemotherapy-induced rupture. Some present as acute abdomen, diagnosis being made at surgery.
Tumors at risk include: neuroblastoma, Wilms, hepatoblastoma, and ovarian tumors.
Methods: We retrospectively reviewed 10 cases of malignant hemoperitoneum between 2004 and 2010.
Results: Five males and five females (two to 16 years), underwent surgery for malignant hemoperitoneum. Diagnoses included ovarian germ cell tumor (oGCT), followed by Wilms tumor (WT) and hepatoblastoma (HB), then neuroblastoma (NB), ovarian leukemic infiltrate, and rhabdomyosarcoma of the urachus (uRMS). Seven had history of malignancy, three more presented as acute abdomen, the diagnosis being made at laparotomy. Most underwent primary tumor resection, while two (NB and HB) underwent damage-control surgery alone. Free peritoneal blood found at surgery was 300 to 1,500 ml. All required intensive care after surgery. Five patients are alive without evidence of disease. One with WT and four with oGCT. Five children did not survive. Three (WT, NB and HB) died from multiple organ failure 72 hours after the event. The patient with RMS died from disease progression. One with HB died later of multiple organ failure, not related to the hemoperitoneum.
Conclusions: Delayed cancer diagnosis is commonin developing countries. 30% of our patients presented with acute abdomen, the tumor being incidentally found at laparotomy. Not all patients present hemodynamic instability. Signs include abdominal mass/distension, compartment syndrome, and hematocrit drop. CT-scan is ideal for diagnosis. However, in unstable patients, bedside ultrasound identifies the mass/free fluid, and guides a diagnostic paracenthesis. Malignant hemoperitoneum is a serious complication in pediatric cancer patients, which entails a dismal prognosis with elevated mortality rate. A high index of suspicion for a timely diagnosis cannot be over-emphasized. Management should be individualized according to tumor characteristics and patient status.

O-156

MANAGING OVARIAN MASSES IN CHILDREN – WHEN IS OVARIAN SPARING SURGERY APPROPRIATE?

R. Clark[1], R. Roberts[1], O. Burdall[1], T. Rogers[1]

[1]Department of Paediatric Surgery, Bristol Royal Hospital for Children, Bristol, United Kingdom

Objectives: Ovarian sparing surgery in children presenting with an ovarian mass is controversial. We aimed to report preoperative findings that may be predictive of the safety of this approach.
Methods: Retrospective review of all children (0-16 years) presenting with an ovarian mass from January 2006 to December 2013. Operative approach was at the discretion of the operating surgeon. Ovarian sparing surgery was performed with gynaecological expertise present.
Results: Fifty six children were treated during the study period (51 benign, 1 borderline and 4 malignant). Forty two oophorectomies were performed and fourteen ovarian sparing procedures (all benign). Of the oophorectomies, thirty seven (92%) had a benign histology, of which nineteen (51%) had histologically viable ovarian tissue.
All malignant tumours had large mass size (mean 21.4 cm ± 5.4[SD]), positive tumour markers (BHCG, Ca125 or AFP) and mainly solid elements on preoperative ultrasound scan. Benign masses were smaller (mean 9.9 cm ± 7.1 cm [SD]). 31 of these had preoperative tumour markers taken, 9 of whom were positive (29%). Appearance on USS was cystic in (64%), mixed (27%) or solid (9%). Of the benign masses with predominantly solid elements all underwent oophorectomy; two had torted ovarian cysts (no viable ovarian tissue in either); two were considered for ovarian sparing surgery but due to suspicious intraoperative appearances oophorectomy was performed.
Conclusions: In our experience ovarian sparing surgery (performed by a surgeon with appropriate expertise) in children presenting with ovarian masses is safe and effective. Combining preoperative findings may be helpful in selecting those for ovarian-preserving surgery. Masses that were <15 cm in diameter, primarily cystic and had negative tumour markers were all benign. Viable ovarian tissue was frequently seen in benign masses and therefore consideration of ovarian sparing surgery in patients with these three preoperative findings is desirable.

O-157

SINGLE TROCAR LAPAROSCOPIC ASSISTED SURGERY FOR BENIGN OVARIAN CYST IN CHILDREN

S. Tran[1], Q. Tran[1]

[1]Surgical Department, National Hospital of Pediatrics, Hanoi, Vietnam

Objectives: To report our technique and results of single trocar laparoscopic assisted surgery (STLAS) for benign ovarian cyst (BOC) in children.
Methods: Medical records of patients with diagnosis BOC undergoing STLAS at our center from February, 2009 to February, 2014 were reviewed. For the STLAS, a 10 mm umbilical trocar was placed and a 10 mm camera with engrafted 5 mm working channel was used. The ovarian cystic wall was grasped and brought to the umbilical site and then the cystic fluid was aspirated outside the peritoneal cavity. The cyst then was brought out of abdomen via the umbilical incision and excision of the cyst was performed extracorporally, sparing ovarian tissue when possible. When delivery of the cyst to the umbilical site was impossible due to short adnexal pedicle, the cyst was delivered out of the abdomen via a minimal transversal suprapubic incision after fluid aspiration and cystic removal was performed as described.
Results: Thirty patients were identified, with median age of 4 years (range: 8 days - 15 years). The median size of the cyst was 7.0 cm (range: 3 - 13 cm). In 16 cases (53.3%) the cyst was

mature teratoma, in 10 cases (33.3%) – simple cyst and in 4 cases (13.3%) – dermoid cyst. In 25 patients (83.3%) the cyst was excised via the umbilical incision and in 5- via the suprapubic incision. Sparing of the ovarian tissue was performed in 27 cases (90%). The mean operative time was 48 ± 15.3 minutes. There was no perioperative complication. The mean postoperative hospital stay was 1.8 ± 0.6 days. At a median follow up of 24 months, all patients were in good health, without recurrence. The postoperative cosmesis was excellent.
Conclusions: STLAS is feasible, safe, with excellent cosmesis and could be a viable approach in minimally invasive management of BOC in children.

O-158

POSTERIOR SAGITTAL APPROACH FOR SACROCOCCYGEAL TERATOMAS – AN EXCELLENT ALTERNATIVE

S. Bhatnagar[1]

[1]Pediatric Surgery, B.J. Wadia Hospital for Children, Mumbai, India

Objectives: Chevron shaped buttock incision which is the standard surgical approach for sacrococcygeal teratomas has a major disadvantage due to an ugly scar and deformed buttocks which persist throughout life. Modification in the surgical approach through a posterior sagittal incision in the midline natal cleft provides an excellent cosmetic result, almost non-noticeable scar and no buttock deformity.
Methods: A prospective descriptive study was performed between March 2001 till December 2013. All patients with sacrococcygeal teratomas presenting in the neonatal age group or later who were operated through a posterior sagittal approach by a single surgeon were included in the study. The pre-operative features of the tumor, the difficulties faced during surgery with this approach and the post-operative outcome were analysed.
Results: Nineteen patients with sacrococcygeal teratomas (8 males, 11 females) were operated through midline posterior sagittal approach. Majority (16/19) presented in the neonatal period, whereas 3/19 presented at 1-3 years of age. The sizes of the tumor varied from 5.5 to 13 cms in horizontal dimensions of which 9 were type 1, 7 were type 2, 3 of type 3 as per Altman's classification. Excision of the tumor with the posterior sagittal incision was done with ease in all except in type 3 tumors wherein a slight lateral or superior extension of the incision was needed for adequate exposure. Complete excision including coccygectomy was done in all. Wound healed well in all except 3 patients having superficial wound gapes which healed spontaneously.
Conclusions: As compared to the chevron incision, the posterior sagittal approach requires meticulous midline dissection and raising of the flaps on both sides without damaging the external anal sphincter and the surrounding structures. With slight extension of the incision even the presacral component could be completely excised. Cosmetic results were excellent in all without any deformity of the buttocks.

O-159

GASTROINTESTINAL STROMAL TUMOR IN CHILDREN: A CLINICAL-PATHOLOGICAL REPORT FROM THE ITALIAN PEDIATRIC RARE TUMOR PROJECT (TREP)

M. Ilari[1], A. Ferrari[2], G. Bisogno[3], G. Cecchetto[4], V. Kiren[5], P. Tamaro[5], S. Ladogana[6], P. Pierani[7], A. Martino[1]

[1]Pediatric Surgery, "G. Salesi" Children's Hospital, Ancona, Italy; [2]Pediatric Oncology, National Cancer Institute, Milano, Italy; [3]Pediatric Oncology, University of Padova, Padova, Italy; [4]Pediatric Surgery, University of Padova, Padova, Italy; [5]Pediatric Oncology, IRCCS Burlo Garofolo, Trieste, Italy; [6]Pediatric Oncology, Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; [7]Pediatric Oncology, "G. Salesi" Children's Hospital, Ancona, Italy

Objectives: Gastrointestinal stromal tumours (GISTs) are the most important group of mesenchymal smooth muscle neoplasms that can arise anywhere within the gastrointestinal tract. However, their incidence during childhood, is about 0.02 cases per 1 million per year. All tumors of mesenchymal origin that express the membrane protein kit (CD117) or which have a mutation in platelet-derived-growth factor a (PDGFRA) should be considered as GISTs. Purpose of this study is to define the clinical-pathological characteristics of GISTs in patients recruited in the study Italian TREP.
Methods: All patients enrolled in this study were less than 16 years old at the diagnosis. Staging and follow-up workup included the following investigations: digestive endoscopy, magnetic resonance imaging (MRI), and, in some cases, computed tomography (CT). Samples of tumour tissue were also stained with the antibodies against KIT and PDGFRAa. Histomorphologically, GISTs were subtyped according to Fletcher et al. into three categories: spindle cell type, epithelioid type, or mixed type.
Results: Nine patients (5 male and 4 female) with GIST were enrolled in this study. Tumour was located in the stomach in 8 patients and 50 cm proximal to the ileocecal valve in 1. The most common symptom in gastric GIST was the anemia, associated with bleeding; patient with jejunal GIST complained abdominal pain. All patients underwent sparing surgery. One patient with gastric GIST required afterward a radical gastrectomy because of a local recurrence. All patients are alive at the most recent follow-up, although 3 patients are currently undergoing chemotherapy with Sunitinib because of hepathic/peritoneal metastases before a second look surgery.
Conclusions: Currently, there are no international guideline-concordant treatment for GIST during childhood. However, it is important to remember that in children with a GIST the 5-year probability of survival is 90%, therefore sparing surgery should be considered even in cases of multifocal disease or local nodal metastases.

O-160

INCIDENCE AND OUTCOMES OF PEDIATRIC EXTREMITY MELANOMA: A PROPENSITY SCORE MATCHED SEER STUDY

E.A. Perez[1], J. Tashiro[1], A. Rosa[1], J.E. Sola[1]

[1]Division of Pediatric Surgery Department of Surgery, Miller School of Medicine University of Miami, Miami, USA

Objectives: There is a paucity of literature on the treatment of melanoma in children with surgical management often extrapolated from the adult experience. We sought to determine the incidence, surgical treatment, and outcomes of extremity melanoma in pediatric patients.
Methods: The SEER registry was analyzed for all patients <20 years of age with extremity melanoma between 1973 and 2010. Multivariate and propensity-score matched analyses were performed to identify independent predictors of survival.
Results: Overall, 917 patients were identified with an overall age-adjusted incidence of 0.2 per 100,000 persons/year, with an annual percent change of 0.96 ($p < 0.05$). Patients were most commonly female (66%), age 15-19 years (72%), and white (91%). Most were diagnosed with localized disease (77%), lower extremity (54%), melanoma-NOS (52%), superficial spreading (33%), and nodular histology (7%). Surgical procedures included wide local excision (50%), excisional biopsy (32%), surgery-NOS (14%), major amputation (0.2%), sentinel lymph node biopsy (SLNB) (15%), and lymphadenectomy (LA) (28%). SLNB/LA was performed in 32% of patients with localized disease and 95% with regional disease. Overall, 20-year disease specific mortality was 7% with lower survival for males (89%), regional (79%) and distant disease (36%), nodular histology (69%), and upper extremity (90%) (all $p < 0.05$). For regional and distant disease there was no survival advantage for SLNB or LA vs no sampling. Multivariate analysis revealed localized disease (OR 5.247), lower extremity site (OR 2.145) as significant independent prognostic indicators of survival, while distant disease (OR 0.249), and nodular histology (OR 0.338) were indicators of poor survival (all $p < 0.02$). Propensity-score matched analysis found no differences in survival rates between SLNB or LA vs no sampling for localized and regional disease.
Conclusions: Multivariate and propensity score matched analysis of pediatric extremity melanoma in SEER demonstrates no survival advantage between children undergoing sampling procedures or no sampling for localized/regional disease.

O-161

THE ASSESSMENT OF QUALITY OF SURGICAL TREATMENT IN CHILDREN WITH AGGRESSIVE FIBROMATOSISS - THE STUDY OF 50 PATIENTS

K. Bronowicki[1], M. Rapala[1], B. Kazanowska[1], W. Sulka[1], A. Balcerska[1], E. Bien[1], J. Bohosiewicz[1], M. Chrupek[1], K. Dylewska[1], A. Kurylak[1], W. Madziara[1], K. Muszynska-Roslan[1], D. Perek[1], M. Perek-Polnik[1], A. Prokurat[1], A. Raciborska[1], M. Rybak[1], M. Rychlowska-Pruszynska[1], G. Sobol[1], T. Stachowicz-Stencel[1], W. Wozniak[1], M. Wysocki[1], E. Zielinska[1], J. Godzinski[1]

[1]Polish Paediatric Solid Tumours Study Group, Wroclaw, Poland

Objectives: Aggressive fibromatosis (AF) is locally destructive proliferative process with marked tendency to recur.
The Aim of the studywas to assess the risk factors for failure of the surgical treatment in children with AF.
Methods: Between 1981-2014, 50 children (median age 8,43 yrs) with AF were treated in centres cooperating within Polish Paediatric Solid Tumours Study Group. Clinical data regarding localisation of tumour and treatment modalities (resections: wide-R0, marginal-R1, incomplete-R2) were retrospectively evaluated and correlated with the results of treatment (complete remission-CR, stable disease-SD, progressive disease-PD, occurrence of the relapse).
Results: Twenty-five of fifty patients (pts) had R0 resection, 13 R1, 8 R2. Cht was used in 21 and XRT in 6 cases. After a median follow up of 33 months 31/50 pts had CR, 14 SD, 5 PD. Relapses developed in 17/50. 24/25 pts achieved CR after R0 resection, 7/13 after R1, 0/8 after R2 ($p < 0.0001$). All 38pts after R0 and R1 resections entered CR or SD vs 4/8 pts after R2 entered SD ($p = 0.00043$). 7/13 pts had CR and 6 SD after R1 resection vs 4 SD and 4 PD after R2 ($p = 0.00446$). 26/36 pts without symptoms of mutilation achieved CR vs 5/14 ($p = 0.0441$). Rates of relapses by quality of resection were as follow R0-8/25, R1-6/13, R2-3/8 ($p = 0,692$). Resections R0 and R1 were more likely in extremity and trunk (32/35 vs 6/11; $p = 0.0127$), however localisation of tumour did not have influence on the outcome ($p = 0.480$) and the occurrence of relapse ($p = 0.220$).
Conclusions: The importance of the radical surgical margin (R0) seems not clear. Patients after R1 resections can also achieve good outcomes. Mutilating surgery does not improve outcome. The achievement of SD should not be classified as the negative treatment result. Extremities and trunk seem to be favourable sites regarding possibility of R0 and R1 resection.

MISCELLANEOUS

O-162

RESECTABILITY FOR STAGE IA LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA

J. Aldrink[1], B. Appel[2], J.O.E.L. Kaplan[3], C. Schwartz[4], K.A.R.A. Kelly[5], K. McCarten[6], P. Ehrlich[7]

[1]Pediatric Surgery, Nationwide Childrens Hospital, Columbus, USA; [2]Pediatric Oncology, Hackensack University Medical Center, Hackensack, USA; [3]Pediatric Oncology, Levine Cancer Institue, Charlotte, USA; [4]Pediatric Oncology, MD Anderson, Houston, USA; [5]Pediatric Oncology, Morgan Stanly Childrens Hospital, New York City, USA; [6]Radiology, Rhode Island Hopsital, Rhode Island, USA; [7]Pediatric Surgery, University Of Michigan, Ann Arbor, USA

Objectives: Outcomes for children withHodgkin lymphoma (HL) are excellent, but short and long term toxicities may be significant. Lymphocyte predominant Hodgkin lymphoma (LPHL) is a subtype of HL that typically presents with localized peripheral disease. A recent Children's Oncology Group (COG) study, AHOD03P1, demonstrated excellent outcomes for LPHL stage IA, single node disease treated by surgery alone. The purpose of this analysis was to assess the feasibility of extending surgery only treatment to all children with stage IA LPHL.
Methods: Initial imaging for patients enrolled on COG AHOD03P1 with stage I disease >1 lymph node was reviewed independently by two pediatric surgical oncologists for disease location, extent of nodal involvement, and resectability. Concordance between the surgeons was compared, and reasons for unresectablity were noted.
Results: Forty-seven patients were identified. There were 36 males (77%) and 11 females (23%). Median age was 12.3 years (range 4.4 to 20.7 years). Eleven cases were not evaluable due to insufficient imaging available for review. Of the 36 cases that were evaluated, involved nodal locations included submandibular (1), inguinal/iliac (5), and cervical (30). Mean number of nodes requiring resection was 5 (range 1-15). Thirty-four cases (94%) were felt to be resectable by at least one of the surgeons. Surgeon agreement on resectability was 81% (29/36). The resectability opinion differed between surgeons in 5 cervical and 2 iliac cases. Reasons for unresectability and disagreement included morbidity due to extent of the anticipated operation, and proximity to vital structures. Surgeon agreement on type of operation required occurred in 97% of cases.
Conclusions: The technical feasibility of surgery for children with stage I LPHL is high. However, this approach to the treatment of stage 1 LPHL should not be considered the standard of care and must be studied within the context of a clinical trial.

O-163

LONG-TERM PHYSIOLOGIC AND ONCOLOGIC OUTCOMES OF INFERIOR VENA CAVA (IVC) THROMBOSIS IN MALIGNANT ABDOMINAL SOLID TUMORS IN CHILDREN

A.H.P. Loh[1,5], M.W. Bishop[2], M.J. Krasin[3], A.M. Davidoff[1,6], M.R. Langham[4,7]

[1]Department of Surgery, St Jude Children's Research Hospital, Memphis, USA; [2]Department of Oncology, St Jude Children's Research Hospital, Memphis, USA; [3]Department of Radiological Sciences, St Jude Children's Research Hospital, Memphis, USA; [4]Division of Pediatric Surgery, Le Bonheur Children's Hospital, Memphis, USA; [5]Department of Paediatric Surgery, KK Women's and Children's Hospital, Singapore; [6]Department of Surgery, University of Tennessee Health Science Center, Memphis, USA; [7]Department of Surgery, St Jude Children's Research Hospital, Memphis, USA

Objectives: To evaluate the physiologic and oncologic outcomes of IVC thrombosis in children with abdominal malignancies, in order to better understand the long-term risks and benefits of multimodal interventions employed in their management.
Methods: Retrospective review of 15 children with malignant IVC tumor thrombosis treated between January 1996 and December 2011. Extent of tumor thrombus was classified according to Hinman levels I-III. Completeness of thrombus resection and caval patency on follow-up imaging was evaluated. For 12 patients with Wilms tumor, disease characteristics, treatment, and oncologic and physiologic outcomes were correlated with overall survival (O.S.).
Results: Twelve patients had Wilms tumor, 2 had hepatoblastoma, and 1 had adrenocortical carcinoma. Thirteen (87%) patients received neoadjuvant chemotherapy, which reduced the Hinman level in 2 patients. Six (40%) patients had complete thrombus resection, 7 (47%) had partial resection, 1 (7%) had no resection, and in 1 (7%) patient the extent of resection was unknown. On follow-up imaging, 8 (53%) patients' IVCs were patent, 6 (40%) had residual thrombus, and 1 (6.7%) was surgically interrupted. On follow-up imaging, all 6 patients with complete thrombus resection and 2 of 8 patients with partial or no thrombus resection had patent IVCs. These 2 patients both received additional boosts of adjuvant IVC radiation. Only 3 (20%) patients had perioperative complications and 2 (13%) patients experienced transient effects related to IVC occlusion. Among Wilms tumor patients, O.S. was associated with histologic subtype ($P = 0.096$) and IVC patency on follow-up imaging ($P = 0.027$, Log-rank test).
Conclusions: In children with malignant IVC thrombosis, complete resection of the thrombus is associated with maintenance of long-term caval patency. Adjuvant radiation may be effective in clearing residual IVC thrombus. Complete clearance of malignant IVC tumor thrombus in Wilms tumor may confer a survival benefit. Independent of the surgical management of the thrombus, few perioperative and long-term physiologic complications were encountered.

O-164

ONCOLOGICAL AND FUNCTIONAL OUTCOME WITH MULTIMODALITY MANAGEMENT OF MALIGNANT PEDIATRIC MUSCULOSKELETAL TUMORS OF THE PELVIS AT A TERTIARY CANCER CENTER IN INDIA

A. Gulia[1], A. Puri[2], S. Laskar[3]

[1]Orthopedic Oncology Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Orthopedic Oncology Surgical Oncology, TATA Memorial Hospital, Mumbai, India; [3]Radiation Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: To evaluate the morbidity, functional outcome, and oncologic results in pediatric patients with malignant tumors of the pelvis treated with surgical resection as part of their multimodality treatment.
Methods: From Nov. 2000 to Dec 2009, 30 patients with pelvic tumors had undergone surgical excision. the medical records, imaging, oncological and functional status were reviewed. There were 20 males and 10 females, mean age 13 years, range 2to 18 years. The diagnosis included Ewing sarcoma in 22, Osteogenic sarcoma in 4, chondrosarcoma in 2 and synovial sarcoma of bone in 2 cases.
Results: Eighteen resections included the acetabulum and 12 did not. Two of 30 patients had involved margins. Of the 26 patients in whom histologic response to chemotherapy was assessed, 19 patients showed a good response to chemotherapy and seven were poor responders. Five patients with Ewing sarcoma had postoperative radio-therapy (four poor responders and one good responder with a very large soft tissue component). Two patients died because of chemotherapy complications at 6 and 4 months, respectively. One patient had an intra-operative urethral injury, two had wound dehiscence that required secondary suturing, and three had infection. One patient had progressive painless ankylosis of hip. Twenty-seven patients were available for follow-up. Follow-up ranged from 4 to 158 months (mean 48 months). Nineteen patients are currently alive. There were two local recurrences. The overall survival was 68% at 5 years. The Musculoskeletal Tumor Society Score ranged from 22 to 29.
Conclusion: Surgery in malignant pelvic tumors is extremely challenging and requires utmost surgical planning and its careful execution. It provides good local control and oncologic outcomes with acceptable function in these patients.

SUPPORTIVE CARE: WHAT CAN NURSES DO?

O-165

AN EVALUATION OF THE PEDIATRIC ONCOLOGY NUTRITION SCREENING TOOL

A. Murphy[1], M. White[2], P.S.W. Davies[1]

[1]Children's Nutrition Research Centre, Queensland Childrens Medical Research Institute The University of Queensland, Brisbane, Australia; [2]Department of Dietetics and Food Services, Royal Children's Hospital, Brisbane, Australia

Objectives: The Pediatric Oncology Nutrition Screening (PONS) tool is proposed as a method of assessment of nutritional risk in children with cancer. The aim of this study was to assess the validity of the PONS Tool for determining current nutritional status in children with cancer.
Methods: Validity of the PONS tool was tested in children being treated for cancer at the Queensland Children's Cancer Centre. The PONS tool was performed for each subject and involved 5 questions relating to cancer type, therapy and side effects, oral intake, weight loss and a measure of body size. To represent current nutritional status; body mass index (BMI), mid upper arm circumference (MUAC), triceps skinfold and percent fat (%fat) from the Bodpod®, were measured in each child.
Results: A total of 59 inpatients and outpatients ($n = 34$ liquid cancers) were assessed between 5.4 and 17.1 years. Using the PONS Tool cut-offs, 36% of population were classed as low nutritional risk, 34% as moderate risk and 30% as high nutritional risk. The PONS tool was strongly correlated ($p < 0.01$) with weight Z score ($r = -0.62$), BMI Z score ($r = -0.68$), triceps skinfold ($r = -0.34$), MUAC ($r = -0.43$) and%fat ($r = -0.44$). The mean weight Z score (-1.1), BMI Z score (-1.4) and MUAC (18.5 cm) of the high risk group was significantly ($p < 0.05$) lower than the moderate and low risk group. The%fat of the high risk group (25.2%) was significantly lower ($p < 0.05$) than the low risk group (35.3%).
Conclusions: The PONS tool identifies current nutritional status in children undergoing treatment for cancer and significant nutritional differences are evident between the groups classified by PONS as low, moderate and high risk. The next steps in the evaluation involve assessing the concurrent and predictive validity of the tool, and assessing the feasibility, reliability and applicability in international sites.

O-166

THE IMPACT OF NUTRITIONAL STATUS ON HEALTH-RELATED QUALITY OF LIFE IN CHILDREN TREATED FOR CANCER

A. Brinksma[1], R. Sanderman[2], P.F. Roodbol[3], E. Sulkers[3], J.G.M. Burgerhof[4], E.S.J.M. De Bont[5], W.J.E. Tissing[5]

[1]Department of Pediatric Oncology and Hematology / School of Nursing and Health, University Medical Center Groningen, Groningen, Netherlands; [2]Department of Health Sciences Health Psychology Section, University Medical Center Groningen, Groningen, Netherlands; [3]School of Nursing and Health, University Medical Center Groningen, Groningen, Netherlands; [4]Department of Epidemiology, University Medical Center Groningen, Groningen, Netherlands; [5]Department of Pediatric Onoclogy and Hematology, University Medical Center Groningen, Groningen, Netherlands

Objectives: Malnutrition in childhood cancer patients has been associated with lower levels of health related quality of life (HRQL). However, this association has never actually been tested. Therefore, we aimed to assess the impact of nutritional status on HRQL in children treated for cancer.
Methods: In 104 children, aged 2-18 years and diagnosed with hematological, solid, or brain malignancies, nutritional status and HRQL were assessed at diagnosis and at 3, 6, and 12 months using the child- and parent-report versions of the PedsQL 4.0 Generic Core scale and the PedsQL 3.0 Cancer Module. Scores on both scales range from 0-100.
Results: Undernourished children (BMI or FFM<-2SDS) reported significantly lower PedsQL scores compared with well-nourished children on the domains physical functioning (−13.3), social functioning (−7.0), cancer summary scale (−5.9), and nausea (−14.7). Overnourished children (BMI or FM>2SDS) reported lower scores on emotional (−8.0) and cognitive functioning (−9.2) and on the cancer summary scale (−6.6); whereas parent-report scores were lower on social functioning (−7.5). Weight loss (>0.5 SDS) was associated with lower scores on physical functioning (−13.9 child-report and -10.7 parent-report), emotional (−7.4) and social functioning (−6.0) (child-report), pain (−11.6), and nausea (−7.8) (parent-report). Parents reported worse social functioning and more pain in children with weight gain (>0.5 SDS).
Conclusions: Undernutrition and weight loss were associated with worse physical and social functioning; whereas overnutrition and weight gain affected the emotional and social domain of HRQL. These findings stress the importance of adequate nutritional care during treatment. Measures that improve nutritional status will contribute to enhanced health outcomes in children treated for cancer.

O-167

PEDIATRIC ONCOLOGY NURSES INVESTIGATE SOCIALIZATION CHALLENGES RELATED TO NUTRITION: A SOUTH AFRICAN STUDY

S. Mngomezulu[1]

[1]Pediatrics, Chris Hani Baragwanath Academic Hospital, Soweto, South Africa

Objectives: The effect of cancer and treatment modalities affect and compromise nutrition intake, but socialization has an even greater impact on individuals and society in general. When taken in a well-planned balanced meal, nutrition is beneficial for preventing and reducing cancer and treatment side effects, while providing wellness and preventing cancer-related malnutrition and obesity. The benefits of nutrition are only achievable if nurses have insight into the importance of environmental socialization for patients and its effect on proper nutrition. We highlight how socialization impacts on a patient and family's interpretation of nutrition in terms of lifestyle, culture, norms, beliefs, religion, age, gender and education. We emphasize that simple changes in diet interpretation, availability, preparation and provision can increase the benefits of nutritional intake and improve the patient's quality of life regardless of their socio-economic status.
Methods: A prospective observational and cross-sectional survey of 32 parents (30f-2m) and 78 children ages 3-19 [3-6 (15); 7-12 (39), 13-19 (28;15f-13m)] was performed on a day-to-day basis and twice a week on clinic days for three months. The subjects signed written informed consent. The survey included questions on the environment, attitude, presentation and serving of meals while on therapy for cancer. Verification of cultural-socio-economic background was done in relation to food preference, attitude, eating times, hospital and home environment, and served portions especially for teenagers even when at home.
Results: Compliance with nutritional recommendations was found to be the main problem due to diverse social issues and ignorance. Patients' nutritional intake remained compromised when they were introduced to new eating habits while on treatment for cancer that went against their food socialization norms.
Conclusions: Despite socialization challenges, nurses must provide children, adolescents and their parents/guardians with nutritional information that is appropriate for all levels of cultural-socio-economic status so that adequate nutrition remains a cornerstone for improving chances of recovery throughout treatment.

O-168

DECISION MAKING IN CHILDREN WITH CANCER: IT'S NOT ABOUT MAKING "BIG" TREATMENT DECISIONS

K. Kelly[1], C. Mowbray[2], K. Pyke-Grimm[3], P. Hinds[1]

[1]Nursing Research and Quality Outcomes, Children's National Health System, Washington DC, USA; [2]Center for Cancer and Blood Disorders, Children's National Health System, Washington DC, USA; [3]Center for Cancer and Blood Disorders, Stanford Children's Health, Palo Alto CA, USA

Objectives: Informed by the control preferences construct, we developed the Child and Adolescent Decision Involvement Scale (CADIS) for use in children and adolescents with cancer. Cognitive interviews were undertaken to ascertain content validity of the new instrument before initiating large scale psychometric evaluation. Interview techniques provoked in-depth discussion of what being involved in their treatment decisions meant to child and adolescent participants, which focused on access to information along with decision involvement. We conducted additional analyses to better understand how children perceived the interchange between information and decision involvement.
Methods: Twenty children and adolescents (9-17 years) with cancer participated in audio-recorded cognitive interviews. We asked participants to recount their previous treatment decision making (TDM) experiences and to interpret the CADIS statements. We employed constant comparative analysis of verbatim interview transcripts to generate codes and descriptive statements using Atlas.ti.
Results: A majority of participants aligned the five CADIS statements according to Degner's original Control Preference Scale metrics. Participants interpreted the statements using both their personal and theoretical TDM experiences. Children recognized their limited authority/ability for making "big" treatment decisions. They described how being part of TDM helped them gain disease and treatment knowledge, understand why decisions are made and to know what to expect. Children discussed how they had information needs that were both independent of and necessary for TDM. Children also had unique information about themselves that they wanted to contribute to TDM. Children described a larger role for their involvement in "small" supportive care decisions. A few participants of all ages related a desire for limited information and decision involvement.
Conclusions: Child descriptions of their TDM role did not follow a traditional shared decision making paradigm. Additional research is needed to understand TDM from the child's perspective before intervention research can be intiatied.

O-169

IT'S THE ONLY THING HE ENJOYS ABOUT THE WHOLE (HOSPITAL) EXPERIENCE: EXPERIENCE OF MASSAGE THERAPY WHEN RECEIVING CANCER THERAPIES

F. Gibson[1], M. Bluebond-Langner[2], J. Hallman[3], L. Pratt[4], J. Bayliss[5]

[1]Centre for Outcomes and Experience Research in Children's Health Illness and Disability, Great Ormond Street Hospital NHS Foundation Trust and London South Bank University, London, United Kingdom; [2]Palliative Care, Louis Dundas Centre for Children's Palliative Care University College London Institute of Child Health, London, United Kingdom; [3]ICI-LM, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom; [4]Centre for Outcomes and Experience Research in Children's Health Illness and Disability, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom; [5]Louis Dundas Centre for Children's Palliative Care and ICI-LM, Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom

Objectives: While the use of complementary and alternative (CAM) therapies in children with cancer has been reported (as high as 84%) there are few systematic accounts of families experiences, let alone proper investigations of their impact on pain and symptom relief and quality of life. This study was occasioned following identification of a therapies room and the introduction of a Complementary Therapy Nurse Specialist in a children's cancer unit. Our aim was to capture the child's experience of receiving massage alongside conventional cancer therapy and to examine its impact on child and family.
Methods: All children, young people (4-12 years) and their parents, as well as parents of infants (under 4 years) admitted to a large tertiary centre in the UK and accessing the service during the period of recruitment were approached. Participatory research methods, such as symptom sorting cards, were used alongside scales to measure sleep and pain with children. Qualitative content analysis was used to detail 28 stories of children's experiences, and 22 accounts from parents, of their reflections on their child's experience.
Results: Children's and parents' descriptions of the experience were only positive. Massage helped with a range of symptoms including pain, and anxiety. It also provided a safe space for children to relax, think about something else and enjoy calming thoughts. Children spoke about the 'special room' and clearly for many the nurse specialist had taken on an important role in their care. Head massages were particularly popular with some children, helping them with headaches and sleep. In the majority of cases where scales were completed there was indication of perceived improvement.
Conclusions: This presentation will focus on these accounts that suggest massage has a place in the care for children with cancer. Further research is needed to assess specific impact and outcomes in different populations (e.g. children receiving palliative care).

O-170

COMPLEMENTARY ALTERNATIVE MEDICINE USED FOR THE MANAGEMENT OF FATIGUE AND PSYCHOLOGICAL STRESS IN PEDIATRIC ONCOLOGY POPULATION

L. Lopes-Júnior[1], E. Bomfim[1], M. Nunes[1], L. Nascimento[1], M. Flória-Santos[1], G. Bisson[1], R. Lima[1]

[1]Department Maternal-Infant Nurning and Public Health, University of São Paulo at Ribeirão Preto College of Nursing, Ribeirão Preto São Paulo, Brazil

Background: Cancer-related fatigue (CRF) has been described as the most stressful and prevalent symptom in pediatric oncology patients, occurring in 35.6% to 93% of cases. Psychological stress generated during hospitalization can negatively influence the immune system through neuroendocrine and behavioral pathways. For these patients, other modalities of treatment such as the Complementary Alternative Medicine (CAM) can be necessary. Scientific evidence supports the use of CAM for the management these symptoms in adults with cancer, however, the pediatric oncology population studies are still scarce.
Purpose: To identify and analyze scientific evidence about the use of CAM for the management of fatigue and psychological stress inpediatric oncology population.
Material and Methods: We conducted an integrative literature review in which eight databases were accessed for the search: PubMed, Web of Science, CINAHL, LILACS, EMBASE, SCOPUS, PsycINFO and Cochrane Library. Full-text articles were included, studies in English, Spanish or Portuguese published in the last 14 years (2000 until 2013). Controlled and uncontrolled descriptors, as well as its synonyms, were crossed for location of the articles, for example: 'fatigue; cancer-related fatigue; cancer/neoplasm; stress, psychological; child; adolescent; complementary alternative medicine and non-pharmacological interventions'. Two researchers independently analyzed the studies. Initially, 273 articles were found. After the exclusion of duplicate articles and of those that did not match inclusion criteria, and after full reading, we obtained a final sample of nine articles.
Results: The nine studies were grouped into five themes: physical exercises, therapeutic touch, music therapy, massage therapy and nursing interventions & health education. Among the nine studies, six (66.6%) showed a significant p value for CRF and/or psychological stress, evidencing that after the use of CAM there was a decrease in symptoms.
Conclusions: The use of CAM can improve symptoms of CRF and psychological stress in pediatric oncology population.

EDUCATION AND COLLABORATION IN NURSING PRACTICE

O-171

BASELINE STANDARDS FOR PROVIDING PAEDIATRIC ONCOLOGY NURSING CARE IN LOW AND MIDDLE INCOME COUNTRIES: POSITION STATEMENT OF THE SIOP PODC NURSING GROUP

S. Day[1], R. Hollis[2], J. Challinor[3], E. Bosomprah[4]

[1]Division of Nursing Education, St Jude Children's Research Hospital, Memphis, USA; [2]Paediatric Oncology and Haematology, Leeds Teaching Hospitals Trust, Leeds, United Kingdom; [3]School of Nursing, University of California, San Francisco, USA; [4]Paediatric Oncology, Korle-Bu Teaching Hospital, Accra, Ghana

Objectives: Paediatric oncology nurses in low and middle-income countries (LMICs) lack education, resources, support and adequate staffing needed to provide quality care. This is a major impediment for any childhood cancer program and contributes to the low survival rates in LMICs, where most childhood cancers occur. At the 2011 Congress of the International Society of Pediatric Oncology (SIOP), the Nursing Working Group was established as one of 12 new working groups within the Pediatric Oncology in Developing Countries (PODC) structure. The group partners with and advocates for nurses and healthcare teams worldwide to improve paediatric oncology in LMICs. One of our first goals as a group was to develop a position statement regarding baseline standards for providing paediatric oncology nursing care in LMICs.
Methods: In 2013, the SIOP Nursing Working Group, representing 23 countries, collaborated to develop a position statement on baseline nursing standards needed to safely implement quality pediatric oncology nursing care.
Results: Six baseline standards were developed and included recommendations for staffing plans based on patient acuity, paediatric oncology orientation programme, continuing education and training, acknowledgement of nurses as core members of the multidisciplinary team, available resources for safe care, and evidence-based nursing policies and procedures to guide delivery of care.
Conclusions: These baseline standards represent what is needed to provide the minimum level of quality care; however, they are rarely met in LMICs, even in those programs supported by a twinning partnership with a high-income country. This is an international issue that needs addressing in order to improve the survival rate of children with cancer in LMICs. These standards can serve as a critical tool for allocating much needed nursing resources.

O-172

DELIVERING CULTURAL COMPETENT NURSING CARE: A GLOBAL PERSPECTIVE

L. Abramovitz[1], C. Baggott[2]

[1]Nursing, University of California San Francisco, San Francisco, USA; [2]Pediatrics, Stanford University, Palo Alto, USA

Objectives: Pediatric oncology nurses must develop cultural competency to care for children of varying backgrounds. Cultural competency includes self-awareness, knowledge about different cultures, languages, values and beliefs. The purpose of this study was to explore nurses' delivery of culturally competent care in both high income countries (HIC) and low/middle income countries (LMIC).
Methods: A brief web-based survey on cultural competence was developed, focusing on nurses' attitudes, practices and challenges. In March 2014, nurses from both LMIC and HIC who care for children with cancer received emailed invitations to complete the survey with multiple choice and open-ended questions.
Results: Data from 66 surveys were analyzed. Nurses from 12 LMIC comprised 26% of respondents; the remainder included nurses from 9 HIC. Commonly identified challenges included language barriers, obtaining information about specific cultures and developing trusting relationships. Nurses shared successful strategies to deliver culturally competent care (e.g., recognizing non-verbal cues, listening, being respectful and non-judgmental, consulting with knowledgeable staff members, using humor), as well as desired resources (e.g., increased access to interpreters, written information for patients/parents, accessible online/written resources). Prior education in cultural competency differed between the groups. Only 24% of the nurses from LMIC received prior cultural training, compared to 71% of the nurses from HIC ($p = 0.001$). Overall, 86% of the nurses stated that more education was needed to develop cultural competence (100% among LMIC nurses). Lectures, written modules and videos were the top formats identified.
Conclusions: Nurses from LMIC and HIC viewed cultural competency as vital to their practice and felt that exposure to other cultures provides opportunities for individual and professional growth. In addition, they gain new perspectives on life and show increased sensitivity in nurse/patient relationships. Survey results will guide the development of resources and educational programs to support nurses. A written teaching module is proposed for implementation in LMIC and HIC.

O-173

INTERNATIONAL PEDIATRIC ONCOLOGY NURSING PARTNERSHIPS ARE COMPLEX: AN OVERALL HISTORY AND A NORWEGIAN/US AND ETHIOPIAN EXAMPLE

H. Frøland Hauge[1], M. Morken[2], J. Challinor[3]

[1]Children's Division, Oslo University Hospital, Oslo, Norway; [2]Pediatrics, Akershus University Hospital, Lørenskog, Norway; [3]School of Nursing, University of California San Francisco, San Francisco, USA

Objectives: To describe the complexity of international pediatric oncology nursing partnerships between a high-resource country and a low-resource country by reviewing the history of twinnings and using specific examples from an on-going collaboration in Ethiopia.
Methods: Review the history of pediatric oncology twinnings starting in the late 1980s when nurses from Italy collaborated with nurses in Nicaragua. Early St. Jude Children's Research Hospital's International Outreach Program and World Child Cancer twinnings will be included. Provide examples of local (low-resource partner) nursing training, equipment purchases, and travel for nurses from local partner sites to attend international conferences within the context of the larger twinning agenda. Review early models of didactic and clinical teaching such as short-term nursing trainings (1-2 weeks), distance learning, and specific curriculum materials/strategies that have been utilized in the past.
Results: How nurses' collaborations and training are operationalized in low-resource country settings is complex. The role of a nurse in many of these countries may be understood as entirely distinct from the nurse's role in high-resource countries. How nursing practice is defined and constricted by local hospital administration regulations can dramatically impact visiting nurses' ability to provide up-to-date specialized training. Local nurses' and community perceptions of the hazards of working with children with cancer and chemotherapy complicate educational efforts.
Conclusions: An understanding of the history of international pediatric oncology nursing twinning programs reveals the challenges of nursing training and collaborations in countries with low resources. Cultural, language, and educational differences are identified that complicate collaboration, notwithstanding the local nurses', experience, knowledge and strengths. A current twinning in Ethiopia that includes nurses from the US and Norway is highlighted to provide specific examples of the complexity of partnering with and providing 'training' programs for pediatric oncology nursing specialization in a low-resource country.

O-174

NURSING CARE PRIORITIES OVER TIME IN A NEW PEDIATRIC ONCOLOGY UNIT IN A RESOURCE-LIMITED AFRICAN COUNTRY

A. Seifu[1]

[1]Tikur Anbessa Specialized General Hospital (Black Lion Hospital), Addis Ababa, Ethiopia

Purpose: Describe nursing care priorities over time in a setting with limited resources on Ethiopia's newly opened (April 2013) only dedicated ward for childhood cancer.
Materials and Methods: The 26-bed unit has 14 non-rotating nurses and about 257 children on treatment. Approximately 95% of patients receive free care because they are officially

recognized as living in extreme poverty; most have no/little education. Generally, children arrive at the hospital with advanced cancer; survival is <5%.
Results: The ward has newly dedicated pediatric oncology nurses who are learning to manage complex disease and social issues. Advancements have been made in the scope of nursing care since two newly graduated pharmacists on the ward mix some chemotherapy and a newly graduated volunteer psychologist provides play therapy thus assuming some non-nursing tasks. New outpatient housing from a Mother Teresa House has reduced nursing attention to this family support issue. Teaching pediatric nurses about cancer care from other government hospitals has begun.
Conclusions: Remaining challenges: nursing concerns about side effects of preparing chemotherapy, high death rate, low staffing, and lack of parent teaching about the child's disease, infection control and side effects of chemotherapy. Families' extreme poverty is reflected in low levels of personal hygiene and exposure to health care and education. Families arriving from remote areas often speak dialects that local hospital personnel do not understand, thus compounding the challenge of family teaching. The nurses must use critical thinking skills, including their knowledge of multiple Ethiopian cultures and practices, to strive for safe and supportive care for the children and their families. This presentation highlights how the nurses continually prioritize their care over time in this public hospital with severely limited resources, and in a setting of significant professional hierarchy where nursing does not always have a strong voice.

O-175

ESTABLISHING PEDIATRIC ONCOLOGY NURSING EDUCATION DEPARTMENT AT CHILDREN CANCER HOSPITAL, PAKISTAN

R. Punjwani[1], A. Khatoon[1]

[1]Nursing, Children Cancer Hospital, Karachi, Pakistan

Objectives: Developing countries are far behind in sub-specialty care such as pediatric oncology where 80% of children with cancer live. Pakistan is a developing country with total population of 180 million. Nursing in Pakistan like other profession is also in transition phase with emerging new sub-specialties there is a dire need for education and training programs in all areas.
Methods: Keeping in sight the identified need for educational/training programs for nurses children cancer hospital initiated Pediatric Oncology Nursing Education Department (PONED). The Department developed three major programs for nurses over the period of four years with two courses already successfully running and one to start in September 2014. Pediatric Oncology Technician Course is a diploma certification one year course for young adults interested in health care career. Secondly a short course for Registered Nurses already working in pediatric oncology setup is offered twice a year it is a two weeks certification course designed to enhance knowledge and practice. Thirdly a one year post RN diploma first ever in Pakistan to be started in September 2014 with focus on creating sub-specialty case management nurses.
Results: We now have a first ever fully operational pediatric oncology nursing education department with courses registered with licensure bodies that is technician course with Sindh medical faculty and RN diploma with Pakistan nursing counsel. Have completed 4 cycle of technician course with 25 successful nurse technician and 6 courses for RN with 82 trained nurses from all over Pakistan.
Conclusions: Children Cancer Hospital has taken the lead in professional training of Pediatric Oncology Nursing with vision to create centre of excellence in Pediatric Oncology. This can be a model for other health care institutes looking after childhood cancer.

THE CHALLENGES OF THE PROFESSIONAL ROLE

O-176

A SWEDISH PERSPECTIVE ON CARING SCIENCE RESEARCH IN PAEDIATRIC ONCOLOGY: A LITERATURE REVIEW

K. Enskär[1], M. Björk[1], L. Darcy[2]

[1]Department of Nursing, School of Health Sciences, Jönköping, Sweden; [2]Child research group, School of Health Sciences, Jönköping, Sweden

Objectives: The body of research-based knowledge in paediatric caring sciences has been increasing thanks to a dramatic improvement in outcomes related to research and advances in treatment.
The aim of this review was investigate the content of published studies in paediatric oncology related to caring sciences.
Methods: A systematic literature review of 137 published articles on paediatric oncology related to caring science in Sweden was performed.
Results: The result shows that most of the studies were descriptive or comparative studies with a quantitative design. Most of them had parents in focus, and only 22% had focus on the child. Most of the studies investigated wellbeing, using questionnaires or interviews. The result, as stated in the articles, demonstrated that the child's disease has affected the wellbeing of all people coming in contact with the child, in both positives and negative ways. Also the child's disease causes distress related to physical, psychological, existential and social aspects. Several mediating factors for the experience of distress and wellbeing were found, as; disease and treatment severity, gender, time since diagnose, and the use of internal and external support. Frequent reported health promoting aspects were: family togetherness, coping strategies and engaging in activities and normal life, as well as quality of care; as emotional support, information and family participation in care. Suggestions for clinical implications, stated in the articles, were often described in a diffuse manner making translation into clinical practice difficult. However, some areas of clinical implications could be identified and described.
Conclusions: To reflect the child's perspective in paediatric oncology requires that future researchers take on the challenge of including children. The biggest challenge for the future would be to make a shift from explorative studies to intervention studies. There is an urgent need to transform research results into clinical practice.

O-177

AN EXPLORATION OF NURSES' VIEWS REGARDING PROFESSIONAL BOUNDARIES WHEN CARING FOR A CHILD OR YOUNG PERSON AND THEIR FAMILIES WITH A LIFE THREATENING CONDITION

J. Cargill[1]

[1]Teenage and Young Adult Cancer Service, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom

Objectives: Professional boundaries (PB's) are central for the establishment of therapeutic relationships. Tensions exist between the balance of involvement that is beneficial in the therapeutic relationship, to one that is too close and potentially destructive. This challenge is one that is of common occurrence in nursing, where prolonged involvement, caring, and intimacy form the basis from which nursing care is delivered. This presentation reports on the findings from a small exploratory study conducted to uncover experienced nurses' views of PB's when caring for a child or young person with a life threatening condition.
Methods: Conducted in a large teaching hospital within the south of England. Semi-structured interviews were undertaken with six experienced nurses caring for a child or young person and their families with a life threatening condition. Content analysis was utilized to extrapolate meaning from the transcribed interviews.
Results: Knowledge and understanding of PB's and awareness of meaning was good yet PB's are a routine concern. Management of PB's are currently insufficient for nurses working in this area of practice. Strategies are required to improve awareness and support nurses. Support from senior staff could help to reduce the incidence and consequence of boundary crossing and violations.
Conclusions: The study suggests that the determination of PB's within a professional yet therapeutic relationship is one of the most significant challenges for nurses caring for a child or young person. Because of the levels of intensity, and the emotive nature of working with a child or young person with a life threatening condition the study suggests that the crossing or violation of PB's should be considered as an occupational hazard that must be given due attention. The motive that drives boundary crossing and violations, and the governance that is placed to determine such behavior is important. Further research is required to understand such behavior to develop improved coping techniques.

O-178

BALANCING BETWEEN COMPASSION AND PROFESSIONALISM – INTERPRETERS EXPERIENCES OF CHILDHOOD CANCER CARE

J. Granhagen Jungner[1], P. Pergert[1], K. Lützén[1], K. Blomgren[1], E. Tiselius[2]

[1]Women's and children's health, Karolinska Institutet, Stockholm, Sweden; [2]Department of Swedish Language and Multilingualism, Stockholm University, Stockholm, Sweden

Objectives: Linguistic and cultural diversity is an integral part of our society, and so even in childhood cancer care. Children with cancer and their families not sharing a common language with health care staff are in a fragile and vulnerable situation. The purpose of this paper is to describe interpreters' experiences of interpreting in childhood cancer care in a paediatric cancer care unit at Astrid Lindgren Children's Hospital, Sweden.
Methods: Ten (n = 10) interpreters with interpreting experience in childhood cancer care were interviewed in individual semi-structured interviews. Data from the interviews were analysed using qualitative content analysis.
Results: The analysis of the data resulted in the sub-theme reported in this paper: *Balancing between compassion and professionalism*. Interpreters strive constantly to keep a balance between their empathy and compassion, and to perform their task professionally. This balance is sometimes complex to keep because of the difficult circumstances their clients face. The interpreters will handle this balance by "*sparing them my tears*" while, feeling compassion. There is a basic desire to help from a humane perspective, but also since they are countrymen with the same cultural background. In particularly vulnerable situations, interpreters sometimes step outside their professional role e.g. in terms of neutrality, to become, in their view, a fellow human instead.
Conclusions: Interpreters are struggling to be the "neutral party" their professional code of conduct requires in the relation to the families. Interpreters explicitated two phenomena of struggle. First, emotional involvement (children suffering from cancer). Secondly, striving for a meeting point of understanding, this requires commitment beyond interpreters' obligation of

neutrality. Establishing a meeting point of understanding requires explanation of both context and cultural aspects. You cannot only "translate" words. Creating a meeting point of understanding and opening up multi-dimensional understanding requires creation of a relationship between the parties.

O-179

CREATING A TAXONOMY OF TEENAGE AND YOUNG ADULT CANCER CARE IN ENGLAND THROUGH A MAPPING STUDY

C. Vindrola[1], S. Finlayson[1], L. Hooker[2], S. Pearce[3], R. Taylor[1], J. Whelan[4], F. Gibson[1]

[1]Children's Nursing, London South Bank University, London, United Kingdom; [2]Teenage and Young Adult Cancer Service, Southampton University Hospitals NHS Trust, Southampton, United Kingdom; [3]Patient Safety Infection Control, CNWL NHS Foundation Trust, London, United Kingdom; [4]Department of Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom

Objectives: Cancer services for teenagers and young adults in England are currently organised around 13 Principal Treatment Centres. We know that place of care, in terms of both disease and age appropriate specialist settings, is increasingly acknowledged as impacting on outcome. The objectives of this study were to undertake a mapping exercise of the 13 Principal Treatment Centres and develop a national taxonomy of care.
Methods: Our study combined observations, a review of annual reports, interviews with young people, family members, and healthcare professionals, and an activity with young people modelled after the Mosaic approach in 11 of the centres. The main purpose of the interviews was to document different views on care. Each interview transcript was analysed for content and organized in a framework to facilitate data management. Each framework was then summarized into a list of components of care. This list was then grouped in three broader categories created through thematic analysis of the list and which included: staff, environment of care, and activities. The information included in these categories was then used to develop the taxonomy of care in England.
Results: The analysis of the interview transcripts revealed shared perceptions of care in England, despite the wide diversity of models of specialised services currently in operation and the different contexts of care. Even though we found some differences in perceptions of care, all three groups agreed that the overall goal of teenage and young adult care is an individualized and specialised service which is made possible by: caring and supportive staff, an environment that feels like home, and age-appropriate activities.
Conclusions: The taxonomy allowed us to highlight the most important components of care in England. This taxonomy could be useful for other countries currently developing and shaping their own teenage and young adult services.

NURSES AND PSYCHO-ONCOLOGY GROUP

O-180

UNDERSTANDING BODY IMAGE, SEXUALITY, DATING, FRIENDSHIPS, AND FERTILITY IN ADOLESCENTS WITH CANCER FROM AN ADOLESCENT AND PARENT PERSPECTIVE

J. Stinson[1], L.A. Jibb[2], S. Luca[1], M.E. White[1], M. Barrera[2], A. Gupta[2], M. Greenberg[2]

[1]Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada; [2]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: To assess: (1) the impact of cancer and its treatment on adolescents' body image, dating relationships, sexuality, as well as fertility from the perspective of adolescents and their parents, (2) the information needs of adolescents and parents regarding these issues, and (3) whether an Internet-based intervention is an appropriate tool for addressing these needs.
Methods: Twenty adolescents (12-18 years) either under cancer treatment or in remission and 20 parents were recruited from one pediatric tertiary care center. Participants completed demographic and medical history (adolescents only) questionnaires. Semi-structured interviews and participant observation were the primary data collection methods. All interviews were audio-recorded and transcribed. Transcribed data were entered into NVivo 10.0 and independently coded according to the study objectives by two trained analysts. Codes were organized into categories that reflected emerging themes. Discrepancies in coding were resolved through third-party discussion.
Results: Analysis revealed main themes for adolescents and parents around the impact of cancer on: (a) body image (i.e., hair loss, scarring, weight loss/gain, amputation), (b) dating relationships (i.e., relationships 'put to the test', [sexual] relationship readiness), (c) friendships (i.e., social isolation, needed support networks), and (d) fertility (i.e., lack of knowledge). For parents specifically, a change in family and work dynamics was noted. Parents and adolescents generally thought a web-based resource would be beneficial, and especially endorsed the notion of an interactive and engaging site. The anonymity and privacy of a website were cited as main advantages of the medium.
Conclusions: Findings from this study highlight the specific body image-, relationship- and sexuality-issues facing adolescents with cancer. Information gleaned from this study will inform the creation and evaluation of a developmentally appropriate online program for adolescents, parents and healthcare providers. This online program will provide information related to body image, relationships and fertility to ultimately improve the psychosocial health of adolescents with cancer.

O-181

THE CREATIVE BOX: A PATIENT CENTERED COMMUNICATION TOOL FOR USE IN ADOLESCENTS AND YOUNG ADULTS WITH CANCER

V. Van de Velde[1], N. Belpaeme[2], E. Decoene[3], M. Quaghebeur[4], L. Dillen[3], K. Smet[2], S. Vandierendonck[2], A. Raes[3], V. Cocquyt[3], S. Verhaeghe[2]

[1]Pediatrie Hemato Oncologie en Stamceltransplantatie, University Hospital Ghent, Ghent, Belgium; [2]University Centre for Nursing and Midwifery, University Ghent, Ghent, Belgium; [3]Oncologisch Centrum UZ Gent, University Hospital Ghent, Ghent, Belgium; [4]Hematologie, University Hospital Ghent, Ghent, Belgium

Objectives: There is a growing recognition that taking care of adolescents and young adults (AYAs) is distinctive from that of children or adults.
A study has been conducted to explore the personal views of AYAs with cancer in order to get insight in their perspectives during treatment and survivorship.
The integration of study results in a patient centered tool in order to enhance the communication with the AYA and the multidisciplinary team was a secondary objective.
Methods: A qualitative study based on the principles of Grounded Theory was conducted. Twenty four adolescents aged 15 to 25 years were interviewed. Interviews were transcribed and coded using NVIVO 7. Constant comparison was used to analyse the data. Datacollection and –analyse took place in a cyclic process.
Results: From the AYAs' perspective, cancer is something temporarily passing their life-path. The diagnosis is a shock but their coping strategies are focused on preserving identity and guarding normal life. Three phases were identified: cancer freezes life – maintaining normal life is hard and cancer changed their life forever. The AYA is the director in his treatment and customized information, social network, contact with friends, … are key aspects in AYA care. A creative AYAbox has been developed to meet these specific needs and to enhance the communication with the AYA. The box belongs to the AYA and contains a booklet with revealing stories of AYAs' experiences, postcards, a unique AYA tag, stickers mentioning feelings or concerns, cards with information or instructions and smart aids in communication with their relatives and professional caregivers.
Conclusions: The results are translated in a practical and meaningful tool, based on the experiences of the AYAs, inspiring caregivers on our pediatric ward to provide patient centered care in accordance to the specific preferences and wishes of the AYA.

O-182

THE DEVELOPMENT OF AN ONLINE PSYCHOLOGICAL SUPPORT INTERVENTION FOR TEENAGERS AND YOUNG ADULTS (TYA)

J. Cheshire[1], S. Dolby[2], P. Spencer[1], T. Anstiss[3], P. Beynon[1], V. Britton[4], J. Cargill[4], M. Stevens[1]

[1]On Target, University Hospitals Bristol NHS Trust, Bristol, United Kingdom; [2]Psychological Health Services, University Hospitals Bristol NHS Trust, Bristol, United Kingdom; [3]Strategic Health Ltd., Strategic Health Ltd., Buckinghamshire, United Kingdom; [4]TYA Cancer Service, University Hospitals Bristol NHS Trust, Bristol, United Kingdom

Objectives: Findings by the Bristol On Target programme identified 55% TYA received no psychological support after a diagnosis of cancer and showed a significant gap between patient need and availability of information/advice on specific issues. This highlighted a need for accessible information on common psychological problems and for coping strategies/self-management tools. Using a co-creation approach, patients were asked to engage in the development of content, design and functionality of an online psychological/emotional support website.
Methods: Patients and professionals worked collaboratively through a variety of techniques including design studio events, co-design sessions, focus groups, 1:2:1 meetings and email correspondence. Engagement with both patients and professionals allowed the prioritisation and development of content, with a focus on self-management approaches to common psychological distress areas (anxiety, body image, low mood and anger). A series of events were held which brought together patients, healthcare professionals and website developers to establish and refine the required functionality and agree aspects of design for the site.
Results: The creation of a prototype website produced a tangible product for evaluation by the co-creation team, and formed the basis of the specification to develop the final product. The process ensured that the intervention has been built in a way that represents how TYA have asked for psychological support to be delivered, and what will engage them in the content. The format is multi-media based and TYA appropriate in its approach and content, and includes an interactive wellbeing tracker and the ability for user customisation.
Conclusions: The ability to engage and fully integrate the patient into service development, demonstrates the ability for TYA to work with healthcare professionals to design and deliver complex interventions. Further evaluation will confirm acceptability of a product created using this approach to increase availability of psychological support to TYA at times of immediate need.

O-183

USABILITY TESTING OF AN ONLINE SELF-MANAGEMENT PROGRAM FOR ADOLESCENTS WITH CANCER

J.N. Stinson[1], L.A. Jibb[2], A.M. Gupta[2], F. Dupuis[3], B. Dick[4], C. Laverdiere[5], S. LeMay[3], L. Sung[2], E. Dettmer[6], S. Gomer[7], J. Lober[8], C.Y. Chan[9]

[1]Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada; [2]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [3]Health Outcomes, Sainte-Justine University Hospital Research Center, Montreal, Canada; [4]Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada; [5]Viral and Immune Disorders and Cancers, Sainte-Justine University Hospital Research Center, Montreal, Canada; [6]Psychology, The Hospital for Sick Children, Toronto, Canada; [7]Multi-Organ Transplant, The Hospital for Sick Children, Toronto, Canada; [8]Research Institute, McGill University Health Centre, Montreal, Canada; [9]Research Institute, St. Michael's Hospital, Toronto, Canada

Objectives: This study utilized a user-centered design approach to develop a bilingual (English and French) "Teens Taking Charge: Managing Cancer Online" Internet-based cancer self-management program that is acceptable, understandable and easy to navigate for adolescents and their parents.
Methods: Iterative cycles of qualitative usability testing involving user observation were used to refine the intervention. English- (Cycle 1: n = 6, Cycle 2: n = 6) and French-speaking (Cycle 1: n = 6, Cycle 2: n = 4) 12-18 year olds with cancer and one of their parents were recruited from two pediatric tertiary care centers. A brief intervention demonstration was provided. Participants used the website while "thinking aloud" about issues encountered with the interface and content, while a trained observer recorded difficulties and navigation errors. Participants then answered open-ended questions addressing their experience and recommendations for website improvement. Audio-recorded data were transcribed verbatim. French interviews were transcribed into English by a bilingual transcriptionist. Content analysis of transcripts and observer field-notes captured emergent themes related to intervention usability.
Results: French and English adolescents, as well as parents provided similar feedback on needed intervention changes. Overall, participants liked the website aesthetics and content. Both groups rated intervention content as appropriate, credible, and relevant to their cancer experiences. Usability issues identified after Cycle 1 of English and French testing related to (1) aesthetics (i.e., recommendation to eliminate 'blank-spaces' on pages), (2) navigation tools, and (3) English to French translation. Changes were made and no new issues were identified following the second phase of either French or English testing.
Conclusions: The multifaceted usability approach utilized provided insight into how Internet-based self-management programs can be made amenable to adolescents with cancer. Next steps will include feasibility testing before ultimately testing intervention effectiveness in a multicenter randomized controlled trial. It is expected that an acceptable, trusted and cultural competent intervention will improve health outcomes for adolescents with cancer.

O-184

IMPROVING QUALITY OF LIFE OF SIBLINGS OF CHILDREN WITH CANCER AFTER PARTICIPATION IN A PSYCHOSOCIAL GROUP INTERVENTION: A RANDOMIZED CONTROLLED TRIAL

A. Rokeach[1], K. Hancock[1], F. Schulte[2], E. Atenafu[3], P. Nathan[4], M. Barrera[5]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Oncology and Paediatrics, Alberta Children's Hospital, Calgary, Canada; [3]Biostatistics, University Health Network, Toronto, Canada; [4]Pediatrics, The Hosptial for Sick Children, Toronto, Canada; [5]Psychology, The Hosptial for Sick Children, Toronto, Canada

Background: The social and emotional needs and overall quality of life (QOL) of siblings of children with cancer are often ignored. Systematic research assessing psychosocial interventions designed *exclusively* for siblings of children with cancer is rare.
Objective: To determine if participating in *Siblings Coping Together* (SCT), a manualized group intervention (Experimental Group, EG), improves siblings' QOL relative to an Attention Control Group (CG).
Methods: This study employed amulti-siterandomized controlled trial (RCT) design with repeated measures. Inclusion criteria:Siblings, ages 7 to 16 years, of patients at least three months from diagnosis. Both groups completed 8 two-hour weekly group sessions and three assessments (pre-, T1; immediate post-intervention, T2; and three months later, T3). In the **EG,** sessions were designed around a theme, following the SCT plan of educational, social, and therapeutic problem-solving activities through games and crafts; **CG** sessions focused only on the social component through games and crafts. Outcome measures included parent proxy and self-reported QOL (PedsQL4.0). Analyses: Repeated-measures ANOVAs with partial eta-squared as indices of effect size. Institutional approval was obtained and participants signed consent forms.
Results: Preliminary analyses were based on completed data for 53 siblings at T1 and T2 and 26 at all 3 assessments. *Parent Report*. At T3, significant group by time interactions suggested improved t*otal* PedsQL ($\eta^2 = 0.18$) and *school functioning* ($\eta^2 = 0.26$) in the EG compared to the CG over time. Both groups improved *emotional* PedsQLover time ($\eta^2 = 0.25$) with greater scores in the EG ($n = 0.21$). *Self-Report*. There were some trends suggesting general improvements in siblings' t*otal* PedsQLscores ($\eta^2 = 0.20$), and greater improvement in EG's PedsQL scores compared to the CG in *school functioning* ($\eta^2 = 0.14$) and *feelings* ($\eta^2 = 0.19$).
Conclusions: Preliminary findings suggest the manualized group intervention is an effective program, resulting in major improvements in emotional and school related quality of life in siblings of children with cancer.

O-185

PSYCHOSOCIAL HEALTH-RELATED QUALITY OF LIFE IN A COHORT OF CHILDHOOD CANCER SURVIVORS: IMPLICATIONS FOR SURVIVORSHIP CARE

K. Ruccione[1], J. Wood[2], R. Sposto[1], J. Malvar[1], O. Zavala[1], C. Chen[3], D. Freyer[4]

[1]Division of Hematology Oncology and Bone Marrow Transplantation, Children's Hospital Los Angeles, Los Angeles, USA; [2]Divisions of Pediatric Cardiology and Radiology, Children's Hospital Los Angeles, Los Angeles, USA; [3]Keck School of Medicine, University of Southern California, Los Angeles, USA; [4]Children's Hospital Los Angeles, Division of Hematology Oncology and Bone Marrow Transplantation, Los Angeles, USA

Objectives: As part of a larger study characterizing transfusion-derived iron deposition among childhood cancer survivors (CCS), health-related quality of life (HRQOL) constructs including psychosocial health, physical health, and fatigue were assessed.
Methods: Design: single institution cross-sectional cohort study. Participants and parents/guardians completed validated patient-/parent-reported outcomes (PRO) measures in English or Spanish. The primary outcome variable was psychosocial HRQOL.
Results: Participants completed the PedsQL^{TM} 4.0 Generic Core Scale (70 CCS/63 parents) and PedsQL^{TM} Multidimensional Fatigue Scale (71 CCS/63 parents). CCS rated their overall HRQOL as good, although there were subsets (ranging from 13% to 17%) with scores indicating at-risk status for diminished HRQOL. CCS endorsed more fatigue symptoms on every scale than did healthy children, with cognitive fatigue most often reported. Sex, age at study evaluation, duration of follow up, tumor resection, cumulative red blood cell transfusion volume, physical health, and fatigue were considered in a multivariate analysis of psychosocial HRQOL. In the final reduced multivariate model, higher psychosocial HRQOL was associated with older age at evaluation ($p = 0.0003$), better physical health ($p < 0.0001$), and fewer fatigue symptoms ($p < 0.0001$). There was a statistically significant positive correlation between patient self-report and parent proxy report on all aspects of HRQOL and fatigue, although cross-informant variance was noted in ratings of individual items on study measures.
Conclusions: Findings underscore the clinical value of systematically assessing HRQOL, fatigue/other symptoms using validated PRO measures during survivorship care, with both patient and parent as informants whenever possible/applicable. HRQOL assessment may identify symptoms and risk factors that may not otherwise be elicited, and can be used to guide personalized interventions to mitigate adverse psychosocial effects of the cancer experience to improve long-range HRQOL.
Acknowledgements: St. Baldrick's, Concern, ThinkCure, Oncology Nursing, and DAISY Foundations; and Grant Number UL1TR000130, CHLA, National Center for Advancing Translational Sciences at the National Institutes of Health.

IMPROVING PRACTICE THROUGH EVIDENCE AND EVALUATION

O-186

AN EVIDENCE-BASED PRACTICE PROGRAM WITHIN THE CHILDREN'S ONCOLOGY GROUP NURSING DISCIPLINE

C. Rodgers[1], J. Withycombe[2], W. Landier[3], M. Hockenberry[1]

[1]School of Nursing, Duke University, Durham, USA; [2]Pediatrics, Palmetto Health, Columbia, USA; [3]Cancer Center, City of Hope, Duarte, USA

Objectives: Evidence-based practice (EBP) is an increasingly important component of nursing care, especially within pediatric oncology where nurses administer intense therapies. Despite the significance of EBP, much of nursing care lacks evidence based recommendations. In an effort to promote EBP, nursing leaders within the Children's Oncology Group (COG) Nursing Discipline developed a mentorship program to train pediatric oncology nurses on the EBP process. The program was launched in 2012 and to date, has completed four EBP projects. This presentation provides an overview of the EBP mentorship program and highlights the projects.
Methods: The focus for each EBP project was solicited from nursing discussions regarding nursing practice care variations for pediatric oncology patients. Interested groups of nurses applied for the mentorship program, through a formal call sent out to the COG membership. One team was selected in 2012 and three teams were selected in 2013. These teams received didactic information and individual mentorship on the EBP process that included developing a focused question, performing a comprehensive literature search, summarizing and evaluating evidence, creating recommendation statements, and disseminating the information.
Results: All teams completed the EBP process and provided positive feedback on the program. The 2012 team identified physical activity recommendations for childhood cancer survivors with a single kidney. The 2013 teams identified fertility preservation recommendations for childhood cancer patients, prevention and treatment recommendations for post-lumbar puncture headaches in pediatric patients, and hydration recommendations to prevent bladder toxicity in patients receiving cyclophosphamide.

Conclusions: Pediatric oncology nurses are interested in developing EBP recommendations for the pediatric oncology population. A structured mentorship program of didactic information along with guidance of EBP skill application is a successful process. Future COG nursing EBP projects are planned.
Acknowledgement: This project was supported by the National Cancer Institute - Children's Oncology Group Chair's Grant (U10 CA098543).

O-187

WHAT CAN SERVICE DESIGN DO FOR THE PEDIATRIC RADIOTHERAPY EXPERIENCE?

T. Mullaney[1], T. Nyholm[2], J. Lindh[3], V. Lindh[4], K. Nilsson[5], G. Wickart-Johansson[6], A.M. Svärd[7]

[1]Umeå Institute of Design, Umeå University, Umeå, Sweden; [2]Department of Radiation Sciences - Radiation Physics, Umeå University, Umeå, Sweden; [3]Department of Radiation Sciences - Oncology, Umeå University, Umeå, Sweden; [4]School of Nursing, Umeå University, Umeå, Sweden; [5]Oncology, Uppsala University & Akademiska Hospital, Uppsala, Sweden; [6]Oncology, Karolinska University Hospital, Stockholm, Sweden; [7]Oncology, Umeå University Hospital, Umeå, Sweden

Objectives: While radiotherapy is considered a non-invasive treatment for cancer, it can be both stressful and challenging for children to endure, and often requires the use of sedation or general anesthesia which are both costly and have negative side effects. Procedures aimed at reducing distress for both parents and children are important for the child's coping and health during radiotherapy. This research project investigates the benefits of using service design to create supportive pediatric radiotherapy experiences for children ages 2-12, focusing on decreasing fear and anxiety through preparation.
Methods: Service design methods were employed to research the pediatric patient experience in three radiotherapy clinics in Sweden in a controlled study. Observational fieldwork, as well as interviews with care staff, pediatric patients and their parents about the current radiotherapy experience were conducted. This material was analyzed using service design mapping techniques, and used to identify opportunity areas for designing a new pediatric patient journey focusing on preparation.
Results: The final result is a preparation kit comprised of digital and physical elements that uses visual storytelling and play therapy as a way to introduce radiotherapy to younger pediatric patients before the start of treatment. These preparatory materials are directly connected to the treatment experience at the clinic through different tangible touch points. The service involves both designed materials as well as minor changes in clinical routines to ensure the consistency and cohesiveness of the information provided to the child and parents, and has been implemented within the three participating clinics, and is currently undergoing evaluation.
Conclusions: Service design is a useful approach for studying the pediatric patient experience and creating new services aimed at properly preparing and supporting young pediatric patients and their parents throughout the radiotherapy treatment experience.

O-188

EFFORTS OF CHEMOTHERAPY ERROR REDUCTION BY COMPUTERIZED PEDIATRIC CHEMOTHERAPY ORDER ENTRY SYSTEM

H. Shin[1], S. Lee[1], E. Choi[1], K. Koh[1], H. Im[1], J. Seo[1]

[1]Pediatric Hematology/Oncology, Asan Medical Cencer, Seoul, Korea

Objectives: Chemotherapy medication error occurred in a pediatric cancer unit. Chemotherapy administration is a high risk process because of high toxicity and low therapeutic index. While analyzing the causes, a number of near miss cases related to chemotherapy order errors were discovered which had not been reported. We organized multidisciplinary team to work out a feasible solution.
Methods: Computerized pediatric chemotherapy order entry system (CPCOES) was designed by one pediatric hemato-oncologist, clinical nurse specialist, pharmacist and one computerized system developer from March to August 2012. CPCOES was gradually applied to prescribe patient's chemotherapy orders from September 2012. We collected data of prescribing and administration errors from January to October 2012 at a pediatric cancer unit and surveyed doctors and nurses satisfaction before and after the system application.
Results: Total of 14 diagnosis, 135 protocol sheets were set. Three months after CPCOES was put into practice, the monthly average of chemotherapy order errors dramatically decreased by 67% (from 22 to 7.3 cases). The levels of doctors and nurses' satisfaction increased in terms of perceived ease and reduced time consumption for entering and verifying the orders. It also increased the levels of total process satisfaction of doctors and nurses administering chemotherapeutic treatments.
Conclusions: Prospective, CPCOES helped minimize chemotherapy order errors and promote patient safety. Absolutely preventing chemotherapy errors is impossible, but we should take an effort to reduce chemotherapy errors if possible by multi-disciplinary team approach.

O-189

EFFECTIVE PREVENTION AND MANAGEMENT OF TUMOR LYSIS SYNDROME: THE IMPORTANT CONTRIBUTIONS OF ONCOLOGY NURSES

H. Li[1]

[1]School of Nursing, The University of Hong Kong, Hong Kong, Hong Kong China

Objectives: At present there is no published guideline that describes the corresponding nursing interventions for the prevention and management of tumor lysis syndrome. This study has aimed to identify appropriate nursing management procedures for the prevention and treatment of tumor lysis syndrome, in line with the currently available evidence-based medical guidelines in the literature.
Methods: A systematic approach was used to identify relevant studies. The reference materials collected included reviews, reports, guidelines, journal articles, randomized controlled trials, studies and conference reviews. The search results were then limited to publications from the past 10 years (Jan. 2004–Jan. 2014) for which the full texts were available.
Results: Based on the comprehensive literature review, the treatment algorithm for the prevention of tumor lysis syndrome from both the medical and nursing perspectives have been established. In particular, the study highlights the importance of oncology nurses in contributing to the prevention and management of tumor lysis syndrome, which has been commonly overlooked in the existing literature. Moreover, this study provides oncology nurses with the most up-to-date information on the prevalence, pathophysiology and the prevention and treatment interventions for tumor lysis syndrome. This information is crucial for delivering appropriate, high quality care to improve patient outcomes. Most importantly, this study describes a multidisciplinary approach that involves the collaboration of both medical healthcare professionals and oncology nurses in the prevention and treatment of tumor lysis syndrome.
Conclusions: This study has addressed a gap in the literature by describing nursing management in accordance with the currently available evidence-based medical guidelines for risk identification, prevention and treatment of tumor lysis syndrome.

O-190

PHYSICAL ACTIVITY AND FATIGUE IN CHILDREN WITH CANCER

M.C. Hooke[1], L. Gilchrist[2], J. Withycombe[3], L. Tanner[2], N. Hart[2]

[1]School of Nursing, University of Minnesota, Minneapolis, USA; [2]Cancer and Blood Disorders Program, Children's Hospitals and Clinics of Minnesota, Minneapolis, USA; [3]Chldren's Center for Cancer and Blood Disorders Program, Palmetto Health, Columbia, USA

Objectives: Children with cancer identify fatigue as a pervasive, distressing symptom. Fatigue increases during the corticosteroid pulse given during acute lymphocytic leukemia (ALL) maintenance. We explored the feasibility of the FitBit®, an inexpensive device that measures steps and motion, in an activity and fatigue-prevention program. Data uploads to the internet allowing real time access. Aims were: 1. To evaluate if children, who have a step/day goal and receive daily Fitbit® coaching for 2 weeks before a maintenance steroid pulse, have increased steps, 2. To determine the relationship between steps/day pre-pulse and fatigue after the pulse.
Methods: Participants included 17 children in ALL maintenance, age 6- 15, who were receiving a steroid pulse and had a home internet access. The Child Fatigue Scale was administered at baseline, after 2 weeks/before the steroid pulse, and after 5 days of steroids. Participants wore the FitBit® for 3 days pre-intervention, to establish a baseline of steps/day. A tailored weekly step goal was then set by phone with the child and parent. Daily e-mails with FitBit® screen shots were sent with encouraging feedback. During the steroid pulse, participants determined their own level of activity while still wearing the FitBit®.
Results: There was a significant increase in steps/day from week 1 ($10{,}282 \pm 2773$) to 2 (10945 ± 2903) ($p < .001$) and a decrease in fatigue. A significant correlation ($r = -.60$, $p = .02$) was identified between the steps/day during week 2 and fatigue during the steroid pulse with more steps associated with lower fatigue.
Conclusions: The intervention was feasible and effective in this small sample. The mean steps/day each time period (week 1, 2, and during steroids) was over 10,000; an important finding that demonstrates that children with ALL are able to reach the recommended 10,000 steps/day.
Funding: St. Baldrick's Foundation

O-191

PEDIATRIC PALLIATIVE CARE IN CHILDHOOD CANCER PATIENTS:USING FUDAN'S MODEL TO IMPLEMENTATION IN CHINA

Y. Wang[1], G. Shen[2]

[1]Hematology/Oncology Division, Children's Hospital of Fudan University, Shanghai, China; [2]Nursing Department, Children's Hospital of Fudan University, Shanghai, China

Objectives: Many children with childhood cancer in China could not benefit from pediatric palliative care. One national barrier is that we don't have the Medicare hospice reimbursement regulation. In response to the critical need to provide palliative care earlier for these kinds of children, Hematology/Oncology Division of Children's Hospital of Fudan University develop and implement an model of pediatric palliative care in Shanghai, China. Our objective was to describe Chinese experiences in designing, implementing the model.
Methods: Surveys were conducted with parents and staffs firstly. Then, according to the results of the surveys, we constructed the Fudan model of pediatric palliative care in developing area of China, which included multidisciplinary working team and a comprehensive intervention protocol. In the team there were nurse, pediatric oncologist, psychologist, therapist, hospital social worker and volunteer. The protocol contained three sessions: hospital, home and community. In these three sessions, we met children's and family members' needs, supported their emotional and financial difficulty.
Results: From July 2013 to February 2014, 62children have been enrolled in the program. Approximately 72% of parents report they are satisfied with the program and 85% of parents would recommend the program.
Conclusions: Fudan's model is the first in the nation to provide Hospital-Home-Community model of pediatric palliative care from the point of diagnosis onwards. Lessons learned from Fudan's experiences will help guide other city in China.

SUPPORTING CHILDREN AND FAMILIES THROUGH TREATMENT AND BEYOND

O-192

DEPRESSIVE SYMPTOMS IN CHILDREN DURING HEMATOPOIETIC STEM CELL TRANSPLANT RECOVERY

C. Rodgers[1], P. Wills-Bagnato[2], M. Hockenberry[1]

[1]School of Nursing, Duke University, Durham, USA; [2]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: Depressive symptoms such as anxiety and sadness have been reported among pediatric patients prior to and during hematopoietic stem cell transplant (HSCT) hospitalization. These symptoms occur less frequently at one year post HSCT; however, little is known about their prevalence during the immediate months following HSCT hospitalization. This study describes depressive symptom scores as reported by pediatric patients during the first 6 months post HSCT and evaluates the association between the scores and quality of life (QOL).
Methods: A repeated measures design was used to evaluate depressive symptoms and QOL among 23 children and adolescents during HSCT recovery. Demographic and transplant information was obtained from the medical record and patients completed questionnaires monthly for a total of six months post HSCT. Depressive symptoms were measured with the Children's Depression Inventory 2 questionnaire and QOL was measured with the Peds Quality of Life Cancer Module.
Results: Although no significant difference, total depressive symptom mean scores fluctuated over time with the highest score at 1 month and the lowest at 4 months post HSCT. The emotional problem subscale mean scores steadily declined during the first 4 months post HSCT then increased at months 5 and 6. The functional problem subscale mean scores had minor fluctuations over time with the highest score noted at 3 months and the lowest at 4 months post HSCT. Depressive symptom scores were statistically associated with QOL ratings at months 1, 2, and 3 following HSCT.
Conclusions: Pediatric patients experience depressive symptoms throughout HSCT recovery that may be affecting their QOL. Nurses should perform routine assessments for depressive symptoms so that appropriate interventions can be promptly initiated.

O-193

STUDY ON RELATIONSHIP BETWEEN CHINESE CHILDREN'S QUALITY OF LIFE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION AND PARENTING COPING

X.-M. Wang[1], X.Y. Wu[1], F.J. Chen[1], Y. Wu[1], L.L. Liu[2]

[1]Hematology/Oncology Center, Beijing Children's Hospital Capital Medical University, Beijing, China; [2]Nursing Department, Beijing Children's Hospital Capital Medical University, Beijing, China

Objectives: The aims of this study were to assess relationship between quality of life in children after hematopoietic stem cell transplantation (HSCT) and parenting coping.
Methods: A cross-sectional descriptive study was designed using Pediatric Quality of Life Inventory™ 4.0 Generic Core Scale (PedsQL4.0) and Coping Health Invention for Parents (CHIP). All 78 children from the outpatient clinic in Beijing Children's Hospital between December 12, 2011 and March 2, 2013 were recruited. 2 were lost to follow-up and 43 were admitted to inpatient ward. Final sample included 33 patients and 33 parents. Parents were asked to complete CHIP, children age 5 years and over completed age appropriate PedsQL™4.0; for 2∼4 year's children, parent proxy-report was used. Independent sample t-test and spearman correlation were performed.
Results: The median age of children was 5 years (range 2-16 years), the median post-transplant period was 15.5 months (range 3-53 months). 11 were fathers aged 28-43 years and 22 were mothers aged 27-49 years. The physical function scores were 62.51 ± 26.88, the emotional function scores were 71.25 ± 17.73; the social function scores were 83.44 ± 14.67; the school function scores were 59.39 ± 20.89; the overall total scores were 69.44 ± 16.15 (table1). Coping scores of mothers was relatively higher than fathers, the list from most helpful to least helpful in CHIP was: family coping style, medical coping style and support coping style (table2). Spearman correlation coefficients revealed statistically significant positive correlations between children' physical, emotional function and parenting support coping style ($r = 0.41$, $p = 0.02$; $r = 0.31$, $p = 0.03$), between children' social function and parenting family coping style ($r = 0.42$, $p = 0.01$). No significant difference was found between parenting medical coping style and children' quality of life ($p > 0.05$) (table 3).

Table1 Scores of PedsQL™4.0(n = 33)

Scale	Mean ± *SD*
Physical function	62.51±26.88
Emotional function	71.25±17.73
Social function	83.44±14.67
School function	59.39±20.89
Total	69.44±16.15

Table 2 Descriptive Statistics of CHIP (n = 33)

Scale	*Father*(Mean ± *SD*)	*Mother*(Mean ± *SD*)	*Helpfulness ratings*
family coping style	46.00±9.22	46.15±9.17	most helpful
support coping style	23.00±3.79*	33.10±11.61*	least helpful
medical coping style	16.86±6.07	18.20±5.16	moderate helpful
CHIP Overall Score	87.86±16.39	97.45±22.58	

Notes: (1) Independent sample *t* test was used; (2) * $p < 0.05$ father vs. mother

Table 3 Relationship between quality of life in children and parenting coping

Scales		family coping style	support coping style	medical coping style
physical function	r	0.16	0.41	0.01
	P	0.21	0.02*	0.49
emotional function	r	0.03	0.31	0.07
	P	0.44	0.03*	0.36
social function	r	0.42	0.08	0.03
	P	0.01*	0.35	0.44
school function	r	0.01	0.07	0.23
	P	0.48	0.39	0.17

Notes: (1) Spearman correlation was used; (2) * $p < 0.05$

Conclusions: Quality of life in Chinese children after HSCT was low, Chinese mothers coped well than fathers, parents maintaining family integration, social support and self-esteem could increase children's quality of life.

O-194

PARENTS' EXPERIENCE OF THEIR HEALTHY CHILDREN'S PARTICIPATION IN E-HEALTH SUPPORT WHEN A CHILD IN THE FAMILY HAS CANCER

M. Jenholt Nolbris[1], B. Hedman Ahlström[2]

[1]Centrum for childrens right, Queen Silvia's Children's Hospital Sahlgrenska University, Gothenburg, Sweden; [2]Department of Nursing Health and Culture, University West, Trollhättan, Sweden

Objectives: The aim of this study was to investigate parents' experience of their healthy children's participation in e-health support when a child in the family has cancer.
Methods: A qualitative descriptive method was employed in this interview study. Parents from families with a child with cancer and healthy siblings were individually interviewed about their experience of their healthy child's participation in a person-centered support intervention combining education, learning and reflection. The sick child was newly diagnosed with cancer and had been receiving treatment for a maximum of 1 month. The data were collected during spring 2012. Seven parents participated in the study, 5 mothers and 2 fathers in 5 families with 14 healthy children. The interviews were conducted more in the form of a conversation between the interviewer and parent. A qualitative content analysis was used to draw a systematic conclusion from the text and to extract its message.
Results: The result comprises 3 preliminary themes. The parents perceived that: 1) 'The healthy child via his/her contact could think and form an opinion through asking questions and receiving answers'; 2) 'The healthy child was acknowledged and involved during the intervention'; and 3) 'The child became calmer and more hopeful'. The parents felt unburdened as professionals in healthcare provided their healthy children with professional information about the sick child's cancer and also support in understanding and managing their own reactions.

Conclusions: These results allow for a better understanding of the parents' experiences of the situation of their healthy children. The study also indicates that a person centred nursing intervention using e-health in order to help the families may ease family burden.

O-195

SURVIVING THE INCOMPREHENSIBLE - PARENTS' LIVED EXPERIENCES OF LOSING A CHILD TO CANCER

M. Björk[1], A. Sundler Johansson[2], K. Hammarlund[3], I. Hallström[4]

[1]Department of Nursing, School of Health Sciences, Jönköping, Sweden; [2]Department of Nursing, School of Health Care and Social Welfare, Västerås, Sweden; [3]Department of Nursing, School of Life Sciences, Skövde, Sweden; [4]Department of Nursing, Health Sciences Centre, Lund, Sweden

Objectives: The aim of the study was to illuminate parents' lived experience of losing a child to cancer.
Methods: This study is part of a longitudinal research project about family members' experiences of living with childhood cancer within the family. Seventeen families with a child diagnosed with cancer were followed during their child's cancer trajectory. Seven of these families lost their child to cancer, of these, three families participated in this study. Interviews were performed with three mothers and three fathers either at one, two or seven years after the child's death. The interviews were analyzed utilizing a hermeneutical phenomenological approach.
Results: Preliminary results: The essential theme was identified as "Surviving the incomprehensible". In relation to the essential theme, four related themes emerged "Wanting to keep the child, but not to see it suffer", "Wanting to protect the dead child and keep its spirit alive", "Feeling vulnerable and empty" and "Trying to see the light".
Conclusions: For staff, it is important to offer more than one meeting with the parents after the child's death, to be able to identify those in need for extensive support. To enable the contact, the responsibility should lie on the staff, not the parents. The preliminary results suggest that the parents need one contact close to the child's death and then one or two more contacts after a year of more.

O-196

IMPACT OF SOCIAL SUPPORT ON BEREAVED SIBLINGS' ANXIETY: A NATIONWIDE FOLLOW-UP

M.-E.B. Eilertsen[1], A. Eilegård[2], G. Steineck[3], T. Nyberg[3], U. Kreicbergs[2]

[1]Faculty of Nursing, University College Sør-Trøndelag, Trondheim, Norway; [2]Division of Women's and Child's Health Childhood Cancer Research Unit, Karolinska Institutet, Stockholm, Sweden; [3]Division of Oncology-Pathology Department of Clinical Cancer Epidemiology, Karolinska Institutet, Stockholm, Sweden

Objectives: To assess adolescent and young adult siblings' perception of social support prior to and following the loss of their brother or sister to cancer, two to nine years earlier, and their anxiety at follow-up.
Methods: In 2009 a nationwide, long-term follow-up study in Sweden was implemented, using an anonymous study-specific questionnaire. Adolescent and young adult siblings who at the age of 12 to 25 years of age lost a brother or sister to cancer between January 1, 2000 and January 1, 2007 and lived in Sweden were invited, 174 (73%) bereaved siblings participated. The Hospital Anxiety and Depression scale (HADS) was used to measure self-assessed anxiety, relative risks (RR) with 95% confidence interval (CI) were calculated to show the proportion reporting anxiety within dichotomized groups of bereaved siblings. Written informed consent was obtained.
Results: Siblings had a higher risk of anxiety if they perceived their need for social support was unsatisfied during their brother or sisters last month before death, RR = 3.6 (1.8-7.3), time after death, RR = 2.9 (1.5-5.6) and at follow-up, RR = 3.8 (2.0-7.2). Furthermore, a higher risk for anxiety was shown for siblings if they did not perceive that their parents and neighbours cared for them after their brother or sisters' death RR = 2.7 (1.3-5.5), RR = 5.4 (1.3-21.9) respectively.
Conclusions: Bereaved siblings had a greater probability to report self-assessed anxiety if they perceived that their need for social support was not satisfied prior to and following death. Information from both nurses and other health-care professionals to families about the impact of social support may contribute to lessen the siblings' risk of anxiety.

FREE PAPER SESSION 1

O-197

NOTHING ABOUT YOU WITHOUT YOU!: PARENTS' AND PATIENTS' VIEWS ON CLINICAL TRIALS AND BIO-BANKS. RESULTS FROM THE EU-FP7 ENCCA PROJECT AND LESSONS FOR THE FUTURE?

S. Karner[1], J.C.K. Dupont[2]

[1]Österreichische Kinder-Krebs-Hilfe, Österreichische Kinder-Krebs-Hilfe, Vienna, Austria; [2]Département d'oncologie Pédiatrique, Institut Curie, Paris, France

Objectives: In the ethics work-package (WP18) of the "European Network for Cancer Research in Children and Adolescents (ENCCA) ", parents, patients and survivors had the possibility to identify main expectations and concerns about ethical issues in paediatric oncology research, especially on clinical trials and bio-banks.
Methods: Two literature reviews on clinical trials and bio-banks ensured to address the relevant ethical issues. The literature review was followed by collecting the views of stakeholders (professionals, parents' and patients' representatives). Due to this process it was possible to characterise areas of agreement and discrepancies between the stakeholders.
Results: On one hand the views of the stakeholders were collected in two workshops on the topic "Are my tissue-samples available for research? Who knows, who cares?". Parents' and survivors' representatives of the European branch of the International Confederation of Childhood Cancer Parent Organizations (ICCCPO) and young people from the Young Person's Advisory Group (YPAG) at Birmingham Children's Hospital expressed their expectations and concerns about samples and data in paediatric cancer bio-banks. On the other hand, views about clinical trials, the consent procedure and the decision-making process were given by a questionnaire with the topic "Nothing about you without you". The expertise on paediatric cancer research, gained by the parents' and patients' representatives - based on their personal experiences and their activities in national and international levels – was central in the ethical consultation process.
Conclusions: Ethical deliberation does not preclude disagreements between professionals and parents and patients or within these groups. Discrepancies as well as agreements are clues about ways to improve research practices. Therefore, the feedback of parents, patients and survivors is highly appreciated in the definition of ENCCA guidelines on confidentiality in bio-banks and in ENCCA guidelines on clinical trials. Potential for development of long-term interactions is openly discussed.

O-198

QUALITY CARE, RESEARCH AND IMPACT (QCRI) AT CANKIDS…KIDSCAN – ANOTHER DIMENSION TO CHILDHOOD CANCER SUPPORT AND ADVOCACY GROUPS

R. Arora[1], S. Ahuja[2], S. Lederman[2], R. Bhalla[2], S. Prabha[2], P. Arora[3], R. Misra[4], P. Bagai[2]

[1]Medical Oncology, Max Super-Speciality Hospital, New Delhi, India; [2]Quality Care Research and Impact, Cankids…Kidscan, New Delhi, India; [3]Reproductive Medicine, Nova IVI Fertility Clinic, New Delhi, India; [4]Medical Oncology, Medanta - The Medicity, Gurgaon, India

Objectives: Through its presence in 34 centres, Cankids…Kidscan provide awareness, advocacy and patient support to over 13,000 children with cancer every year in India. Our national footprint naturally lends us to participating in research with/without partnering national and international individuals and/or institutions. At the same time any initiatives to assess and improve quality of care have the potential to create a larger impact.
The QCRI team was formed in April 2013 and the idea was to bring together under one umbrella all projects/studies which were being done in Cankids to evaluate service, assess impact and conduct research. The role of the team is to initiate such new projects when appropriate, provide input in ongoing projects and act as a focal point for such activities. The plan has been to put mechanisms into place to deliver the above desired output by setting up a team, holding regular meetings, monitoring progress and eventually assessing performance.
Current **quality care improvement initiatives** include
1. Immunisation for children with cancer – survey of practice in India; developing and disseminating guidelines; patient support for implementation
2. Fertility preservation and support for children with cancer – pilot fertility clinic for survivors; developing and disseminating fertility preservation guidelines.
3. Nutritional support of children with cancer - develop algorithms for nutritional assessment and interventions appropriate for the local setting; patient support for implementation
Current **research projects** include
1. Pilot study of cost of illness in children with cancer
2. Patient Navigation and Tracking to Reduce Abandonment of Treatment in Children with Cancer (PANTRACC) in India – Pilot to start
3. Incidence of cancer in children and young adults in India
4. Multi-centre study on delays in diagnosis and treatment of children with cancer in India – Protocol under development.

O-199

WHEN TRAGEDY INSPIRES HOPE: A PARENTS' CALL TO ACTION TO CREATE AND IMPLEMENT A PSYCHOSOCIAL STANDARD OF CARE FOR CHILDHOOD CANCER

V. Sardi-Brown[1], P. Brown[1]

[1]Psychosocial Programs, Mattie Miracle Cancer Foundation, Washington DC, USA

Objectives: The Mattie Miracle Cancer Foundation will share their experiences with childhood cancer and their mission to create a national standard of psychosocial care. The importance of assembling a multidisciplinary team of professionals, the challenges of operating a large initiative, and the complexities of implementation will be discussed.
Methods: An oral presentation with Power Point slides will discuss:
1) the history of the project,
2) the nature of our multidisciplinary team of leaders and how such a team was assembled,
3) the methodology used to establish a standard of care, and
4) an update on where the project currently stands

O-200

CLOSING THE GAP: BUILDING A FRAMEWORK FOR OPTIMAL ORGANIZATION OF PEDIATRIC PALLIATIVE CARE WITH INPUT FROM EXPERTS AND PARENTS

L.C.M. Kremer[1], M.R.N. Uitdehaag[2], L.M.A.J. Venmans[3], A.A.E. Verhagen[4]

[1]Paediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [2]NA, Saxion University of Applied Sciences, Deventer, Netherlands; [3]NA, Pediatric Association of The Netherlands, Utrecht, Netherlands; [4]Pediatrics, University Medical Center Groningen, Groningen, Netherlands

Objectives: To create a national framework for optimal organization of pediatric palliative care using the 'Idea Factory' method with input from professionals and parents. Recommendations on organization of pediatric palliative care are important for high quality palliative care.
Methods: We extracted recommendations on the optimal organization of pediatric palliative care from selected (inter) national guidelines categorized in prioritized topics. We sent this information to the participants of a work conference. The Idea
Factory is a method to create intensive knowledge exchange about an important theme, to generate good ideas on how to take the theme forward and to create energy and support to implement the best ideas generated. During the conference the participants discussed in small teams their own ideas and a jury in pediatric palliative care scored these ideas using five predefined criteria. After the work conference, the expert panel reduplicated, discussed and prioritized these ideas and defined a final set of recommendations.
Results: We identified eight guidelines focusing on the organization of pediatric palliative care for extracting recommendations. General practitioners, pediatricians, pharmacists, nurses from different care settings, students, psychologists, remedial educationalists, chaplains, social workers, policy staff/managers, healthcare insurers, and parents participated in the working conference. The interactive session and written and verbal commentary rounds resulted in a list of 49 high-quality care recommendations for the organization of pediatric palliative care based on input of professionals and parents.
Conclusions: This study defines a unique set of recommendations for a national framework on the organization of optimal pediatric palliative care, based on literature and creative ideas of experts, including parents. The final set of recommendations provides a basis for improvement programs regarding the organization of pediatric palliative care.

FREE PAPER SESSION 2

O-201

THE OPACC PARENT INTERVENTION GROUP AND PARENT LIAISON PROGRAM AT THE HOSPITAL FOR SICK CHILDREN

S. Kuczynski[1]

[1]Parent Liaison Program at the Hospital for Sick Children (Toronto), Ontario Parents Advocating for Children with Cancer, Barrie, Canada

Objectives: Parents play a crucial role in the care of a child with a cancer diagnosis. Social isolation, fear, and anxiety are realities for families of children admitted to a pediatric oncology ward. The need for a social network and a support community for families of children with a cancer diagnosis is significant (Richards et al, 1986). Peer navigation helps to normalize the experience for those embarking on a similar journey (Boyle-Bride et al, 2013).
Methods: Ontario Parents Advocating for Children with Cancer (OPACC's) mission is to educate, advocate, support, and enable families of children with cancer. Collaborating with The Hospital for Sick Children (HSC), OPACC identified a gap and piloted co-facilitated parent support groups and a dual track peer-to-peer support initiative. Survey results from 2009 suggested 72% of parents wanted a co-facilitated parent support group (i.e. two facilitators, one a member of the psychosocial team and the other a parent of a child treated at HSC), while as many as 70% of parents wanted peer support groups. In response, OPACC engaged in a collaborative initiative with HSC to offer co-facilitating parent intervention groups since 2010. The Parent Intervention Group and Parent Drop-in Group create a safe and supportive environment for parents to connect and provide peer-to-peer support. The Parent Liaison Program began in a volunteer capacity in 1997 and has been active as a member of the Haematology/Oncology Program at HSC since its inception. The OPACC-funded Parent Liaison program has evolved to two Parent Liaison positions at the hospital.
Results: Consistent offering of these programs and participation validate a need is being met by these initiatives, having a positive impact overall for family-centred care.
Conclusions: The OPACC Parent Intervention Group and Parent Liaison Program have bridged a gap and facilitated a social network for families facing a pediatric cancer diagnosis.

O-203

ENGAGING THE YOUTH IN A NATIONAL AWARENESS CAMPAIGN FOR YOUTH AND GENERAL PUBLIC IN LEBANON

R. Farah[1], A.M. Nasr[2], N. Najjar[2], B. Tohme[3], D. Bou-Saba[2], C. Asmar[2], N. Ghantous[2]

[1]Pediatrics, St George Hospital University Medical Center, Beirut, Lebanon; [2]CHANCE, CHildren Against Cancer Association, Beirut, Lebanon; [3]CHANCE, Children Against Cancer Association, Beirut, Lebanon

Objectives: Although childhood cancer is highly curable, cancer remains the leading cause of disease-related deaths among children in several countries. Awareness campaigns are extremely needed in our country.
Methods: In order to raise awareness against cancer in an interactive way, a nationwide poster competition with the theme: "A Healthy Environment and a Balanced Lifestyle for a Cancer Free World" was launched by CHANCE association in collaboration with the Ministry of Environment, among all professional media companies, universities and schools. Eighteen universities were visited over a period of 3 months by our team who delivered awareness lectures on site.
Results: 129 entries were obtained (101 from students in 10 major universities and 28 from professionals), in addition to numerous entries from middle and high school students from 20 public and private schools. A jury was composed of several well-known public figures in the country. Posters were judged according to their power in conveying the message. The top 10 posters were selected and prizes were then awarded personally by the Lebanese Minister of Environment and CHANCE team. All the posters were exposed in the capital Beirut Waterfront for general public viewing. Beautiful posters with powerful messages were viewed live by hundreds of people and seen on TV by thousands on several national and regional television stations.
Conclusions: This nationwide campaign was highly effective and achieved the goal of raising awareness against cancer among the youth in the schools and the universities and in the general public. Such initiatives are rare in the Middle East and should be widely encouraged due to their immediate impact.

FREE PAPER SESSION 1

O-206

POOR OUTCOME OF BRAIN TUMOR IN A DEVELOPING COUNTRY: EXPERIENCE OF A TERTIARY CARE CHILDREN CANCER HOSPITAL IN PAKISTAN

S. Hamid[1], M. Ashraf[1], S. Belgaumi[2]

[1]Pediatric Oncolgy, Children Cancer Hospital, Karachi, Pakistan; [2]Life Sciences, University of Michigan, Michigan, USA

Objectives: To study the clinico-pathological features and the survival of brain tumors in a Pediatric cancer referral centre in Karachi.
Methods: Retrospective chart review of children with brain tumors at Children Cancer Hospital (CCH) from 1997-2013. Data collected on demographics age, sex, location of residence, primary site, morphology, investigations, timing of interventions, treatment modalities and outcome.
Results: 231/3315 (7%) of all registered patients were diagnosed with brain tumors. Male to female ratio was 11:9 with a mean age of 7 years (0.1-19).45% of patients were from karachi and remaining were from distent areas of Pakistan. Mean duration of first symtom to the presentation was 6 months. MRI was the first diagnostic modality in only 40% of the cases. Average interval from first scan until any surgical intervention was 30 days. Posterior fossa was the commonest site in 40% of patients. Gliomas (31%), medulloblastoma (21%) and Ependymoma (13%) were the three most common tumors. There were 129/231 (56%) either visited once or abandoned treatment.50/231 recieved only palliative treatment mostly radiotherapy. Only 50/231 (23%) treated with curative intent.79 (34%) of this cohort had tumor resection (STR or GTR), remaining were either inoperable or only had shunt surgery for hydrocephalus. Immediate post-operative scans were performed in only 40 (17.3%). Chemotherapy and radiotherapy were given as per protocol. Only 24/52 (46%) actively treated patients are alive with a mean follow up at 3 years. For whole cohort of 231 patients, survival is only 10%.
Conclusions: The outcome of brain tumors in our group is very dismal. delays in suspecting, diagnosing and intervention lead to poor outcome. Poor socio-economic status, distence from treating centres and low literacy rates among parents might be the cause of high rate of abandonment in children with brain tumors.

O-207

SURVIVAL IN METASTATIC NEUROBLASTOMA WITH NON-AVAILABILITY OF STANDARD TREATMENT OPTIONS IN PODC SETTINGS

S. Bhatnagar[1]

[1]Pediatric Surgery, B.J. Wadia Hospital for Children, Mumbai, India

Objectives: The standard treatment options in metastatic/advanced Neuroblastoma are chemotherapy, surgery, stem cell transplant, radiation therapy, isotretinoin, anti-GD2 antibody, interleukin-2/GM CSF. In RCN (resource challenged nations) set-ups all of the standard treatment options are not feasible. The survival rates in such situations with judicious use of chemotherapy, surgery, radiation therapy and isotretinoin are presented herewith.
Methods: Retrospective case cohort study was conducted wherein data of all children with metastatic Neuroblastoma was collected from January 2001 to December 2013. The treatment details and survival rates were analysed.
Results: Forty-three children (26 males, 17 females) presented with metastatic Neuroblastoma in the departments of pediatric oncology and pediatric surgery over a period of 12 years. 5/43 abandoned therapy. Upfront chemotherapy was given to all patients after confirmation of diagnosis with CT-Guided biopsy. 26/38 received CECA (Cis-platin, Etoposide, Cyclophosphamide, Adriamycin), whereas others received OPC/OJEC regime (Oncovarin, Cisplatin, Etoposide, Cyclophosphamide/Oncovarin, Carboplatin, Etoposide, Cyclophophamide). All, except 9 patients (29/38) underwent surgical intervention of which incomplete excision and residual tumor was present in 14/29. Isotretinoin was given to 13/38 pateints. 17/29 (58.6%) patients died due to uncontrolled disease spread. 40% of the surviving 41.4% children are on some form of treatment and show non-functional residual lesions at the primary site.
Conclusions: With long-term and diligent management with the available resources for treatment of metastatic Neuroblastoma, the survival rate is about 41.4%. Inspite of residual disease (majority being non-functional), the children remain well. Regular follow-up and immediate intervention is planned for these children in case of disease spread. Loco-regional control along with long term systemic therapy helps in controlling the tumor spread to a great extent.

O-208

KAPOSI SARCOMA IN HIV-INFECTED CHILDREN: A NOVEL CLINICAL STAGING CLASSIFICATION DETERMINES RISK STRATIFICATION

N. El-Mallawany[1], W. Kamiyango[2], J. Villiera[2], C. Kovarik[3], G. Schutze[4], S. Ahmed[2], P. Kazembe[2], P. Mehta[4]

[1]Pediatrics, New York Medical College, Valhalla, USA; [2]Pediatrics, Baylor College of Medicine Children's Foundation Malawi, Lilongwe, Malawi; [3]Dermatology, University of Pennsylvania, Philadelphia, USA; [4]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: Kaposi sarcoma (KS) is the most common HIV-associated malignancy in Africa. Pediatric KS is distinct from adult disease. We aimed to evaluate the clinical characteristics of pediatric KS.
Methods: We retrospectively analyzed 53 HIV+ children with KS between 8/2010 – 9/2012 in Lilongwe, Malawi. Diagnosis was biopsy-confirmed in 24.5%. Local 1st-line chemotherapy included bleomycin and vincristine. HAART was based on local protocol. Statistical analysis was performed using Kaplan-Meier survival curves.
Results: Median age was 8.7 years (1.7-17.4); 27 females & 26 males. Common sites of presentation were: lymph node (75%), skin (56%), subcutaneous nodules (36%), oral (29%), woody and facial edema (21.8%/16.4%), pulmonary (14.5%), and gastrointestinal (3.6%). Severe CD4 suppression occurred in 50.9%. 22.6% presented with platelet count < 50 and 20.7% with hgb < 6. Twelve-month disease status revealed: 50.9% in complete remission (CR), 11.3% with stable disease, and 37.7% died. A pediatric KS clinical staging classification was devised as follows: Stage 1: limited to skin or flat oral mucosa lesions, total < 10 lesions. Stage 2: lymph node involvement, subcutaneous nodules, facial edema, +/- skin or palatal lesions, without visceral involvement and < 20 skin lesions. Stage 3: woody edema +/- any of above. Stage 4: clinical pulmonary or gastrointestinal involvement, or having > 20 skin lesions, +/- any of above. There were zero Stage 1 patients. 53.8% were in Stage 2, 21.1% Stage 3, and 25% Stage 4. This staging classification revealed dramatically different outcomes. 75% of Stage 2 patients were in CR at 12 months. Stage 3 patients had 55% CR but 91% overall survival (OS). Outcomes for Stage 4 patients were unfortunate—12 month OS 8% (all p-values < 0.0001).
Conclusions: This novel pediatric clinical KS staging system differentiates patterns with dramatically contrasting prognoses. Identifying high-risk patients is critical to guide treatment strategy and improve overall outcomes.

O-209

THE DF/BC-HITO OBSERVERSHIP PROGRAM – AN EXAMPLE OF HOW ACADEMIC CENTERS IN RESOURCE-RICH SETTINGS CAN HELP BOOST PROFESSIONAL DEVELOPMENT

P. Friedrich[1], M. Nicola[1], I. Albanti[1], G. Escamilla[2], L. Vega[2], L. Lehmann[1], L. Diller[1], C. Rodriguez-Galindo[1]

[1]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Pediatric Oncology, Hospital Infantil Teletón de Oncología (HITO) Queretaro Mexico, Queretaro, Mexico

Objectives: The DF/BC-HITO Observership Program was a professional training project developed by DF/BC, HITO, Fundación Teletón México, and the Children's Trust. The goal was to ensure HITO's faculty and nurses were expertly prepared to begin treating patients when the hospital opened in November 2013. HITO is a free-standing pediatric oncology hospital and aims to become a Center of Excellence in pediatric oncology care. The medical curriculum aimed to (a) familiarize and acculturate HITO clinicians to the practice of oncology at a Center for Excellence, (b) provide assistance in the creation of multidisciplinary clinical programs, clinical protocols, and policies and procedures and (c) expose providers to a rich clinical research environment and motivate incorporation of research into clinical practice.
Methods: The Program was grounded on adult learning principles. It (a) assumed learners were independent, intrinsically motivated, and self-directed, (b) combined formal with informal and practical experiences, and (c) encouraged participation, ongoing peer-support, and one-on-one coaching.
Results: The Program ran for 18 months. A total of 14 physicians, 5 nurses, 1 pharmacist, and 2 administrators visited DF/BC between February-November 2013; 1-6 months each. Nursing and pharmacy experience is reported separately. Physicians included oncologists, intensivists, pathologists, infectious disease specialists, radiologists, radiation oncologists, pain and palliative care specialists, and surgeons. Observers developed their goals based on interests, roles, and responsibilities, observed direct patient care, attended clinical and educational conferences, national conferences, and formal course work in quality and research methods, improved their English skills, had one-to-one meetings with disease-specific attendings to review protocols, met regularly with organizers to monitor progress, and presented a summary of their experience at the conclusion of their stay.
Conclusions: Academic institutions and Centers of Excellence can meaningfully contribute to boosting the professional development of providers from low-and-middle-income countries. Support from leadership and foundations is essential for success.

O-210

FROM PAPER TO POLICY TO PATIENT OUTCOMES: THE PRIORITIZATION OF CHILDREN IN NATIONAL CANCER CONTROL PLANS IN AFRICA

M. Weaver[1], C.G. Lam[1], J.J. Atteby Yao[2]

[1]Pediatric Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Pediatric Oncology, University Teaching Hospital of Treichville/Medical Sciences Training and Research Unit of Abidjan, Abidjan, Côte d'Ivoire

Objectives: With the increasing burden of noncommunicable diseases, prevention, early detection, treatment completion and palliative care are essential priorities. A country-specific cancer control framework is necessary to organize services, including for pediatric populations.
Methods: We identified African countries reporting to the World Health Organization (WHO) as having national cancer plans, and conducted a comparative content analysis with a health systems perspective. Structured analysis was based on existing development and evaluation frameworks, and elements of cancer control outlined by WHO; items included: timeliness; scope; World Bank country income group; organizing framework; stakeholders; comprehensiveness, and specificity of plan element for pediatrics.
Results: Of 18 African countries reporting a cancer control plan in 2010 and two that have published since, nine current national plans and one continental plan (7 English, 3 French) were accessible through the International Cancer Control Plan portal, representing 4 low-income, 3 lower-middle, and 2 upper-middle income settings: Benin, Cote d'Ivoire, Ghana, Kenya, Mauritius, Morocco, South Africa, Togo and Zimbabwe. Plans spanned from 3 to 9 years (range 2010 to 2019), and four discussed cancer control in the context of other noncommunicable diseases. National plans reported incidence data from national ($n = 4$), subnational ($n = 3$), and hospital ($n = 2$) registries. Two plans explicitly noted families as participatory stakeholders along with government and civil society organizations. All proposed pediatric prevention through public health measures. Early detection, diagnosis, and treatment for children were specified in five plans. One budget itemized pediatric cancer. Palliative care strategies frequently emphasized analgesic access, with specified pediatric needs in two plans. Resources for palliative care were strategized in eight plans and itemized in five budgets.
Conclusions: Explicit strategies and funding for pediatric and palliative services in national cancer plans may help guide prioritized development. Implementation advocacy and funding accountability remain essential to shift plans from paper to improved population outcomes.

FREE PAPER SESSION 2

O-211

PARENTAL EXPERIENCES OF CHILDHOOD CANCER TREATMENT IN KENYA

F. Njuguna[1], S. Mostert[2], A. Seijffert[2], J. Musimbi[1], S. Langat[1], R.H.M. van der Burgt[2], J. Skiles[3], M.N. Sitaresmi[4], P.M. van de Ven[5], G.S.L. Kaspers[2]

[1]Department of Child Health and Pediatrics, Moi Teaching and Referral Hospital, Eldoret, Kenya; [2]Department of Pediatric Oncology-Hematology and Doctor 2 Doctor program, VU University Medical Center, Amsterdam, The Netherlands; [3]Department of Pediatrics, Division of Hemato-Oncology, Indiana University School of Medicine, US; [4]Department of

Pediatrics, Dr Sardjito Hospital, Yogyakarta, Indonesia; [5]Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

Purpose
This study explores the socio-economic, treatment-related and psychological experiences of parents during cancer treatment of their children at an academic hospital in Kenya.
Methods: This cross-sectional study used semi-structured questionnaires. Parents whose children came for cancer treatment consecutively between November 2012 and April 2013 were interviewed.
Results: Seventy-five families were interviewed. Cancer treatment resulted in financial difficulties (89%). More information about cancer and treatment was required (88%). More contact with doctors was needed (83%). At diagnosis, cancer was perceived as curable (63%). However, parents were told by health-care providers that most children with cancer die (49%). Parents had difficulties with understanding doctors' vocabulary (48%). Common reasons to miss hospital appointments were: travel costs (52%) and hospital costs (28%). Parents (95%) used complementary alternative treatment (CAM) for their children. Health-care providers told parents not to use CAM (49%). Parents had not discussed their CAM use with doctors (71%). Community members isolated families because their child had cancer (25%), believed that child was bewitched (57%), advised to use CAM (61%), and stop conventional treatment (45%). Parents shared experiences with other parents at the ward (97%) and would otherwise not understand the disease and its treatment (87%).
Conclusions: Parents suffer financial hardships and are dissatisfied with doctors' communication regarding their children's condition. CAM is very commonly used. Doctors need to improve their communication skills and discuss CAM more openly. A parent support group would be useful, financial support and a facility where the parents and children can stay during the course of therapy.

O-212

A PILOT STUDY TO DETERMINE THE OUT-OF-POCKET EXPENDITURES BY FAMILIES OF CHILDREN BEING TREATED FOR CANCER AT PUBLIC HOSPITALS IN INDIA

S. Ahuja[1], S. Lederman[1], P. Bagai[1], A. Tsimicalis[2], A. Martiniuk[3], R. Arora[4]

[1]Quality Care Research and Impact, Cankids…Kidscan, New Delhi, India; [2]Ingram School of Nursing, McGill University, Montreal, Canada; [3]Faculty of Medicine, University of Sydney, Sydney, Australia; [4]Medical Oncology, Max Super-Speciality Hospital, New Delhi, India

Objectives: In the absence of insurance and/or social support, costs can lead to abandonment of treatment. The objective of this pilot study was to determine the feasibility of assessing the out-of-pocket costs in India (a) two weeks prior and (b) 12 weeks following diagnosis.
Methods: A prospective cost of illness design with twice-weekly, repeated assessments over 12-weeks was piloted from a family household perspective. Parents/caregivers, whose child was being treated for cancer at All India Institute of Medical Sciences and Safdarjung Hospital, had their costs and resource utilization, and impact of these costs recorded.
Results: Eleven families participated. The children (3-19 years) were diagnosed with ALL (n = 5), Neuroblastoma (n = 2), NHL (n = 2), Bone sarcoma (n = 2), or Wilm's tumor (n = 1). Over half of the families' income was from an unskilled worker wage, and at least one parent per family was illiterate or had no schooling. Eight families lived outside New Delhi. The two-week median costs prior to diagnosis were Rs 6565 (US $107) (range: 438-20076 Rs). Nearly 70% of costs prior to diagnosis were: investigations (55%), supportive care (14%) followed by 30% in indirect medical costs (17% travel, 3% lodging, 8% food, 2% other). The median weekly **costs for 12 weeks following diagnosis were** Rs 2263 (US $37)/week (Range: 1071-7102 Rs/week). Half of the weekly costs following diagnosis were direct medical costs (supportive care 15%, investigations 8%, chemotherapy 7%); the other half were indirect medical costs (food 25%,14% travel, 2% lodging, 8% other). To date, five families have been interviewed regarding impact. All have depleted savings, borrowed money, and are in debt. Four families opted selling their assets. Three families indicated their employment was affected and that the schooling of their other children had suffered.
Conclusions: Despite "free treatment" in government hospitals in India significant out of pocket expenses impact employment, schooling and housing.

O-213

REDISCOVERING THE JOY OF LEARNING - YCMOU INITIATIVE FOR CHILDHOOD CANCER SURVIVORS

S. Chawre[1], S. Jha[1], E. Rawat-Pawar[1], D. Chaudhari[2], A. Deshmukh[2], S. Goswami[3], N. Dalvi[3], M. Prasad[3], V. Dhanmankar[3], P. Kurkure[3]

[1]Survivorship, Ugam-Indian Cancer Society, Mumbai, India; [2]Education, Yashwantrao Chawan Maharashtra Open University, Mumbai, India; [3]Pediatric Oncology, After Completion of Treatment (ACT) Clinic Tata Memorial Hospital, Mumbai, India

Objectives: Young survivors of childhood cancers, who were deprived of education due to interruptions as a result of long treatment & socioeconomic constraints, are encouraged & inducted to pursue vocational training to achieve their goals. Yashwantrao Chavan Maharashtra Open University (YCMOU) in collaboration with Tata Memorial Hospital (TMH) offers educational assistance to survivors at subsidized rate or free of cost.
Methods: Ugam, a support group of childhood cancer survivors from After Completion of Treatment (ACT) clinic at TMH functioning under survivorship program of Indian Cancer Society (ICS), has collaborated with YCMOU for empowerment of cancer survivors through educational assistance. YCMOU not only provides graduate and post graduate courses like Management training, Media Graphics and Animation etc.; but also offers preparatory courses in English and Hindi. Patients are able to attain reputed degrees at a very nominal rate or free of cost if survivor is below the poverty line.
Results: Fifteen young survivors have enrolled themselves in different courses such as B.Sc. in Media Graphics and Animation, B.Com, BS-CIT, M.B.A., Civil Supervising etc. and have benefited from such an initiative. These survivors are now capable of achieving a respectable trade or profession owing to the strong educational background. Due to the subsidized fees, they can also opt for multiple degrees as per their choice. The survivors are provided official certificates from the university.
Conclusions: YCMOU has allowed survivors to overcome their limitations and financial obstacles. They are now able to chase their dreams by competing with ever challenging world. More survivors are being encouraged to be a part of this project. Establishing a study center within the premises or near the hospital are being implemented by YCMOU to facilitate overall development of patients and survivors.

O-214

ABSENCE OF SOCIAL SUPPORT NETWORK INCREASES THE RISK OF TREATMENT ABANDONMENT IN CHILDREN WITH CANCER

M. Ospina[1], C.A. Portilla[2], M. Quintero[3], L.E. Bravo[4], M. Aristizabal[5], O. Ramirez[3], On behalf of Vigicancer Working Group[6]

[1]School of Medicine, Universidad del Valle, Cali, Colombia; [2]Pediatric Oncology and Hematology, Fundación POHEMA. Centro Médico Imbanaco. Universidad del Valle. Hospital Universitario del Valle, Cali, Colombia; [3]Pediatric Oncology and Hematology, Fundación POHEMA. Centro Medico Imbanaco de Cali, Cali, Colombia; [4]Registro Poblacional de Cáncer de Cali. Pathology Department, Universidad del Valle, Cali, Colombia; [5]Pediatric Oncology and Hematology, University of California San Diego, CA, USA; [6]Universidad del Valle, Fundación POHEMA, Cali, Colombia

Objectives: Treatment abandonment (TA) is the main reason of therapy failure in children with cancer in low/middle income countries. We explore predictive factors for TA in a cohort of children with cancer in Cali, the third largest city in Colombia.
Methods: We included children diagnosed with cancer at Cali's public university hospital (Jan/01/2010-June/04/2013). We extracted information for predictors from interviews applied by the pediatric oncology unit social worker, and unit psychologist, to caregivers. Outcomes were death, relapse, and TA. Event monitoring was carried-out by Cali's pediatric cancer clinical outcomes surveillance system (VIGICANCER). We estimated rate ratios (RR) among different predictors. We adjusted the hazard ratios (HR) for potential confounders using multivariate Cox regression analyses. Because of the small sample available, we finally applied bootstrapping approach to have a more accurate estimate.
Results: During this period, 162 patients were diagnosed, and 98 psychosocial interviews applied. 55% were male, 18% had colombian-indian ethnicity, 42% came from rural areas, 79% had an income below Colombian minimal wage, and 19% were classified as without social support network (SSN). TA was 18.5%. SSN RR was 7.3 (95%CI: 2.5, 20.5). RR for families with >4 children living in home was 8.6 (95%CI: 2.1, 49.3) and for colombian-indian ethnicity was 4.1 (95%CI: 1.2, 13.7). We did not found a significant association for gender, child or caregiver age at diagnosis, caregiver relationship, caregiver education, household conditions, family monthly income, parental job, and place of origin. In multivariate analyses, only SSN and household children preserved their independent relationship with TA. Bootstrapping adjusted HR for SSN was 2.4 (95%CI 1.1, 33.8).
Conclusions: We found a strong association between being classified as without SSN and TA. It was independent of other covariates, including surrogate measures of wealth. This highlights the imperative understanding of social ties around families with children with cancer, for planning strategies to prevent TA.

PSYCHOSOCIAL INTERVENTIONS: EVIDENCE FOR EFFECTIVENESS

O-215

DOES DEXAMETHASONE INDUCE MORE NEUROPSYCHOLOGICAL SIDE EFFECTS THAN PREDNISONE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA? A SYSTEMATIC REVIEW

L. Warris[1], M.M. van den Heuvel - Eibrink[1], M.A.H. den Hoed[1], F.K. Aarsen[1], R. Pieters[1], E.L.T. van den Akker[2]

[1]Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Pediatric Endocrinology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands

Objectives: Steroid-induced neuropsychological side effects have a major impact on the quality of life in a large proportion of children treated for acute lymphoblastic leukemia (ALL). Dexamethasone is preferred over prednisone because of its higher anti-leukemic activity at the cost of a higher potency to induce metabolic side effects. To evaluate whether

dexamethasone also leads to more neuropsychological side effects than prednisone, we performed a systematic review of the literature.
Methods: Articles were selected in PubMed, Embase and Cochrane on the basis of title and abstract by two independent reviewers using the following inclusion criteria: children with leukemia were receiving dexamethasone and/or prednisone; short and/or long term neuropsychological side effects (mood, cognition, behavior, sleep) were compared between both steroids; original research; written in English. We excluded case series (<10 subjects). We graded their level of evidence using the GRADE system.
Results: Of the 243 potentiallyrelevant articles identified, we included 13 studies for review. Half of the included studies report more neuropsychological side effects with dexamethasone compared to prednisone. However, none of the randomised controlled trials with neuropsychological outcome primarily in view, showed a significant difference between dexamethasone and prednisone on mood and behavior. The randomized trials on long-term cognitive function only showed a subtle significant difference between dexamethasone and prednisone, limited to a minor decrease in word reading and a minor decrease on a IQ measure of fluid reasoning in the dexamethasone group, but both with absence of a clinically significant difference.
Conclusions: Based on this review of the literature, we conclude that the for clinical outcome valuable drug, dexamethasone, does not seem to induce more neuropsychological side effects than prednisone in children with ALL.

O-216

EFFECTS ON QUALITY OF LIFE OF PARTICIPATION IN A COMBINED PHYSICAL EXERCISE AND PSYCHOSOCIAL INTERVENTION PROGRAM FOR CHILDHOOD CANCER PATIENTS

E.M. van Dijk-Lokkart[1], K.I. Braam[2], G.J.L. Kaspers[2], M.A. Veening[2], M.A. Grootenhuis[3], I. Streng[4], T. Takken[5], E. van Dulmen-den Broeder[2], J. Huisman[6]

[1]Medical psychology, VU University Medical Center, Amsterdam, Netherlands; [2]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [3]Psychosocial, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [4]Pediatric Oncology/Hematology, Erasmus MC/Sophia Children's Hospital, Rotterdam, Netherlands; [5]Pediatric Physiotherapy and Exercise Physics, Wilhelmina Children's Hospital/UMC Utrecht, Utrecht, Netherlands; [6]Medical Psychology, Wilhelmina Children's Hospital/UMC Utrecht, Utrecht, Netherlands

Objectives: The QLIM (Quality of Life in Motion) study was designed to evaluate the effects of an intensive 12-weeks intervention program, combining physical exercise and psychosocial support. In this multi-center randomized controlled trial physiotherapist-led exercise therapy program and a psychosocial intervention aimed to enhance patient wellbeing and self-belief were offered simultaneously. Improved wellbeing and health-related quality of life (HrQoL) is hypothesized to increase the willingness and motivation to engage in sport activities and, as a result, to enhance the efficacy of the exercise program and vice versa.
Methods: Childhood cancer patients, aged 8 to 18 years and on or within the first year after treatment, were asked to participate. All participants underwent physical performance tests and completed questionnaires prior to randomization (T0) and after the 12-week intervention (T1). This abstract presents results of the HrQoL-assessments. Patients and parents filled in the PedsQoL generic core scale, cancer module and multidimensional fatigue module, both on T0 and T1.
Results: Sixty-eight patients (mean age = 13.1; SD 3.1) participated. Parents in the intervention group (N = 30) reported a significant improvement in HrQoL of their children compared with the parents of children in the control group (N = 38) on the subscales Physical Functioning (mean (T1-T0 = 16.0 and 6.0 respectively; $p = 0.02$), Pain and Hurt (mean (T1-T0 = 15.7 and -4.5; $p = 0.00$) and Procedural Anxiety (mean (T1-T0 = 12.0 and -1.1; $p = 0.04$). No significant differences in improvement between the two groups were found by patient self-report.
Conclusions: In children with cancer short-term positive effects on HrQoL, as perceived by parents, were found for Physical Functioning, Pain and Hurt, and Procedural Anxiety after participation in a combined physical exercise and psychosocial intervention program. The study is continued to determine the longer-term changes.
Grant: Supported by Alpe d'Huzes/KWF (grant number ALPE-VU 2009-4305).

O-217

COGNITIVE-BEHAVIORAL TREATMENT FOR INSOMNIA IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER

E. Zhou[1], L.M. Vrooman[1], P.E. Manley[2], C.J. Recklitis[1]

[1]Perini Family Survivors' Center, Dana-Farber Cancer Institute, Boston, USA; [2]Pediatric Neuro-Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: Pediatric cancer survivors are at high risk for the development of insomnia due to treatment side effects, inpatient hospitalizations and medical late effects. Insomnia is linked to behavioral and emotional disturbances, substance use, and compromised school/work performance in adolescents and young adults. However, insomnia is an undertreated medical issue in pediatric survivors. Cognitive-behavioral treatment for insomnia (CBT-I) has been empirically validated in other cancer populations, but has not been adapted for use with pediatric cancer survivors, and is not offered as part of routine clinical practice even in major cancer centers delivering specialized survivorship care.
Methods: We are piloting an abbreviated CBT-I program in our regional cancer center's survivorship clinic, and evaluating whether this modified treatment (3 in-person sessions, and up to 2 telephone follow ups) would be feasible, acceptable, and effective in a cancer survivorship setting. Participants monitored their sleep using sleep logs, and completed sleep questionnaires and program evaluations.
Results: 5 adolescent/young adult survivors of childhood cancer (ages 16-41 years) completed our ongoing CBT-I protocol. All reported improved sleep efficiency (pre to post-intervention: 72.9% to 88.4%), and improved Pittsburgh Sleep Quality Index (10.3 to 7.8), and Insomnia Severity Index (15.5 to 9.5) scores. Participants indicated that the abbreviated intervention was preferred to standard treatment, and were open to web/mobile interventions in the future. All indicated that the intervention was helpful, and would recommend the program.
Conclusions: There is a clinical need to incorporate effective treatment for insomnia into routine care for this at-risk population. Ongoing pilot data suggest that brief CBT-I is feasible, acceptable, and effective for improving insomnia in a pediatric oncology survivorship setting. Our findings support the potential to adapt this treatment model to a web/mobile CBT-I platform. We will discuss our plan to improve dissemination of insomnia treatment for childhood cancer survivors through technologically-enhanced intervention delivery.

MEASUREMENT: WHAT'S NEW AND NECESSARY/SCREEN OR NOT TO SCREEN

O-218

CAREGIVER DISTRESS AND PATIENT HEALTH-RELATED QUALITY OF LIFE: PSYCHOSOCIAL SCREENING DURING PEDIATRIC CANCER TREATMENT

L. Pierce[1], J. Fleischer[2], M.C. Hocking[2], M. Alderfer[3], A.E. Kazak[3], L. Barakat[4]

[1]Oncology/Pediatrics, The Children's Hospital of Philadelphia/The University of Pennsylvania School ofNursing, Philadelphia, USA; [2]Oncology/Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, USA; [3]The Center for Healthcare Delivery Science, Nemours and the Alfred I.duPontHospital for Children/The Children's Hospital of Philadelphia, Wilmington, USA; [4]Oncology/Pediatrics, The Children's Hospital of Philadelphia/The University of Pennsylvania School of Medicine, Philadelphia, USA

Objectives: Prior research has focused on identifying family psychosocial risk factors at cancer diagnosis in order to improve pediatric cancer care. This study aimed to evaluate presence of family risk/resources and caregiver distress in the first year from diagnosis and to determine the associations of family risk/resources and caregiver distress with patient health-related quality of life (HRQOL).
Methods: Sixty-seven parents of children with cancer completed the Check-in About Recent Experiences and Strengths (CARES) protocol via iPad during clinic visits within one year of diagnosis. CARES includes: Psychosocial Assessment Tool (family risk/resources), Strengths and Difficulties Questionnaire (patient adjustment), PedsQL 4.0 (patient HRQOL), Distress Thermometer (caregiver distress), and PTSD Checklist-Civilian 6 (caregiver traumatic stress).
Results: Patients ranged in age from 3 months to 18 years (M = 9.3, SD = 5.5 years), and 49% were female. The sample was equally distributed across leukemia/lymphoma, solid tumor and brain tumor diagnoses, and mean time since diagnosis was 158.27 days (SD = 94.6 days). Distress thermometer scores indicated moderate distress (M = 4.86, SD = 2.69). Gender, age, type of cancer, and time since diagnosis were not significantly correlated with family risk/resources, caregiver distress, and caregiver traumatic stress. Reduced patient HRQOL was significantly correlated with family risk ($r = -.41$, $p < .001$), caregiver distress ($r = -.43$, $p < .001$), and caregiver traumatic stress ($r = -.33$, $p < .01$).
Conclusions: Moderate levels of distress regardless of time since diagnosis and the association of caregiver distress with reduced patient HRQOL highlights the importance of psychosocial screening and care throughout the course of pediatric cancer treatment. To target timing and focus of psychosocial interventions, our future research aims to screen psychosocial risk based on patient self- and parent report using an adapted version of CARES during and after cancer treatment.

O-219

HEALTH CARE PROVIDERS' RATINGS OF THE UTILITY OF PSYCHOSOCIAL SCREENING TOOLS IN CHILDHOOD CANCER

A. Di Battista[1], K. Hancock[1], D. Cataudella[2], D. Johnston[3], A. Punnett[4], W. Shama[5], U. Bartels[4], P.C. Nathan[4], M. Barrera[1]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Psychology, London Health Sciences Centre, Toronto, Canada; [3]Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Canada; [4]Pediatrics, The Hospital for Sick Children, Toronto, Canada; [5]Social Work, The Hospital for Sick Children, Toronto, Canada

Objectives: The clinical use of standardized psychosocial screening tools in pediatric oncology is rare, and how useful these tools are perceived to be by health care providers' (HCPs) is unknown. This study examined HCPs' perceived utility of two psychosocial screening tools designed for use in pediatric oncology, the Psychosocial Assessment Tool-Revised (PATrev) and (2) the Psychosocial Care Checklist (PCCL).

Methods: Pediatric oncologists (ONC), nurses (NUR) and social workers (SWK) treating patients at four pediatric cancer centres participated. Institutional approval was obtained for the study at each site and participants signed consent forms. Participants were asked to rank how useful they found: (1) psychosocial summary information derived from the parent-completed PATrev; and (2) the PCCL, an instrument completed by HCPs regarding the psychosocial needs of participating families before they received the psychosocial summary information. Usefulness was assessed using a Visual Analogue Scale (VAS). The VAS had a minimum score of 0 and a maximum score of 10; higher scores indicated greater endorsement for the utility of the measure. X^2 were used for analyses; effect sizes are reported.
Results: Seventy-three HCPs participated (32 ONC, 24 NUR, 10 SWK). Nurses reported the greatest utility endorsement of the PATrev summary compared to pediatric oncologists ($d = 0.77$) and social workers ($d = 2.94$). Similar results were found for the PCCL utility for nurses compared to pediatric oncologists ($d = 0.87$), and nurses compared to social workers ($d = 1.94$). Overall, nurses reported psychosocial screening to be more useful than the other HCPs.
Conclusions: These results suggest that there is variable belief in the utility and endorsement of these psychosocial screening tools among practitioners. Future research should examine specific barriers to uptake and implementation of these tools.

FUNCTIONING AND INTERVENTIONS FOR SIBLINGS

O-220

SIBLINGS OF CHILDREN WITH CANCER: PERCEIVED CHANGES IN THEIR PLACE AND ROLE WITHIN THE FAMILY AFTER CANCER DIAGNOSIS

A. Neville[1], M.R. Simard[1], K. Hancock[1], A. Rokeach[1], L. Brister[2], P. Yogalingam[1], A. Saleh[1], M. Barrera[1]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Child Life, The Hospital for Sick Children, Toronto, Canada

Objectives: Siblings of children with cancer have often been reported as expressing a number of social and emotional difficulties. This qualitative study aimed to examine siblings' perceptions of their place and role within the family when a brother or sister is diagnosed with cancer.
Methods: Institutional approval was obtained and participants signed written informed consent. Participants included 22 siblings, aged 7-17 years, who participated in four rounds of the Siblings Coping Together (SCT) Program, an 8-week, manualized, group intervention program for siblings of children with cancer. Data consisted of materials completed by siblings during the sessions ("feelings trees" and "mind maps"), 49 in-between session homework sheets, 33 pieces of artwork/posters, and 31 logs recording events within group sessions completed by observers and group facilitators. A grounded theory framework was used for thematic data analysis.
Results: Three themes emerged regarding changes in siblings' perceptions of their place and role within the family since their brother or sister was diagnosed: *Being treated differently* (perceptions of being a burden in the family, ways they are included or left out of the cancer experience), *perceptions of being less important than the child with cancer* (seeing themselves as less loved than the affected child, having less privileges), *and perception of changes in their role in the family as a whole* (assisting in care giving for the ill child, a sense of increased responsibility for themselves and within the family, e.g. having to do more chores, becoming more independent). Sharing of these thoughts gradually increased over the 8-week sessions and formed the basis for the group intervention.
Conclusions: These preliminary findings provide rich insight of siblings' own views of the changes in their place and role within the family. These views emerged throughout their participation in the SCT intervention, which allowed them to improve their coping strategies.

O-221

HAVING A SIBLING WITH CANCER: EMOTIONAL EXPERIENCE AND GROWTH THROUGHOUT AN 8-WEEK COPING WITH CANCER INTERVENTION

M. Simard[1], A. Neville[1], A. Rokeach[1], K. Hancock[1], L. Brister[2], A. Saleh[1], P. Yogalingam[1], M. Barrera[1]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Child Life, The Hospital for Sick Children, Toronto, Canada

Objectives: This qualitative study examined the emotional experiences and growth of siblings of children with cancer while participating in a manualized group intervention program: *Siblings Coping Together.*
Methods: Participants were 22 youth partaking in four different rounds of an 8-week group intervention for siblings of patients at least three months from diagnosis. Siblings were eligible to participate if they were between 7-17 years old. Data was derived from materials (e.g., "feelings trees" and "graffiti walls") completed by siblings during the sessions, 49 in-between session homework sheets, 33 pieces of artwork/posters completed by siblings, and 31 logs recording events within group. A grounded theory framework was used for thematic analysis of data. This study was approved by the institution and participants provided signed consent.
Results: Several overarching themes emerged regarding siblings' emotional experiences during the group: *feelingsrelated to their personal experiences regarding their exposure to cancer* (sense of loss, sense of being dismissed or brushed aside by their family, guilt for having negative thoughts about the ill child, and emotional confusion), *feelingsrelated to their perceptions of their brother's/sister's experiences with cancer* (feeling badly for them, worry about death and their well-being, and hope for their cure), and *feelingsrelated to the family context* (as stressful, emotionally labile, and dependent on the treated child's health). Siblings reported several different ways of attempting to regulate these feelings, both adaptively (e.g., "find someone to talk to") or maladaptively (e.g., avoiding difficult feelings). Sharing of these emotional experiences and how to cope with them improved over the 8 sessions of intervention.
Conclusions: These findings provide rich evidence capturing siblings' views about themselves, the ill child's and family's experience, progressively emerging throughout a group intervention. This information is critical for treatment planning and ultimately helping siblings to navigate the experience of having a brother or sister with cancer.

O-222

REDUCTION OF ANXIETY LEVELS IN PARENTS AND SIBLINGS OF CHILDREN WITH CANCER AFTER SIBLING PARTICIPATION IN A PSYCHOSOCIAL GROUP INTERVENTION: A RANDOMIZED CONTROLLED TRIAL

M. Barrera[1], A. Rokeach[1], K. Hancock[1], F. Schulte[2], E. Atenafu[3], P. Nathan[4]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Oncology and Pediatrics, Alberta Children's Hospital, Calgary, Canada; [3]Biostatistics, University Health Network, Toronto, Canada; [4]Pediatrics, The Hospital for Sick Children, Toronto, Canada

Objectives: Childhood cancer diagnosis and treatment can result in major psychological distress in the family. Programs targeting the specific psychosocial needs of siblings are rare and examination of the effects of these interventions on sibling and parental distress has not been previously investigated.
To determine if a manualized group intervention program for siblings, *Siblings Coping Together* (SCT), (Experimental Group, EG), improves anxiety in siblings' (directly) and parents' (indirectly) compared to a Control Group (CG).
Methods: Institutional approval was obtained and participants signed consent forms.
A multi-site andomized controlled trial (RCT) with repeated measures. Inclusion criteria: Siblings, ages 7 to 16 years, and one parent, of patients at least three months from diagnosis. Both groups completed 8 two-hour weekly group sessions and three assessments (T1, pre-; T2, immediately post-intervention; and T3, three months later). **EG** sessions followed SCT's educational, social, and therapeutic problem-solving plan through games and crafts; **CG** sessions focused on socializing through games and crafts. Parents and siblings completed standardized self-report measures of Anxiety (*Multidimensional Anxiety Questionnaire* and *Multidimensional Anxiety Scale for Children*). Repeated-measures ANOVAs were conducted with partial eta-squared as indices of effect size.
Results: Preliminary analyses were based on 53 participants at T1 and 26 at all 3 assessment points. *Parent Self-Report*. Two significant group x time interactions were found: *physiological panic* reactions ($(^2 = 0.30)$ and *social phobia* ($(^2 = 0.20$), suggesting improvements for parents in the EG compared to CG across time. Significant effects of time suggested both groups improved on measures of *total anxiety*, *worry-fears*, and *negative affectivity* ($(^2 = 0.36$, 0.29, and 0.43, respectively). *ChildSelf-Report*. A significant group x time interaction in *panic/separation* suggests improvement in the EG relative to CG, maintained over time ($(^2 = 0.24$).
Conclusions: Preliminary findings suggest major improvements in siblings' *and* their parents' anxiety, sustained over time, following participation in the manualized group intervention program.

O-223

A NEW 1-DAY SYSTEMIC INTERVENTION FOR SIBLINGS OF CHILDREN WHO HAVE CANCER AND THEIR PARENTS: A FEASIBILITY AND PILOT STUDY

C. Besani[1], A. Higgins[1], C. McCusker[1], A. McCarthy[2]

[1]Clinical Psychology Department, Royal Belfast Hospital for Sick Children, Belfast, United Kingdom; [2]FRCPCH M MedSc, Haematology and Oncology Department, Royal Belfast Hospital for Sick Children, Belfast, United Kingdom

Objective: The aim of this study was to determine the feasibility and acceptability of a new 1-day systemic intervention for siblings of children with cancer and their parents, and to examine outcomes of a pilot study. Preliminary evidence was gathered to assess whether the current intervention promoted psychological adjustment in siblings in terms of mood, self-esteem, coping, and resilience, reduced psychosocial risk in the family and improved family functioning and communication.
Materials and methods: This study recruited siblings of children who were being treated for all cancer types at a regional pediatric oncology and hematology centre in the UK over a period of 12 months. Twelve families (17 children and 19 parents) participated in the 1-day systemic therapeutic intervention. The intervention was developed combining three therapeutic components: systemic, narrative and problem solving strategies. The study used a

longitudinal repeated measure design and included pre- and post-intervention assessments (4 and 12 weeks follow-up) and a qualitative assessment of participants' experience (8 weeks follow-up).
Results: Enrolment, retention, attrition and satisfaction data support feasibility and acceptability of the intervention, but also highlight challenges. Outcome data showed changes in the desired directions: at 4 and 12 weeks follow-up, siblings in the intervention groups showed improved scores on the self-esteem, psychological competences, resilience and coping scales, and parents showed improvement on the scales of family functioning and communication and a reduction on the psychosocial risk scale (with Effect Sizes from small to large).
Conclusion
The current study filled a gap in the current literature proving the feasibility and acceptability of delivering 1-day systemic intervention study for siblings of children with cancer and their parents in a regional centre in the UK. The authors developed a manual of the current intervention that allows for the replication of the current study in different oncology centres.

PREDICTING AND IMPROVING BEHAVIORAL FUNCTIONING OF CHILDREN AND SURVIVORS

O-224

CEREBROSPINAL FLUID BIOMARKERS OF OXIDATIVE STRESS, MOTOR DEXTERITY AND BEHAVIOR DURING CHEMOTHERAPY FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

K. Krull[1], M. Hockenberry[2], K. Insel[3], A. Pasvogel[3], P. Gundy[3], D. Montgomery[2], O.L. G.A. Taylor[2], I. Moore[3]

[1]Epidemiology and Cancer Control Psychology, St. Jude Children's Research Hospital, Memphis, USA; [2]School of Nursing, Duke University, Durham, USA; [3]College of Nursing, University of Arizona, Tucson, USA

Objectives: To examine associations between cerebrospinal fluid (CSF) biomarkers of oxidative stress, performance on fine motor dexterity tasks, and parent-reported behavior in children undergoing chemotherapy treatment for acute lymphoblastic leukemia (ALL).
Methods: Children diagnosed with ALL (N = 89; mean [range] diagnosis age = 7.1 [2.3-14.7] years) were followed from diagnosis through the end of chemotherapy at one of two pediatric cancer centers in the southwestern United States. No children received cranial radiation therapy. CSF was collected at diagnosis and prior to intrathecal injections, and was analyzed for biomarkers of oxidative stress, including concentrations of oxidized phosphatidylinositol (PI) and F2 isoprostane (F2-I). High performance chromatography and ELISA was used for PI and F2-I assays, respectively. Children competed measures of fine motor dexterity, visual processing speed and visual-motor integration following induction, during continuation and at the end of chemotherapy. Parent completed ratings of child behavior at these same time-points.
Results: Compared to age-adjusted population norms (z-score = 0, SD = 1.0), children demonstrated significantly lower motor dexterity (mean = −1.19; 95% CI = −1.47, −0.91), visual processing speed (−0.24; −0.45, −0.03) and visual-motor integration (−0.22; −0.42, −0.02) following induction. By the end of therapy, visual processing speed normalized (−0.03; −0.26,0.21), while motor dexterity (−0.39; −0.70, −0.09) and visual-motor integration (−0.37; −0.57, −0.18) remained below average. F2-I concentration was significantly correlated with motor dexterity and visual-motor integration at multiple points in therapy. Oxidized PI was significantly correlated with motor dexterity beginning in the continuation phase. Visual processing speed was not related to CSF biomarkers of oxidative stress. Motor functioning during continuation was associated with increased hyperactivity and anxiety, and decreased functional communication at the end of therapy.
Conclusions: Central nervous system oxidative stress occurs following chemotherapy for childhood ALL, and is related to impaired fine motor function. Early intervention should be considered for these children to prevent progressive visual-motor deficits and behavioral problems.

O-225

"LOOKING FOR WHERE THE WILD THINGS ARE": POLYMORPHISMS AS PREDICTORS OF LATE ONSET LONGTERM COGNITIVE AND BEHAVIORAL DISABILITY

J. Blom[1], L. Pomicino[2], L. Montanari[3], C. Migliozzi[3], G. Rigillo[3], M. Cellini[3], G. Zanazzo[2]

[1]Pediatric Ooncology, University of Modena and Reggio Emilia, Modena, Italy; [2]Institute for Maternal and Child Health, IRCCS Burlo Garofolo of Trieste, Trieste, Italy; [3]Pediatric Oncology, University Hospital University od Modena and Reggio Emilia, Modena, Italy

Objectives: 'Good news stories in medicine have two particular things in common, they have led to early detection and early intervention (Insel, 2013). While we have been able to cure a complex disease such as childhood acute leukemia in 80% of the children diagnosed, we have not been so good at reducing long-term morbidity or disability developed by some of these patients. The nature of the disability is often cognitive or behavioral, which are both recognized to constitute a major burden of disease. The question then is what drives this late onset long-term cognitive and behavioral disability? Here, the hypothesis was tested that various polymorphisms can partially explain the individual variation in developing anxiety and mood disorder as well as neuro-cognitive and behavioral disorders.
Methods: 40 patients (1-18 yrs old) diagnosed with ALL belonging to two pediatric oncology centers were enrolled (protocol AIEOP-BFM-2009) and genotyped for 5HTT, BDNF (va66met) and COMT (val158met) polymorphisms. All patients and their families were subjected to psychosocial assessment (PAT2.1) and a short neurocognitive and behavioral age appropriate screening battery while in treatment and during scheduled follow-up visits.
Results: Patients with SL alleles of 5HTTLPR had a significantly more compromised score in some areas of executive functioning than patients with LL alleles; cognitive areas most affected were those involved in the modulation of emotional responses and flexibility to solve tasks and problems. Due to the sample size and the asymmetric division of the polymorphisms, no clear correlations with polymorphisms of COMT and BDNF were found.
Conclusions: Genes regulating neurotransmitters and vulnerability to stress, such as 5HTTLPR, may represent a factor indicating susceptibility towards the development of cognitive late effects in children treated for ALL, thus, offering a partial mechanism for individual variability among those with similar treatment histories, and providing a possible early predictor for cognitive and behavioral disability.

O-226

EFFECTIVENESS OF AN ADVENTURE-BASED TRAINING PROGRAM IN PROMOTING REGULAR PHYSICAL ACTIVITY AMONG CHILDHOOD CANCER SURVIVORS

O.K. Chung[1]

[1]School of Nursing, The University of Hong Kong, Hong Kong, Hong Kong China

Objectives: Research indicates that regular physical activity enhances the physical and psychological well-being of childhood cancer survivors. Nevertheless, there is growing concern about declining levels of physical activity in childhood cancer survivors. This study aimed to examine the effectiveness of an adventure-based training program in promoting changes in exercise behavior and enhancing the physical activity levels, self-efficacy, and quality of life of Hong Kong Chinese childhood cancer survivors.
Methods: A randomized controlled trial, two-group pretest and repeated post-test, between-subjects design was conducted to 71 childhood cancer survivors (9-16-year olds). Participants in the experimental group joined a four-day adventure-based training program. Control group participants received the same amount of time and attention as the experimental group, but not in such a way as to have any specific effect on the outcome measures. Participants' exercise behavior changes, levels of physical activity and self-efficacy and quality of life were assessed at the time of recruitment, 3, 6, and 9 months after starting the intervention.
Results: Childhood cancer survivors in the experimental group reported significantly higher levels of physical activity and self-efficacy than those in the control group. Besides, there was a statistically significant change in the physical activity levels of childhood cancer survivors in the experimental group.
Conclusions: The adventure-based training program was found to be effective in promoting changes in exercise behavior and enhancing the physical activity levels, self-efficacy, and quality of life of Hong Kong Chinese childhood cancer survivors.

O-227

IMPACT OF POSTTRAUMATIC GROWTH ON SELF-ESTEEM AMONG SURVIVORS OF CHILDHOOD BRAIN TUMORS

K. Kamibeppu[1], I. Sato[1], A. Higuchi[1], T. Yanagisawa[2], S. Murayama[1], T. Kumabe[3], K. Sugiyama[4], A. Mukasa[5], N. Saito[5], Y. Sawamura[6], M. Terasaki[7], S. Sibui[8], J. Takahashi[9], R. Nishikawa[2], Y. Ishida[10]

[1]Department of Family Nursing Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; [2]Department of Neuro-Oncology/Neurosurgery Comprehensive Cancer Center, International Medical Center Saitama Medical University, Saitama, Japan; [3]Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Japan; [4]Department of Clinical Oncology & Neuro-oncology Program, Cancer Treatment Center Hiroshima University Hospital, Hiroshima, Japan; [5]Department of Neurosurgery Faculty of Medicine, The University of Tokyo, Tokyo, Japan; [6], Sawamura Neurosurgery Clinic, Sapporo, Japan; [7]Department of Neurosurgery, Kurume University School of Medicine, Fukuoka, Japan; [8]Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital, Tokyo, Japan; [9]Department of Neurosurgery, Uji Hospital Social Welfare Corporation, Kyoto, Japan; [10]Pediatric Medical Center, Ehime Prefectural Central Hospital, Ehime, Japan

Objectives: Self-esteem is an important resource for childhood brain tumor survivors in their adolescence and adulthood. The purpose of this study was to identify the association between posttraumatic growth (PTG) and their self-esteem among childhood brain tumor survivors. We hypothesized that PTG is related to self-esteem independently of severity of disease, combinations of treatment, relapse, or posttraumatic stress symptoms (PTSS).
Methods: One hundred and thirty eight survivors were recruited at eight hospitals and a clinic in Japan. They were asked to answer a set of questionnaires, including Rosenberg's self-esteem scale, the Impact of Event Scale-Revised (IES-R), Sarason's social support questionnaire (satisfaction) (SSS), and the Posttraumatic Growth Inventory (PTGI) / Posttraumatic Growth Inventory for Children (PTGIC). Besides, severity of disease,

combinations of treatment, and relapse, using the intensity of treatment rating scale 2.0 (ITR-2), and information about presence or absence of late effects were collected from their primary physicians.
Results: A total of 108 survivors answered the questionnaires, however, of which 89 were valid for this analysis. As a result of multiple regression analyses, PTG ($\beta = 0.229$, $p = 0.011$), SSS ($\beta = 0.240$, $p = 0.011$), ITR-2 (physician report) ($\beta = -0.342$, $p < 0.001$), perceived treatment intensity (self-report) (($= 0.219$, $p = 0.019$), and PTSS (($= -0.365$, $p < 0.001$), were independently related to self-esteem after adjusted by sex, late effect, higher brain dysfunction, and difference of questionnaires (PTGI or PTGIC).
Conclusions: In conclusions, the hypothesis was proved. PTG was related to their self-esteem independently of the objective and subjective treatment intensity or PTSS of childhood brain tumor survivors. In addition SSS was also related to self-esteem in the same manner. Therefore, even with a severe disease, undergoing harsh treatments, or PTSS, childhood brain tumor survivors can maintain their self-esteem, when they perceive PTG or SSS. Knowledge of this finding may empower survivors, their families, and medical professionals.

SESSION 1

O-228

AVARTHEC STUDY: CEREBROVASCULAR DISEASE FOLLOWING CHILDHOOD AND ADOLESCENCE CANCER RADIATION THERAPY

V. Bernier-Chastagner[1], E. Desandes[2], C. Carrie[3], C. Alapetite[4]

[1]Radiation Oncology, Institut de Cancérologie de Lorraine, Vandoeuvre-les-Nancy, France; [2]Statistiques, Institut de Cancérologie de Lorraine, Vandoeuvre-les-Nancy, France; [3]Radiation Oncology, Centre Leon Berard, Lyon, France; [4]Radiation Oncology, Institut Curie, Paris, France

Objectives: To describe clinical and imaging characteristics of cerebrovascular disease (CVD) in survivors after irradiation of brain tumors (BT) during childhood. To identify high-risk patients to develop CVD and to adapt their long-term follow-up (FU). The study could help elaborating recommendations on new radiation techniques considering potential risk factors of cerebrovascular morbidity.
Methods: This study was performed in 13 French centers. Patients alive at the time of the study were irradiated between 1990 and 2002, at the age 0 to 18 years, for a BT. Patients who signed the consent had to have a clinical exam, an angioMRI and fullfill a questionnaire about their quality of life (QOL). MRI images were reviewed independantly, Finally, a retrospective analysis of the dosimetry collected radiation criteria, and doses received by the abnormalities.
Results: Out of the 173 included patients, 165 are available for analysis because 6 finally refused the MRI after the inclusion. Median age at diagnosis and at the moment of the study are respectively 9 and 24 years, Median FU is 15 years198 CVD have been observed in 118 patients. Most of them are cavernoma (132 cases for 80 patients). Twenty-five serious abnormalities as carotid stenosis and several second tumors have been detected, The average dose received by the site of cavernoma was 43 Gy. One hundred and six QOL questionnaires are available.
Conclusions: There were 71.5% of survivors irradiated for BT during childhood developed a CVD. Characteristics and correlation with dose will be discussed, as well as impact on QOL.

O-229

SINGLE CENTER RESULTS FOLLOWING PROTON BEAM THERAPY WITH ATYPICAL TERATOID RHABDOID TUMORS OF THE CENTRAL NERVOUS SYSTEM

J. Buchsbaum[1], C. Haskins[1], B. Jyoti[1], M. Hines[1], V. Simoneaux[1]

[1]Radiation Oncology, IU Health Proton Therapy Center, Bloomington, USA

Objectives: Atypical teratoid rhabdoid tumor (ATRT) is a rare embryonal tumor seen predominantly in infancy and childhood. Outcomes are generally dismal with median survival estimated at around six months to a year. The purpose of this study was to evaluate proton beam therapy (PBT) outcomes in this population.
Methods: Sixteen patients with a diagnosis of ATRT were treated between November 2007 and January 2013 at our center. All patients were treated with PBT. Fraction sizes of 1.8 Gy/fraction were used to deliver between 28 to 33 fractions. Seven patients received craniospinal PBT. There were 12 male and 4 female patients. The median age at diagnosis was 18.5 months, with a range of 5 months to 39 years. Eight had metastatic disease at diagnosis. Fourteen patients underwent surgery. Fifteen patients received chemotherapy.
Results: Mean survival was 1.2 years (standard deviation 0.3 years). The median radiation dose to the tumor bed for all patients was 54 Gy. Eight patients received craniospinal irradiation (CSI) in addition to cranial irradiation with a median dose of 36 Gy. Median follow-up time was 0.81 years (range 0.0-4.16 years). 11 patients are stable, 3 patients are deceased, and 2 patients developed progression of disease. Four patients suffered nausea and vomiting (CTC Grade 2) as a result of treatment, and four patients also suffered moderate skin erythema (CTC Grade 2). Two patients suffered from both weight loss and general fatigue during treatment. All 8 patients with localized disease are alive while those with metastatic disease have shown a steady decline in survivor numbers ($P = 0.066$).
Conclusions: PBT is well tolerated in this heavily treated population. In the background of poor survival, these early outcome data are promising, especially in those without metastatic disease. Further follow-up is necessary.

O-230

THE ROLE OF CRANIAL RADIOSURGERY FOR PEDIATRIC PATIENTS

E. Murphy[1], S. Chao[1], L. Angelov[2], G. Neyman[1], C. Reddy[1], G. Barnett[2], P. Rasmussen[2], T. Tekautz[3], J. Suh[1]

[1]Radiation Oncology, Cleveland Clinic, Cleveland, USA; [2]Neurosurgery, Cleveland Clinic, Cleveland, USA; [3]Pediatric Oncology, Cleveland Clinic, Cleveland, USA

Objectives: The indications for radiosurgery for pediatric patients are often extrapolated from adult patients. Reduced normal tissue exposure is ideal, but the toxicities of treatment are not well characterized. Outcomes and toxicity are analyzed from our institutional experience of Gamma Knife radiosurgery (GKRS) for pediatric patients.
Methods: A query of the GKRS database was performed to identify patients age ≤ 18 at the time of GKRS. Diagnosis, pre-treatment factors, GKRS data, post-treatment neuroimaging studies, and toxicity information were evaluated. Survival times were calculated using the Kaplan-Meier method.
Results: From 1997 through 2013, 35 pediatric patients were identified; 16 female and 19 male. Median follow up was 43.1 months (Range: 0-204.2). Diagnoses included: AVM (23), schwannoma (3), low-grade astrocytoma (3), pituitary adenoma (1), ependymoma (1), medulloblastoma (1), and metastasis (3). Median age was 14 yrs and and median LPS at GKRS was 90. Six patients had prior fractionated radiotherapy and chemotherapy. Ten patients had prior resection: 7 GTR, 1 NTR, and 2 STR. GKRS was the initial treatment for 24 patients and used for recurrence or progression for 11 patients. Median prescription dose was 15 Gy (Range: 12 to 27 Gy), dose conformality was 1.817, dose heterogeneity was 1.996. Median treatment volume was 2.8 cc., and max tumor diameter was 2.63 cm. Following GKRS, 9 patients had progression: 6 distant, 2 local, and 1 combined. One-and 5-year local progression free survival, progression free survival, and overall survival was 96.7% and 87.4%, 87.3% and 70.3%, and 87.7% and 82.4%, respectively. CTCAE v 4.0 CNS toxicity grade 1-2 occurred in 10 pts, and grade 3 in 1 pt. Median time to toxicity was 9 months, (Range: 0-80.3).
Conclusions: Pediatric patients tolerated GKRS well with reasonable toxicity. Local control was good across the spectrum of diagnoses treated. Prospective evaluations should be performed to develop guidelines for the use of radiosurgery in this population.

FREE PAPER SESSION

O-231

SIGNIFICANCE OF PRIMARY TUMOR VOLUME ON RECURRENCE AND SURVIVAL IN PEDIATRIC PATIENTS WITH NASOPHARYNGEAL CARCINOMA

E. Eldebawy[1], S. Ahmed[2], H. Ammar[3], A. Elnashar[4], M. Zaghloul[1]

[1]Radiation Oncology, Children Cancer Hospital Egypt (CCHE) and National Cancer Institute Cairo University, Egypt; [2]Radiation Oncology, Children Cancer Hospital Egypt (CCHE), Cairo, Egypt; [3]Biophysics, Children Cancer Hospital Egypt (CCHE), Cairo, Egypt; [4]Statistics, Children Cancer Hospital Egypt (CCHE), Cairo, Egypt

Objectives: Primary tumor volume (PTV) has been recognized as a promising prognostic indicator in the treatment of adult nasopharyngeal carcinoma (NPC). Our study was designed to analyze the value of the primary tumor volume [gross tumor volume of the primary site (GTV-P)] in predicting the treatment outcome in pediatric patients with NPC treated with intensity modulated radiotherapy (IMRT).
Methods: A retrospective review of 30 consecutive pediatric patients aged <18 years with stage I–IVB NPC was performed. All Patients received three cycles of Induction chemotherapy with cisplatin and 5-fluorouracil, and three additional cycles of cisplatin alone during radiation therapy. Radiation therapy was administered using intensity modulated radiotherapy (IMRT) technique and inverse planning system. Gross tumor volume of primary tumor plus retropharyngeal nodes (GTVprn) was calculated to be an index of treatment outcome.
Results: The median PTV was 45.9cc. Large GTVprn (>55 ml) was associated with a significantly poorer local control, lower distant metastasis-free rate, and poorer survival. 3-year overall survival in the large tumor volume group (>55 ml) and the small tumor volume ($\leq$55ml) were 58% and 100%, respectively ($p = 0.007$). The 3-year disease free survival was 28% in the large tumor group and 94% in small tumor volume group ($p = 0.002$) while 3 year local recurrence free survival in the large tumor group 77% and 100% in small tumor volume group ($p = 0.02$). The 3-year overall survival, disease-free survival, local control, and distant metastasis-free rates in all patients were 87%, 76%, 92%, and 76%, respectively.
Conclusions: PTV had a close relationship with survival rates and recurrence rates in pediatric patients with NPC. The large tumor volume group (PTV > 55 mL) was associated with more recurrence and poor survival rate.

O-232

COLORECTAL CANCER SCREENING IN CANCER SURVIVORS TREATED WITH RADIATION THERAPY

S. Samiee[1], S. Ahmed[2], K. Hui[2], R. Gryfe[3], A. Pollett[4], M. Cino[5], G. Gingras-Hill[1], A. Ng[6], D. Hodgson[1]

[1]Radiation Medicine, Princess Margaret Hospital, Toronto, Canada; [2]Clinical Research, Princess Margaret Hospital, Toronto, Canada; [3]Dept. Surgery, Mt Sinai Hospital, Toronto, Canada; [4]Dept. Pathology, Mt Sinai Hospital, Toronto, Canada; [5]Dept Gastroenterology, Toronto Western Hospital, Toronto, Canada; [6]Radiation Medicine, Farber Cancer Institute Harvard Medical School, Boston MA, USA

Objectives: Due to increased risk of colorectal cancer (CRC) among childhood cancer survivors who received abdominal or pelvic radiation therapy (RT), guidelines recommend that these survivors should start CRC screening earlier than general population. However, there is no evidence suggesting that earlier CRC screening for these survivors would be effective. We undertook a prospective study to determine the polyp detection rate among young survivors and compare this to the 20% prevalence rate expected among average risk individuals >50 years old for whom CRC screening is accepted.
Methods: Asymptomatic cancer survivors aged 35-49 years who were treated with abdominal radiation or TBI (at least 12Gy), ≥10 years prior were eligible. Patients with past medical history of polyps, Crohn's disease, ulcerative colitis or any colorectal screening within the last 5 years were excluded. All patients underwent a full colonoscopic examination with adequate bowel preparation, and any retrieved polyps were reviewed by a gastrointestinal pathologist.
Results: Fifty five patients (27 males, 28 females), with a median age of 45 years (43-49), were enrolled. A total of 52 polyps were found in 26 patients (47.3% of patients; 95% CI = 31.6%-61.2%). Adenomatous polyps were found in 19 patients (34%; 95% CI = 22%-48%). 32% of all polyps were deemed to be within radiation field (17/52; 95% CI = 20-47%). 61% of all polyps were found beyond the ascending colon beyond the reach of a sigmoidoscope (either in the transverse colon, descending colon or cecum; 32/52; CI = 47%-74%).
Conclusions: The prevalence of adenomatous colorectal polyps in abdominal-RT-treated survivors is comparable to or greater than that described among the general population aged ≥ 50 years, for whom CRC screening is generally recommended. This provides indirect support for guidelines recommending the early initiation of screening. It is recognized that most polyps occurred outside the RT field, which complicates interpretation.

O-233

LIMITED MARGIN RADIOTHERAPY FOR PEDIATRIC PATIENTS WITH EWING SARCOMA ACHIEVES HIGH RATES OF LOCAL TUMOR CONTROL

A. Talleur[1], F. Navid[1], S. Spunt[2], E. McCarville[3], M. Neel[4], A. Davidoff[4], S. Mao[5], J. Wu[5], M. Krasin[3]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Hematology/Oncology, Lucile Salter Packard Children's Hospital, Palo Alto, USA; [3]Radiological Sciences, St. Jude Children's Research Hospital, Memphis, USA; [4]Surgery, St. Jude Children's Research Hospital, Memphis, USA; [5]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Determine the rate of local failure (LF) using limited margin radiotherapy (RT) and dose escalation (for tumors ≥8 cm) in pediatric patients with Ewing sarcoma (EWS).
Methods: Eligible patients with EWS were treated on a Phase II institutional trial of limited margin RT. Treatment volumes were based on CT/MR treatment planning datasets. The clinical target volume (CTV) included gross tumor (GTV) plus a 1 cm anatomically constrained margin. Planning target volumes (PTV) ranged from 0.5-1 cm. Unresected tumors <8 cm received standard RT dose of 45Gy to the CTV (PTV1) and a boost to 55.8Gy to the GTV (PTV2). For tumors ≥8 cm, RT dose was escalated to include a boost to 64.8Gy to the GTV (PTV2). Patients with marginal resections received adjuvant RT of 50.4Gy to the CTV (PTV1). Initial follow-up occurred every 3 months, including imaging of the primary tumor site.
Results: Forty-one patients with EWS who had localized (22) or metastatic (19) disease were enrolled on trial. Thirteen had primary pelvic tumors. Median (range) age, tumor size and follow-up were 13.4 years (2.9-24.7), 8.6 cm (3.0–17.0) and 44.1 months (2-125, {62 months for patients remaining on-study}), respectively. All patients received systemic chemotherapy. The median (range) RT dose for all patients was 56.3Gy (45.0-65.48). Fifteen patients received adjuvant, 12 standard, and 11 dose escalated RT. Ten patients had distant failure and one patient local and distant failure. The 5-year cumulative incidence of LF was 0.0244 ± 0.0244. Within local and metastatic patient groups, differences in failure-free survival were not statistically significant based on initial tumor size, age or site of disease.
Conclusions: Treatment with limited margin RT including dose escalation for unresected tumors ≥8 cm provided favorable local tumor control in this trial. This RT approach warrants further investigation in a larger trial incorporating standardized chemotherapy.

O-234

PRELIMINARY RESULTS FROM THE PEDIATRIC PROTON CONSORTIUM REGISTRY (PPCR): A COLLABORATION OF US PROTON CENTERS TO ACCELERATE PROTON THERAPY RESEARCH

T. Yock[1], D.J. Indelicato[2], W. Hartsell[3], H. Symecko H. Kasper[4], S. Perkins[5], C. Hill-Kayser[6], A. Mahajan[7], A.L. Chang[8], S. Childs[9], F. Laurie[10], J. Buchsbaum[11], L. Raeke[1], C. Neville[1], M. Ladra[1], B.Y. Yeap[1]

[1]Dept. of Radiation Oncology, Massachusetts General Hospital, Boston, USA; [2]Dept. of Radiation Oncology, University of Florida Proton Therapy Institute, Jacksonville, USA; [3]Dept. of Radiation Oncology, CDH Proton Center Chicago, Chicago, USA; [4]Dept. of Radiation Oncology, MGH, Boston, USA; [5]Dept. of Radiation Oncology, Washington University, St. Louis, USA; [6]Dept. of Radiation Oncology, University of Pennsylvania, Philadelphia, USA; [7]Dept. of Radiation Oncology, MD Anderson Cancer Center, Houston, USA; [8]Dept. of Radiation Oncology, Hampton University, Hampton, USA; [9]Dept. of Radiation Oncology, Mayo Medical School, Rochester, USA; [10]Dept. of Radiation Oncology, Qarc University of Massachusetts, Providence, USA; [11]Dept. of Radiation Oncology, Indiana University, Providence, USA

Objectives: Pediatric proton investigators have united to form the Pediatric Proton Consortium Registry (PPCR) to accelerate research on the role of Proton Radiotherapy (PRT) in children. A comprehensive (680+field) REDCap web-based database for pediatric cancer patients was created. The early demographics and PRT patterns-of-use/care are described here.
Methods: All proton patients <22 years treated at PPCR centers are eligible. The registry captures baseline demographics, insurance status, disease/health information, treatment details, and follow-up of consenting children/families. Basic information on demographics/diagnosis are collected on unenrolled patients.
Results: Six sites are IRB approved, 3 enrolling. 242 pts enrolled, 16 refused/or were missed. Nine more sites will open in 2014. The PPCR data reveals: median age 10.1 (0.7-21.9yrs); 41% female; 77.4%white, 5%black, 6%Asian. 98.5% are insured: 68% private/employer-based, 13.3%Medicaid; 14.8%International, 2%self-pay. Referrals are from pediatric oncologists 55.7%, neurosurgeons 15.8%, and radiation oncologists 14.8% of the time. MA, IL, NY, FL states lead enrollment. Europe, Asia, Australia and Canada comprise 71.9%, 18.8%, 6.3%, and 3.1% of international patients.
59.8% have CNS tumors; 40.2% have non-CNS; 71.7% of tumors are primary, 23.7% recurrent, 4.5% metastatic. CNS histologies: glioma (20.2%); medulloblastoma (19.3%); ependymoma (18.5%); craniopharyngioma (16.8%). Non-CNS histologies: chordoma (21.3%); RMS (18.8%); bone sarcoma (16.3%); other STS (10%). 4.1% have a genetic syndrome. 5.9% have KPS/Lansky = <60.
Radiotherapy intent was curative in 97.4%. Type of PRT: 74.4% passively scattered; 9.9% pencil beam scanning (PBS); and 8.1% Proton-SRS. Mean total RT dose is 51.4 GyRBE (12-81). 15.1% received CSI, 54.4% received chemotherapy; 15.2% enrolled on COG trial. 39% return to proton center for f/u care.
Conclusions: The PPCR is a successful multicenter US based registry for children receiving PRT. The early demographics and patterns-of-use/care demonstrate the PPCR can be used to understand the population referred for PRT and track their outcomes. All US proton centers that treat children are invited to join the PPCR.

O-235

HIGH DOSE RATE BRACHITHERAPY IN CHILDHOOD SOFT TISSUE SARCOMAS

G. Scarzello[1], M.S. Buzzaccarini[1], E.E. Pane[1], G. Cecchetto[2], P. Dall'Igna[2], D. Di Carlo[2], D. Canonico[3], G. Bisogno[2]

[1]Radiation Oncology, Istituto Oncologico Veneto-IOV IRCCS, Padova, Italy; [2]Pediatrics, University Hospital, Padova, Italy; [3]Physics, Istituto Oncologico Veneto-IOV IRCCS, Padova, Italy

Objectives: To evaluate the efficacy of HDR-BT in children undergoing treatment for STS.
Methods: From 1998 to 2013, 50 children, 7 year median age, with STS received HDR-BT at IOV. Forty-eight have been treated on primary lesion, 2 for relapse. Extremities were most commonly involved (18), followed by head and neck (11), vagina (11), orbit (5), chest-abdominal wall (5). Histology was embryonal rhabdomyosarcoma (26), alveolar rhabdomyosarcoma (11), Ewing-PNET (5), fibrosarcoma (3), Nos rhabdomyosarcoma (2), leyomyosarcoma (2) and myoepithelial carcinoma (1). Ten children had lesions greater than 5 cm (5 limbs, 3 chest-abdominal wall, 2 vagina). Surgical margins where positive in 27 (11 vagina, 7 limbs, 4 orbit, 3 non parameningeal head-neck, 2 chest-abdominal wall), 1 (orbit) had macro residual. All patients underwent local excision, followed by temporary interstitial HDR-BT using iridium-192. Forty-five patients have been treated with HDR-BT alone, while 5 received HDR-BT plus EBRT. HDR-BT dose has been 36 Gy, in 12 fractions, twice per day. All children receiving EBRT underwent irradiation up to a total dose of 32 Gy in 20 fractions of 1.60 Gy, twice per day, after a 18 Gy HDR-BT boost.
Results: At a 8 year median follow up, 45 patients are alive without disease, 1 is alive without disease after amputation. Two children failed locally and after developed lung metastasis, 2 had nodal and lung metastasis without LR; all died for tumor progression. The 5-year local control, DFS, and OS were 94%, 90%, and 92%, respectively. Late mild subcutaneous fibrosis is evident in near all patients. One female with wrist sarcoma underwent surgery because of finger movements impairment with a very satisfactory outcome. Two children presented esthetically unacceptable scars, very well corrected by plastic surgery. One female presented hematocolpos at menarche.
Conclusions: HDR-BT, in select groups of children, results in excellent local control and functional outcome with reduced treatment-related morbidity.

O-236

SECOND MALIGNANT NEOPLASMS AND CAUSES OF DEATH IN PATIENTS TREATED OF HODGKIN DISEASE IN CHILDHOOD IN SLOVENIA

L. Zadravec Zaletel[1], B. Jereb[1]

[1]Radiotherapy, Institute of Oncology, Ljubljana, Slovenia

Objectives: We studied the frequency of second malignant neoplasms (SMN) and causes of death in patients (pts) treated of Hodgkin disease (HD) in childhood in Slovenia.
Methods: One hundred fifty-six pts under the age of 16 were treated for HD in Slovenia between 1960 and 2007. At diagnosis they were 3 to 16 (med. 12) years old. Nineteen pts died of HD 1 to 8 (med. 2) years after diagnosis. December 2013 the follow-up time of the remaining 137 pts was 5 to 43 (med. 24) years.
Results: Thirty-one SMNs were found in 28 pts 5-42 (med. 22) years after diagnosis; in 1 (breast cancer) of 13 (8%) treated with ChT alone, in 4 (2 thyroid cancers, 2 basaliomas, one malignant melanoma and pleural mesothelioma) of 16 (25%) treated with RT alone and in 23 (10 thyroid cancers, 3 breast cancers, 2 acute myeloid leukemia, 3 basaliomas and parotid cancer, colon cancer, lung cancer, uterine cancer, RMS of maxillar sinus and intracranial meningeoma one of each) of 108 (21%) pts treated with RT and ChT. Twenty-five SMNs arised inside RT field Cumulative incidence for SMN was 11,2% at 20 years, 25,5% at 30 years and 32,1% at 40 years of follow-up. Seven pts died of SMN (2 with AML, one with lung cancer, mesothelioma, colon, breast cancer and RMS 7 to 43 (med. 26) years after diagnosis and 6 of other causes: heart damage in 4 pts 23 to 30 (med. 26) years after diagnosis and infection in 2.
Conclusions: In our study incidence of SMNs after treatment of HD in childhood was high, thyroid cancer being the most frequent. SMNs were the most important cause of death more than 10 years after diagnosis of HD. Longlife follow-up including screening for SMNs and heart disease in those patients is of vital importance.

O-237

CAROTID ARTERY DISEASE AFTER NECK IRRADIATION IN LONG-TERM SURVIVORS OF HODGKIN DISEASE IN CHILDHOOD

L. Zadravec Zaletel[1], M. Zaletel[2]

[1]Radiotherapy, Institute of Oncology, Ljubljana, Slovenia; [2]Vascular Neurology, University Medical Centre, Ljubljana, Slovenia

Objectives: Some studies have shown carotid artery disease in pediatric cancer survivors treated with neck irradiation (RT), although with contradictory results. We compared parameters of carotid artery disease in patients (pts) treated of Hodgkin disease (HD) in childhood with neck RT and cardiovascular risk factors matched controls.
Methods: Fifty-six pts were treated of HD under the age of 16 in Slovenia between 1975 and 1986; 32 of 40 alive pts received neck RT and were eligible for study, 8 refused cooperation, 24 (8 females, 16 males) were included. They were 3 to 16 (med. 11) years old at diagnosis and had evaluation 27 to 38 (med 33) years later at the age of 29 to 48 (med. 43) years. They received neck RT with 20 to 42 (med. 30) Gy, 19 pts received chemotherapy. Aloka alfa 7 was used to determine plaque and intima media thickness in common carotid arteries. Carotid artery stiffness was measured by new high-resolution echo tracking using colour-coded duplex sonography. The following carotid stiffness indexes were calculated: local pulse wave velocity (PWVb m/s), strain pressure elasticity index (Ep) (kPa), beta index and augmentation index (Aix,%). The variables of the two groups were statistically analyzed by SPSS 20.
Results: Values of local carotid stiffness indexes were significant higher: beta stiffness ($p = 0.03$), PWVb ($p = 0.021$), Ep ($p = 0.005$), Aix ($p < 0.000$) and there were significant more arterial wall calcinations ($p < 0.000$) in the group of survivors. The intima-media thickness ($p = 0.285$) and the number of plaques ($p = 0.55$) were not different in the two groups neither was in either group any significant carotid stenosis.
Conclusions: Our results revealed that mild arteriosclerotic changes of carotid arteries are more prevalent in long-term survivors of Hodgkin disease in childhood after neck RT. Follow-up is needed to prevent stroke, associated with advanced carotid disease.

O-238

HELICAL TOMOTHERAPY FOR ASKIN'S TUMOR OF CHEST WALL: CLINICAL OUTCOMES

S. Laskar[1], N. Kalyani[1], N. Khanna[1], T. Vora[2], S. Qureshi[3], G. Chinnaswami[2], S. Kembhavi[4], M. Ramadwar[5], R. Upreti[6], P. Kurkure[2]

[1]Radiation Oncology, Tata Memorial Hospital, Mumbai, India; [2]Pediatric Oncology, Tata Memorial Hospital, Mumbai, India; [3]Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [4]Radiodiagnosis, Tata Memorial Hospital, Mumbai, India; [5]Pathology, Tata Memorial Hospital, Mumbai, India; [6]Medical Physics, Tata Memorial Hospital, Mumbai, India

Objectives: To evaluate the clinical outcomes of patients with Askin's tumor of the chest wall treated using Helical Tomotherapy.
Methods: The treatment comprised multiagent chemotherapy (CTh) and local therapy in the form of surgery (Sx) & radiation therapy (RT) or definitive RT alone.
Results: Sixty-four pts. between 7-21 yrs (Median: 17Yrs) treated with radical intent between January 2008 - December 2013 were included. Most (63%) were males. Median tumor volume was 840cc. Forty-one (64%) underwent Sx+RT. Surgical margins were close/positive in 24 (59%). Median percentage necrosis was 85%. After a median follow-up of 24mths the local control (LC), disease free survival (DFS), & overall survival (OS) were 74%, 54%, & 81% respectively. Tumors with volume more than 850cc had inferior LC (67% vs. 80%, $p = 0.74$) & DFS (58% vs.61%, $p = 0.89$).
Conclusions: Primary tumor volume, surgical resection & margins, percentage necrosis & presence of pleural effusion influenced disease outcomes. The combination of CTh, Sx, & RT resulted in superior outcomes for non-metastatic Askin's Tumor.

O-239

RADIOSURGICAL TREATMENT OF TUMORAL AND VASCULAR BRAIN LESIONS IN CHILDREN

D. Devriendt[1], N. Massager[1], F. De Smedt[1]

[1]Gamma Knife Center, Hôpital Erasme ULB, Brussels, Belgium

Objectives: The objective of the present study is to assess the long-term safety and efficiency of Gamma Knife radiosurgical treatment of brain arteriovenous malformations and tumors in children.
Methods: We reviewed the outcome of a series of 55 children (aged 2.4-15.5 years) who underwent radiosurgical irradiation for a tumoral or vascular brain lesion in our center. This included 21 arteriovenous malformations, 1 cavernoma, 8 pilocytic astrocytoma, 4 grade II glioma, 1 glioblastoma, 3 ependymoma, 3 hypothalamic hamartoma, 8 schwannoma, 2 meningioma, 2 choroid plexus carcinoma, 1 craniopharyngioma, and 1 hemangiopericytoma. All patients had single-session radiosurgery using Gamma Knife C or Perfexion, under general anesthesia for 39 patients. Pathologies with a mean size of 2.8 cc (range 0.1-13.6 cc) were irradiated with a mean margin dose of 16.8 Gy (range 10-25 Gy).
Results: The follow-up period of 45 of these patients ranged from 0.5 to 12 years (mean 4.6 years). The obliteration rate of arteriovenous malformations was 86.6%. No bleeding occurred after radiosurgery. The morbidity was limited to 2 children: 1 patient with AVM had seizures after irradiation and 1 patient with vestibular schwannoma from NF2 lost hearing unilaterally. We observed excellent tumor control for patients with pilocytic astrocytomas, grade II glioma, schwannoma and meningioma, hemangiopericytoma. None of our children with glioblastoma, ependymoma, hypothalamic hamartoma or craniopharyngioma had their tumor controlled in the long term after radiosurgery.
Conclusions: Gamma Knife radiosurgery represents a very safe and quite effective therapy for brain arteriovenous malformations and some brain tumors in children.

SIOP AWARD SESSION

O-240

SERUM FOLATE LEVELS, METHYLENE TETRA HYDROXY FOLATE REDUCTASE (MTHFR) GENOTYPE, AND COMPLICATIONS DURING INDUCTION CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

N. Roy Moulik[1], A. Kumar[1], S. Agrawal[2], A. Mahdi[3]

[1]Pediatrics, King George Medical University, Lucknow, India; [2]Medical Genetics, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India; [3]Biochemistry, King George Medical University, Lucknow, India

Objectives: Majority of the deaths in children from low/middle income countries undergoing treatment for ALL occur during the initial phases of chemotherapy, mostly due to malnutrition and infections. Though folate deficiency is widely prevalent in the developing countries, its effect on the outcome of treatment in these children has not been studied. The present study examines the effect of folate status and the MTHFR genotype on the course and complications of induction chemotherapy.
Methods: Children with ALL registered from September 2011 through August 2013 were assessed for serum folate at baseline and at end of induction and MTHFR genotype (677 and 1298). Clinical and laboratory parameters were monitored during induction chemotherapy. The study was approved by institutional ethics committee.
Results: Folate deficiency was seen in 40 (26%) of 150 children at baseline and 43 (32%) of 134 at end of induction chemotherapy. Folate levels declined from 10.29 ± 7.2 to 8.23 ± 5.9 ng/ml; ($p = 0.02$) after induction, being more marked in mutant 677 genotypes. Low counts at day14 was seen more often in children with baseline folate deficiency ($p = 0.001$) and 677mutation ($p = 0.01$). Higher proportion of folate deficient children 14/40 (36%) experienced episodes of febrile neutropenia as compared to 17/110 (15%) children with normal folate ($p = 0.01$). 6/10 (60%) children succumbing of neutropenia related sepsis had pre-induction folate deficiency as compared to 33/134 (24.6%) induction survivors ($p = 0.02$). Transfusion requirement (both red cell and platelet) was higher in folate deficient children (0.01 and <0.0001 respectively). Higher incidence of mucositis was seen in children with 1298 mutations ($p = 0.007$). Concomitant folate deficiency accentuated the adverse effects of mutated genotypes. Multivariate analysis revealed associations of baseline folate

deficiency with low counts at day 14 ($p = 0.001$) and MTHFR 1298 mutations with mucositis ($p = 0.02$).
Conclusions: Folate deficiency and MTHFR mutations led to higher incidence of hematological complications, mucositis and poorer survival in children with ALL undergoing induction chemotherapy.

O-241

SECULAR TRENDS IN SURVIVAL FOR ACUTE LYMPHOBLASTIC LEUKEMIA AMONG CHILDREN LIVING IN AN AREA WITH LOW SOCIOECONOMIC STATUS IN NORTHEAST-BRAZIL

S.S. Viana[1], L.M.M.R. Lima[1], O.A. Menezes-Neto[1], C.A.F. Cardoso[1], J.B. Nascimento[1], M.R.U. Rangel[1], R. Cipolotti[1]

[1]Medicine, University of Sergipe, Aracaju, Brazil

Objectives: To evaluate the secular trend of survival for acute lymphoblastic leukemia in children living in an area with low socioeconomic status in Northeast-Brazil.
Methods: We evaluated patients up to 19 years with acute lymphoblastic leukemia from 1980 to 2014, treated by pediatric oncologists using standardized protocols in a service linked to a public general hospital. We divided the patients into two cohorts: treated from 1980 to 2004 (cohort A) and from 2005 to 2014 (cohort B). The findings were compared with patients treated from 2005 to 2014 in the single private hospital in the same localization, by the same team and protocols (cohort C).
Results: We obtained 391 patients (cohort A: 287; cohort B: 89; cohort C: 15). The overall mortality rate was 52.4% and the mean overall survival was 148 months (cohort A: 57.5% and 137 months; cohort B: 40.4% and 59 months; cohort C: 26.7% and 106 months respectively). The overall mortality rate was higher in cohort A ($p = 0.005$). It was noted that in the cohort A the mortality rate was higher in infants and adolescents compared to toddlers/school children ($p = 0.006$ and 0.034 respectively) and the median survival ($p = 0.004$ and 0.023 respectively). In cohort B, patients from rural areas had a higher mortality rate ($p = 0.045$) and the males had a longer mean survival ($p = 0.025$). For cohorts B and C we have obtained a higher mortality rate among patients living in rural areas ($p = 0.038$), in the same way that the median survival time ($p = 0.024$), also higher among males ($p = 0.011$) whose mothers had 11 or more years of schooling ($p = 0.044$).
Conclusions: The mortality rate has been considered decreasing, and increased median survival time was associated with male gender, living in urban area, and with mothers with higher level of education.

O-242

OUTCOME AND MORBIDITY OF PRIMARY RESECTION OF HEPATOBLASTOMA IN JPLT-1 AND 2 PROTOCOLS

E. Hiyama[1], T. Hishiki[2], K. Watanabe[3], K. Ida[4], M. Yano[5], T. Oue[6], T. Iehara[7], K. Hoshino[8], K. Koh[9], Y. Tanaka[10], S. Kurihara[1]

[1]Pediatric Surgery, Hiroshima University Hospital, Hiroshima, Japan; [2]Pediatric Surgery, Chiba Chidren's Hospital, Chiba, Japan; [3]Pediatrics, Kyoto University School of Medicine, Kyoto, Japan; [4]Pediatrics, Teikyo University School of Medicine Mizoguchi, Tokyo, Japan; [5]Pediatrics, Akita University School of Medicine, Akita, Japan; [6]Pediatrics, Osaka University School of Medicine, Osaka, Japan; [7]Pediatrics, Kyoto Prefectural Medical University, Kyoto, Japan; [8]Pediatrics, Keio University School of Medicine, Tokyo, Japan; [9]Hemato-Oncology, Saitama Children's Medical Center, Saitama, Japan; [10]Pathology, Kanagawa Children's Medical Hospital, Saitama, Japan

Objectives: The Japanese Study Group for Pediatric Liver Tumor (JPLT) was launched in 1991 and conducted two protocols named JPLT-1 and JPLT-2 to evaluate the cure rate of risk-stratified hepatoblastoma (HB). In these protocols, primary resection was permitted in PRETEXT I and II cases followed by postoperative chemotherapy. In this study, we examined the outcome and surgical complications of primarily resected HB cases.
Methods: Among 154 JPLT1 and 335 JPLT2 cases, 54 primarily resected HB cases were enrolled. 16 were PRETEXT I, 26 were PRETEXT II, and 12 were ruptured HBs. Clinical features, surgical procedures and survival rates were compared among these three groups.
Results: All 16 PRETEXT I cases underwent complete resection by left lobectomy or left lateral segmentectomy ($n = 7$), right lobectomy ($n = 5$) and partial resection ($n = 4$). Among them, two cases showed recurrence; one older case (100 mos.) and one partially resected case. All 26 PRETEXT II cases except for one underwent complete resection by right lobectomy ($n = 8$), left lobectomy ($n = 17$) and other resection ($n = 1$). Three cases had portal or hepatic vein involvement. Among them, operation death occurred in one newborn and there was recurrence in 4 cases including 3 cases involved veins and one older case (114 mos.). Of 12 ruptured cases, 7 showed recurrence. Overall survival rates at 5 years of the PRETEXT I, II and ruptured cases were 94%, 85%, and 42%. Event-free survival rates at 5 years in these groups were 88%, 70%, and 32%, respectively. In these cases, 3 cases showed biliary duct complications, which were all cured.
Conclusions: Outcome of PRETEXT I and II cases with primary resection was unsatisfactory because of some recurrence. Primary resection for these cases should be performed by anatomical resection according to strict surgical guidelines. More intensified chemotherapy should be required for the primarily resected cases where the tumors ruptured.

O-243

COMPREHENSIVE UPDATE OF PEDIATRIC RENAL TUMOR EPIDEMIOLOGY: ANALYSIS OF THE FIRST 4000 PATIENTS ON CHILDREN'S ONCOLOGY GROUP (COG) RENAL TUMOR CLASSIFICATION AND BIOLOGY PROTOCOL AREN03B2

E.A. Mullen[1], J.I. Geller[2], E. Gratias[3], E.J. Perlman[4], P.F. Ehrlich[5], G. Khanna[6], A. Naranjo[7], C.V. Fernandez[8], K. Gow[9], F. Ferrer[9], T. Hamilton[9], R. Glick[9], J. Kandel[9], D. Barnhart[9], Y. He[10], R. Dasgupta[9], F. Hoffer[9], S. Servaes[9], J. Gastier-Foster[9], D.A. Hill[9], V. Huff[9], P.E. Grundy[11], J.S. Dome[10]

[1]Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Hematology/Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [3]Pediatric Hematology/Oncology, Children's Oncology Group, Monrovia, USA; [4]Pathology, Ann & Robert H Lurie Children's Hospital of Chicago, Chicago, USA; [5]Pediatric Surgery, C.S. Mott Children's Hospital, Ann Arbor, USA; [6]Pediatric Radiology, Washington University School of Medicine, St. Louis, USA; [7]Biostatistics, COG Data Center, Gainsville, USA; [8]Pediatrics & Bioethics, IWK Health Centre, Halifax, Canada; [9]Renal Tumors, Children's Oncology Group, Monrovia, USA; [10]Oncology, Children's National Medical Center, Washington D.C., USA; [11]Cancer Care, Alberta Health Services, Calgary, Canada

Objectives: The AREN03B2 study is a conduit to risk-stratified enrollment on COG therapeutic renal tumor (RT) studies via real-time central review, and supports a comprehensive biologic tissue and epidemiologic repository. To define the present day spectrum of pediatric RT, we analyzed the first 4000 patients enrolled.
Methods: 4000 patients with a radiologically identified RT, extra-renal Wilms (WT) or extra-CNS Malignant Rhabdoid Tumor (MRT) enrolled on AREN03B2 between 2/27/2006 - 9/19/2013. Required submissions included: 1. Abdominal CT/MRI, and chest CT 2. Institutional pathology report, formalin-fixed tissue and diagnostic H&E slides 3. Operative report 4. Tissue for LOH (1p/16q) or *INI1* testing. Available blood, urine, tumor and normal kidney tissues were banked.
Results: Overall, 3,949/4000 were eligible. Median age at diagnosis was 3.2 years (range 1 day – 29.7 years), 47.4% were males, 7.6% had congenital anomalies, including 3.5% with predisposition syndromes. Histologic distribution in unilateral patients was Favorable Histology WT (FHWT) 75%, Anaplastic WT 5%, Renal Cell Carcinoma 4.2%, MRT 3.7%, Clear Cell Sarcoma of the Kidney 3.4%, Congenital Mesoblastic Nephroma 2.2%, Cystic Nephroma 2.0%, Metanephric Adenoma 0.4%, and 3.0% Other. 41.5% of patients subsequently enrolled on therapeutic studies. Among patients with FHWT, stage distribution was I 20.4%, II 22.0%, III 31.6%, IV 19.8% and V 6.3%. Of stage IV patients, 78.4% had pulmonary only metastases, 2.7% extra-pulmonary only and 17.5% both. 5.2% had LOH of 1p/16q. The tissue bank has supported over 50 biologic and epidemiologic studies to date.
Conclusions: AREN03B2 is the largest clinical, epidemiologic and biologic databank for pediatric RT, and has presented new insight into pediatric RT epidemiology in the modern era. In contrast to historical cohort studies, only 80% of enrolled unilateral patients had WT, and incidence of rare RTs was increased. The study enables timely risk stratification onto clinical trials and serves as a valuable repository for RT discovery research.

O-244

INTEGRATIVE GENOMIC ANALYSES IDENTIFY RECURRENT STRUCTURAL ALTERATIONS IN ATYPICAL TERATOID RHABDOID TUMOURS (ATRTS)

J. Torchia[1], D. Picard[2], K.C. Ho[2], D.A. Khuong-Quang[3], L. Louterneau[4], M. Bourgey[4], T. Chan[1], B. Golbourn[1], L. Lafay-Cousin[5], M.D. Taylor[6], P. Dirks[6], E. Bouffet[7], C. Hawkins[8], J. Majewski[4], S.K. Kim[9], N. Jabado[3], A. Huang[7]

[1]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada; [2]The Arthur and Sonia Labatt Brain Tumour Research Centre, The Hospital for Sick Children, Toronto, Canada; [3]Human Genetics and Experimental Medicine, McGill University, Montreal, Canada; [4]Genome Quebec Innovation Centre, McGill University, Montreal, Canada; [5]Pediatric Oncology, Alberta Children's Hospital, Calgary, Canada; [6]Division of Neurosurgery, The Hospital for Sick Children, Toronto, Canada; [7]Paediatric Hematology & Oncology, The Hospital for Sick Children, Toronto, Canada; [8]Pathology, The Hospital for Sick Children, Toronto, Canada; [9]Pediatric Neurosurgery, Seoul National University Children's Hospital, Seoul, Korea

Objectives: ATRTs (Atypical teratoid rhabdoid tumours) represent one of the most aggressive pediatric brain tumours. Paradoxically, ATRTs are reported to exhibit balanced genomes with alterations of the *SMARCB1* locus on chr22, as the sole recurrent somatic genetic event. To better define molecular mechanisms underlying ATRT biology we comprehensively interrogated 63 ATRTs using an integrated genomics approach.
Methods: We integrated a combination of ultra-high resolution SNP genotyping whole-genome/exome and RNA sequencing. Copy number and structural alterations were mapped using orthogonal bioinformatics techniques. Structural alterations and mutations were validated by targeted re-sequencing using the Sanger method and/or MiSeq and Ion Torrent analyses.
Results: ATRTs exhibited few recurrent deleterious SNVs with exception of loss of function mutations in *SMARCB1* (15 SNVs in 63 tumours). As reported previously, we observed a low mutation rate in primary ATRTs. Significantly, we observed structural alterations as

predominant genetic mechanisms (~3.2/tumor) in primary ATRTs. Notably, bi-allelic structural events leading to loss of *SMARCB1* function were observed in the majority of primary ATRTs (76% of tumours) and included novel intrachromosomal translocations of *SMARCB1* not detected using conventional diagnostic techniques. We observed novel recurrent structural alterations associated with corresponding copy number driven gene expression changes in novel loci not previously implicated in ATRTs, in nearly 20% of primary ATRTs. These included focal deletions of *BCR*, *MKL1*, *EP300*, *LRP1B*, *CDH13*, *ODZ2* and *ZNF407*.
Conclusions: Our integrated high resolution genomics approach has uncovered novel loci with predicted functions in cell adhesion, DNA damage response and epigenetic regulation that will inform a better understanding of ATRT tumour biology. The identification of novel structural events in *SMARCB1* and other genes indicates that the scope of genetic alterations in ATRTs has to date been underestimated and underscore WGS as an important tool for gene discovery as well as clinical diagnostics in ATRT.

O-245

ARE THERE ANAPLASTIC WILMS TUMORS THAT RETAIN AN INTACT P53 PATHWAY?

A.H.A.G. Ooms[1], S. Gadd[1], D.S. Gerhard[2], M.A. Smith[3], J.M. Guidry-Auvil[2], J.S. Dome[4], M.M. van den Heuvel-Eibrink[5], R.R. de Krijger[6], E.J. Perlman[1]

[1]Pathology, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, USA; [2]Office of Cancer Genomics, National Cancer Institute, Bethesda, USA; [3]Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, USA; [4]Hematology-Oncology, Children's National Medical Center, Washington, USA; [5]Oncology, Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands; [6]Pathology, Erasmus MC, Rotterdam, Netherlands

Objectives: The Therapeutically Applicable Research to Generate Effective Treatment (TARGET) project includes 39 Diffuse Anaplastic Wilms Tumors (DAWT) showing anaplasia in >50% of slides. The goal was to evaluate and characterize the p53 pathway in DAWT and to identify novel mutations/targets.
Methods: A single sample of frozen tissue of each tumor underwent Whole Genomic or Exomic Sequencing, gene expression (Affymetrix U133+2) and copy number analyses (6.0 SNP arrays). TP53 immunohistochemistry was performed on available blocks, taken from a different sample of the respective tumors.
Results: High-quality, somatic, non-synonymous TP53 variants were identified in 26/39 (67%) DAWT. No germline mutations were identified. TP53 variants were associated with 17p13 copy number loss in 23/26 DAWT; the remaining 3 had TP53 variants involving both alleles. Of 13 DAWT lacking TP53 variants, 17p13 copy number loss was identified in 6 and a normal 17p13 copy number was present in 7. Significant upregulation of genes involved in the Biocarta p53 and p53 hypoxia pathways was identified in these 7 DAWT, supporting an active p53 pathway in the sample analyzed. No other variants were identified within the p53 pathway. Only 14% of the 7 tumors lacking TP53 abnormalities relapsed versus 53% in the remaining 32 DAWT. We further examined the 7 DAWT without TP53 abnormalities. Abnormal p53 protein accumulation was identified in anaplastic areas by immunohistochemistry in 3, consistent with TP53 mutation not sampled for sequencing. Anaplasia-containing slides are being requested for the remaining 4 cases.
Conclusions: These results support the key role of TP53 loss in the development of anaplasia in the majority of DAWT. Whether anaplasia arises in the absence of TP53 mutation remains unproven. Tissue heterogeneity, difficulties in the performance and interpretation of p53 immunohistochemistry, and the rarity of DAWT remain important obstacles to stratifying patients with anaplasia based on TP53 abnormalities.

POSTER PRESENTATIONS

ACUTE LYMPHOBLASTIC LEUKAEMIA

P-001

THE CHARACTERISTIC OF IG/TCR GENE ARRANGEMENTS PATTERNS AND ITS APPLICATION IN MRD DETECTION IN CHINESE CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

W. Li[1], L.E.I. Cui[1], Z. Li[1], M. Wu[1], C.H.A.O. Gao[1]

[1]Hematology, Beijing Children's Hospital, Beijing, China

Objectives: According to analyze the characteristics of *Ig/TCR* gene rearrangements patterns and the correlation with the clinical and biological features in childhood ALL, we established up the quantitative detection system targeted by *Ig/TCR* gene rearrangement.
Methods: Using the standardization *Ig/TCR* amplification system proposed by Europe Biomed-2 collaboration group, the clonal gene rearrangement of *IgH, IgK* (including *Kde), IgL, TRD, TRB, TRG* were screened in 259 children with ALL (including 233 B cell precursor ALL and 26 T cell ALL), then sequenced and analyzed for the junction domain for the preparation of RQ-PCR.
Resultsf clonal *Ig/TCR* gene rearrangements in childhood B-ALL and T-ALL was 98.3% and 92.3% respectively. In B-ALL, the positive rate of clonal rearrangement: *IgH* (85.8%) >*IgK* (51.1%) >*TRD* (49.4%) >*TRG* (46.7%) >*TRB* (33.9%) >*IGL* (6%); In T-ALL: the *TRB* (76.9%) >*TRG* (73.1%) >*TRD* (38.5%) >*IgH* (11.5%). The incidence of *TRG* rearrangement in the *TEL-AML1*$^+$ and *BCR-ABL*$^+$ B-ALL was significantly higher than that in the *E2A-PBX1*$^+$ and *MLL*$^+$ rearrangement B-ALL (80.9%, 57.1% and 16.7%, 0 respectively, $p < 0.001$). In childhood B-ALL, *TRG* rearrangement pattern was associated with age, initial WBC count ($p = 0.031$;$p < 0.001$). *IgH* rearrangement occurred mostly in patients who had good prednisone ($p = 0.051$). We established a RQ-PCR quantitative detection system in 91.9% children with ALL.
Conclusions: The incidence of clonal *Ig/TCR* gene rearrangements was high in childhood ALL, and there was diversity in the junction. The rearrangement pattern was different significantly in childhood ALL with different fusion genes, and it was associated with age and initial WBC count. This RQ-PCR by *Ig/TCR* as target displayed wide coverage of molecular markers and higher sensitivity and specificity of quantitative approach, which was applied in MRD detection in childhood ALL.

P-002

LOSS OF TUMOR SUPPRESSOR BTG1 PROMOTES CELL SURVIVAL BY CONTROLLING ATF4 FUNCTION

L. Van der Meer[1], L. Yuniati[1], E. Tychon[1], L. Emst[1], M. Alkema[1], C. Rodenbach[1], P. Hoogerbrugge[1], F. Leeuwen[1]

[1]Pediatric Oncology, Radboud University Medical Centre, Nijmegen, Netherlands

Objectives: The B cell Translocation Gene 1 (BTG1) locus is affected by genomic deletions in 9% of pediatric acute lymphoblastic leukemia patients. However, it remains unclear how loss of BTG1 promotes clonal outgrowth.
Methods: We detected an up to 15-fold increases of BTG1 expression when cells are exposed to various challenge conditions. To test for a functional role for BTG1 in the cellular response to stress, we challenged BTG1 knockout cells with nutrient deprivation and found that BTG1 knockout cells show a 20-30% improved survival rate as compared to wildtype cells.
Results: As Activating Transcription Factor 4 (ATF4) is a master regulator of cellular stress signaling, we hypothesized that the improved survival after BTG1 loss is regulated via ATF4. Indeed, ATF4 target genes are differentially regulated in BTG1 knockout cells. In addition, we showed that BTG1 complexes with ATF4 in immunoprecipitation experiments. BTG1 functions as a transcriptional co-regulator that acts by recruiting Protein Arginine Methyl Transferase 1 (PRMT1) to transcription factor complexes. Methylation assays showed that ATF4 is a direct target for PRMT1 mediated methylation. Furthermore, we found that the PRMT1 interacting domain in BTG1 is essential for BTG1 mediated modulation of ATF4 function. In search for additional evidence for the functional interaction between BTG1 and ATF4 we performed global expression analysis on cells expressing B-cell marker B220. This revealed a significant deregulation of ATF4 target genes in BTG1 knockout cells when compared to wildtype cells.
Conclusions: Together, our data indicate that BTG1 suppresses activation of ATF4 in response to cellular stress. Loss of BTG1 function, as it occurs during leukemia development, enhances ATF4 activity, thereby promoting cell survival under cellular stress conditions such as nutrient deprivation or ER stress. Leukemic cells carrying BTG1 deletions may thus benefit from this increased resistance to cellular stress, not only during leukemia development but also during treatment.

P-003

THE FREQUENCY OF HLA -A, B, DRB1 ALLELES ACCORDING TO RISK GROUPS IN CHILDREN WITH B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

T. Patiroglu[1], H.H. Akar[2]

[1]Department of Pediatric Hematology and Oncology, Erciyes University Faculty of Medicine, Kayseri, Turkey; [2]Department of Pediatric Immmunolgy, Erciyes University Faculty of Medicine, Kayseri, Turkey

Objectives: Previous studies have demonstrated some significant differences in HLA allele frequencies in leukemic patients and normal subjects. The purpose of this study is to evaluate the frequencies of HLA class I (A, B) and class II (DRB1) alleles in patients with acute lymphoblastic leukemia and compare to unrelated healthy subjects in Central Anatolia of Turkey.
Methods: This study was performed in 90 children with ALL, whose ages were ranging between 1-18 years. Twenty nine of 90 patients had standard risk group (SRG) of ALL, 37 moderate risk group (MRG), and 24 high risk group (HRG) respectively according to Berlin Frankfurt Münster (BFM) standards. We have typed for HLA-A, B, DRB1* alleles in patients with ALL and 90 unrelated normal subjects in Central Anatolia of Turkey. PCR-SSO low resolution method (Luminex technology) was used for HLA typing.
Results: Allele frequencies of HLA-A*01, HLA-A*29 and DRB1*07 were higher in patients with ALL compared to the control group ($p = 0.008$, $p = 0.032$, and $p = 0.000$, respectively). On the contrary, HLA-B*08 and DRB1*08 alleles frequencies in patients with ALL lower than controls ($p = 0.010$, $p = 0.016$, respectively). DRB1*04 allele was higher in HRG ALL and MRG ALL than in SRG ALL ($p = 0.009$). DRB1*07 allele was higher in SRG ALL than in HRG and MRG ALL ($p = 0.007$). The most observed haplotype was A*02, B*35, DRB1*13

($p = 0.023$) in patients with ALL. We could not find any haplotypes negatively associated with ALL. The most observed homozygous allele was A*24 ($p = 0.043$) in the presented cohort.
Conclusions: These results suggest that HLA-A*01, A*29, DRB1*07 alleles may play a presumptive predisposing factor in ALL, whereas HLA-B*08 and DRB1*08 alleles have been found to be negatively associated with ALL. In addition, DRB1*04 allele has been found as associated with HRG and MRG ALL. Also, DRB1*07 allele may play a presumptive predisposing factor for SRG ALL.

P-004

PRECLINICAL IN VIVO EFFICACY OF PI3K PATHWAY INHIBITION IN PHILADELPHIA-LIKE ACUTE LYMPHOBLASTIC LEUKEMIA

S.K. Tasian[1], Y. Li[1], T. Ryan[1], S.L. Maude[1], D.T. Teachey[1], M.L. Loh[2], S.P. Hunger[3], C.G. Mullighan[4], M. Carroll[5], S.A. Grupp[1]

[1]Pediatrics, Children's Hospital of Philadelphia, Philadelphia, USA; [2]Pediatrics, UCSF Benioff Children's Hospital, San Francisco, USA; [3]Pediatrics, Colorado Children's Hospital, Denver, USA; [4]Pathology, St. Jude Children's Research Hospital, Memphis, USA; [5]Medicine, University of Pennsylvania, Philadelphia, USA

Objectives: Philadelphia-like B-precursor acute lymphoblastic leukemia (Ph-like ALL) is associated with various genomic alterations known or predicted to activate oncogenic signal transduction. We previously demonstrated constitutive phosphorylation of PI3K pathway proteins in Ph-like ALL, but therapeutic disruption of PI3K signaling in these leukemias has been minimally investigated. We hypothesized that PI3K isoform-selective or dual PI3K pathway protein inhibition would robustly inhibit Ph-like ALL proliferation *in vivo* and abrogate aberrant signaling.
Methods: Immunocompromised mice well-engrafted with pediatric Ph-like ALL were treated with the PI3Kα inhibitor BYL719, PI3K(inhibitor idelalisib, PI3K/mTOR inhibitor PKI-587, TORC1/TORC2 inhibitor AZD2014, or vehicle. Treated mice were assessed for (a) pharmacodynamic inhibition of phosphoproteins at 72 hours by phosphoflow cytometry and (b) residual ALL in murine spleens after 3-4 weeks of treatment by quantitative flow cytometry.
Results: 7 of 7 Ph-like ALL xenograft models (5 *de novo* and 2 relapsed; Table) demonstrated potent *in vivo* inhibition of relevant phosphoproteins (phosphorylated PI3K, Akt^{T308}, mTOR, S6, 4EBP1, Akt^{S473}, and/or ERK) with PI3K pathway inhibition. PKI-587 treatment resulted in near-eradication of ALL in all models with mean 91.8% (range 86.0-99.4%) leukemia reduction versus vehicle treatment ($p < 0.0001$ via ANOVA with Dunnett post-test for multiple comparisons). BYL719, idelalisib, or AZD2014 treatment inhibited ALL proliferation in all models with mean 56.8% (range 38.5-72.9%), 45.5% (range 40.2-53.1%), and 51.8% (range 37.4-69.4%) leukemia reduction, respectively ($p < 0.001$ for all). Models with highest basal PI3K pathway phosphoprotein levels responded most robustly to PI3K pathway inhibitors.

Ph-like ALL genomic lesions
IGH@-CRLF2
IGH@-CRLF2, $JAK2_{R683G}$
IGH@-CRLF2, $JAK2_{GPinsR683}$
IGH@-CRLF2, $JAK2_{R867Q}$
$JAK1_{S646F}$
P2RY8-CRLF2, $JAK2_{R683G}$
IGH@-CRLF2, $JAK2_{R683G}$

Conclusions: PI3K pathway inhibition is an effective, biochemically relevant therapeutic approach for Ph-like ALL. Dual PI3K/mTOR inhibition was the most potent treatment strategy evaluated in these models. These results will continue to inform development of clinical trials testing signal transduction inhibitors with chemotherapy in children with high-risk ALL.

P-005

IMPROVED THERAPEUTIC STRATEGIES USING PREDICTIVE BIOMARKERS IN PEDIATRIC ALL: AN ACTIVITY WITHIN THE EU NETWORK ENCCA TO INTRODUCE NEWLY DISCOVERED MOLECULAR INFORMATION INTO CLINICAL PRACTICE

M. Stanulla[1], G. Te Kronnie[2], G. Cazzaniga[3], A. von Stackelberg[4], M. Dworzak[5], A. Attarbaschi[5], M.L. Den Boer[6], J.P. Bourquin[7], G. Basso[8], M. Schrappe[9]

[1]Department of Pediatric Hematology and Oncology, Hannover Medical School, Hannover, Germany; [2]Department of Women's and Children's Health, University of Padua, Padua, Italy; [3]Children's Hospital, University of Milan-Bicocca, Monza, Italy; [4]Department of Pediatric Hematology and Oncology, Charité University Hospital, Berlin, Germany; [5]Department of Pediatrics, St. Anna Children's Hospital and Children's Cancer Research Institute, Vienna, Austria; [6]Department of Pediatric Hematology and Oncology, Erasmus Medical Center, Rotterdam, Netherlands; [7]University Children's Hospital, University Children's Hospital, Zürich, Switzerland; [8]Department of Women's and Children's Health, University of Padua, Padua, Switzerland; [9]Department of General Pediatrics, UKSH Campus Kiel, Kiel, Germany

Objectives: Lately, major progress has been achieved in pediatric ALL by improved risk stratification of treatment based on the measurement of leukemic cell reduction by minimal residual disease (MRD) analysis. Outcome data clearly indicate, however, that a large proportion of recurrences cannot be predicted solely by their MRD response pattern. As part of the EU-funded network project ENCCA, a stepwise integrated approach by European clinical study groups on ALL was taken to molecularly characterize new risk groups and to systematically adapt existing trial infrastructures for associated common future treatment approaches.
Methods: First, a survey of diagnostics was conducted. Second, development of a harmonized pipeline for molecular diagnostics in a European virtual laboratory setting using very high-risk ALL (VHRL, characterized by molecular persistence under intensified treatment) as a model system was started. Third, the molecular diagnostic pipeline was integrated with preclinical model systems for molecularly targeted treatment and algorithms for identification and prioritisation of targets developed. Fourth, harmonization and integration of clinical platforms was promoted to practically pave the way for introduction of molecularly targeted treatment.
Results: So far, main achievements of this project were: a) implementation of coherent diagnostic strategies by developing recommendations for diagnostic approaches for pediatric ALL; b) implementation of a laboratory software system tailored to ALL and agreement on a shared dataset of ALL biospecimens to promote joint research activities including a meta-database for interfacing additional different laboratory systems; c) coordinated joint evaluation of molecularly defined prognostic entities (e.g., IKZF1-deleted, CRLF2+, ERG-deleted, TCF3/HLF+); d) implementation of a xenotransplant repository; and e) development of access to a functional clinical trial infrastructure (IntReALL).
Conclusions: Overall, this project exemplifies complexities, needs and solutions to adapt current fragmented infrastructures associated with different clinical trial groups to prepare for common future molecularly based treatment approaches of new pediatric ALL entities in Europe.
Funding: EU-FP7, GA HEALTH-F2-2011-261474.

P-006

REFINING RISK CLASSIFICATION OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA BASED ON GENETIC FEATURES AT PRESENTATION AND MINIMAL RESIDUAL DISEASE

I. Sidhom[1], A. Mokhles[2], N. Ali[1], K. Shaaban[3], D. Yassin[3], S. Salem[3], S. Soliman[3], N. Hamdy[3], S. Youssef[4], W. Rashed[5], M. Mehanna[5], A. Haddad[1]

[1]Pediatric Oncology, NCI Cairo University and Children's Cancer Hospital Egypt, Cairo, Egypt; [2]Pediatric Oncology, Beni Suef University and Children's Cancer Hospital Egypt, Cairo, Egypt; [3]Clinical Pathology, NCI Cairo University and Children's Cancer Hospital Egypt, Cairo, Egypt; [4]Clinical Pharmacy, Children's Cancer Hospital Egypt, Cairo, Egypt; [5]Research Department, Children's Cancer Hospital Egypt, Cairo, Egypt

Objectives: To apply genetic characteristics and early response to therapy towards further refinement of ALL risk classification.
Methods: Study included precursor B-ALL patients presenting with low risk (LR) features [age 1-9.9 years and WBC$<50 \times 10^9$/L, or DNA index $\geq$1.16 or TEL/AML1; with no CNS or testicular disease, or unfavorable genetic abnormalities] who were treated at Children's Cancer Hospital Egypt between July 2007 and December 2010 according to St Jude ALL Total Study XV (Pui et al., NEJM 2009; 360: 2730).
Results: Of 356 patients with provisional LR features, 290 (81.5%) who had good early response and end of induction minimal residual disease (day42-MRD) ^{9}/L at presentation but treated on LR arm based on favorable genetic features and MRD response. Their 5-year RFS was $91.7 \pm 5.7\%$. LR patients with MRD day15.
Conclusions: Therapy was successfully de-escalated based on favorable genetic features and MRD irrespective of age and WBC at presentation. MRD day15.

P-007

IMPLEMENTATION OF AUTOMATED ELECTRONIC RISK ASSIGNMENT FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP (COG)

K. Rabin[1], P.A. Zweidler-McKay[2], C. Wood[3], Y. Dai[3], J. Gastier-Foster[4], A.J. Carroll[5], N.A. Heerema[6], B. Wood[7], M.J. Borowitz[8], P. Brown[9], J. Hilden[10], A. Angiolillo[11], W. Salzer[12], M.J. Burke[13], E.A. Raetz[14], M.L. Loh[15], S.P. Hunger[10], M. Devidas[3]

[1]Pediatric Hematology-Oncology, Baylor College of Medicine, Houston, USA; [2]Pediatric Hematology-Oncology, MD Anderson Cancer Center, Houston, USA; [3]Biostatistics, University of Florida, Gainesville, USA; [4]Laboratory Medicine, Nationwide Children's Hospital, Columbus, USA; [5]Genetics, University of Alabama, Birmingham, USA; [6]Cytogenetics, Nationwide Children's Hospital, Columbus, USA; [7]Pathology, University of Washington, Seattle, USA; [8]Pathology, Johns Hopkins Medical Institute, Baltimore, USA; [9]Pediatric Hematology-Oncology, Johns Hopkins Medical Institute, Baltimore, USA; [10]Pediatric Hematology-Oncology, University of Colorado, Denver, USA; [11]Pediatric Hematology-Oncology, Children's National Medical Center, Washington DC, USA; [12]Pediatric Hematology-Oncology, Walter Reed National Military Medical Center, Fort Detrick, USA; [13]Pediatric Hematology-Oncology, Medical College of Wisconsin, Milwaukee, USA; [14]Pediatric Hematology-Oncology, University of Utah, Salt Lake City, USA; [15]Pediatric Hematology-Oncology, University of California San Francisco, San Francisco, USA

Objectives: Risk-directed treatment has significantly improved survival in childhood ALL. The COG ALL Classification Study AALL08B1 and linked clinical trials require timely risk assignment for over 2,000 children annually according to a complex risk stratification scheme

that integrates clinical information, laboratory data from the local site and three centralized reference laboratories that assess minimal residual disease, DNA ploidy, and central review of cytogenetic and fluorescent *in situ* hybridization data. The purpose of this study was to develop, implement and validate an automated risk assignment methodology.
Methods: An algorithm was implemented in the COG web-based remote data entry system (eRDEs) to automatically generate risk assignments for patients, after required data from all sources are entered. Individual sites review and validate the assignment, eliminating the need for manual centralized assignments. The algorithm was successfully modified during the study to accommodate new data on the prognostic impact of intrachromosomal amplification of chromosome 21 which refined the risk classification.
Results: Within 3.5 years, AALL08B1 has enrolled nearly 7,000 subjects. Patients with B-ALL are treated on three frontline studies (Infant-AALL0631, Standard Risk-AALL0932, High Risk-AALL1131) and are risk classified for post induction therapy. Comparison of programmatically generated risk assignments with automatic assignments in eRDEs, demonstrated discordance in only 109 of 4,776 evaluable cases (2.2%). Only one of these cases demonstrated discordant risk assignment between the two methods, due to alteration of a data entry after the site validated the risk assignment. In the remainder, risk assignment was simply missing by one or the other method due to incomplete data, discontinuation of protocol therapy, or patient inevaluability for other reasons.
Conclusions: Automated web-based risk assignment, integrating multiple sources of data, is a rapid, accurate, and flexible mechanism that is well-suited for use in large-scale cooperative group clinical trials.

P-008

SIGNIFICANT CONCORDANCE OF EARLY TIME-POINTS MINIMAL RESIDUAL DISEASE (MRD) LEVELS, ASSASED BY EIGHT-COLOUR FLOW CYTOMETRY AND RQ-PCR IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

M. Dawidowska[1], M. Kosmalska[1], L. Sedek[2], M. Twardoch[2], A. Sonsala[2], B. Szarzynska-Zawadzka[1], K. Derwich[3], A. Szczepankiewicz[4], M. Witt[1], T. Szczepanski[2]

[1]Dept. of Molecular and Clinical Genetics, Institute of Human Genetics Polish Academy of Sciences, Poznan, Poland; [2]Dept. of Pediatric Hematology and Oncology, Medical University of Silesia, Zabrze, Poland; [3]Dept. of Pediatric Hematology Oncology and Transplantology, University of Medical Sciences, Poznan, Poland; [4]Dept of Pediatric Pulmonology Allergy and Clinical Immunology, University of Medical Sciences, Poznan, Poland

Objectives: Minimal residual disease (MRD), assessed by flow-cytometry (FC) or RQ-PCR-detection of rearranged immunoglobulin and T-cell receptor (Ig/TCR) genes, is the most significant prognostic factor in ALL. Compatibility of these methods has not been studied in pediatric T-ALL.
Objective: Comparative analysis of MRD levels in pediatric T-ALL, by 8-colour FC and (Ig/TCR) RQ-PCR aimed at assessment of MRD kinetics and concordance between FC-MRD and RQ-PCR-MRD results.
Methods: MRD was assessed in 30 T-ALL children, treated according to ALL-IC-BFM2002protocol, by RQ-PCR in 30 patients (77bone marrow mononuclear cell samples) and by FC in 26/30 patients (69bone marrow samples), on day15, day33 and before consolidation (week 12). MRD evaluation by RQ-PCR was according to ESG-MRD-ALL protocols, by FC-according to EuroFlow protocol, with informed consent of patients and approval of local review board. MRD results by both methods were available for comparison in 65/77 samples (84%). Spearman's rank correlation test was used to estimate the relation between FC-MRD and RQ-PCR-MRD. In 16/30 patients (53%) comparison of risk-group assignment, based on standard criteria (day15 FC-MRD; day33 & week12 RQ-PCR-MRD) was feasible.
Results: HighMRD levels ($> = 0.001$) were observed at early time-points:96% of results at day15 and 63%-at day33, equally for both methods. Before consolidation lower MRD levels were observed:82% of FC-MRD and 70% of RQ-PCR-MRD results were<0.001. Significant correlation between FC-MRD and RQ-PCR-MRD was observed at day15 ($R = 0.94$; $p = 0.000$) and day33 ($R = 0.87$;$p = 0.000$);before consolidation:$R = 0.66$ ($p = 0.002$). Risk group assignment based on FC-MRD and RQ-PCR-MRD was concordant in 11/16 patients (69%).
Conclusions: Significant concordance, demonstrated for FC-MRD and RQ-PCR-MRD at day15 and day33, results from specific MRD kinetics in T-ALL: considerable proportion of high MRD levels at early time-points, lower-before consolidation. Longer follow-up is needed for prognostic significance of MRD measured by both methods to be assessed.
Research supported by participation of Polish Pediatric Leukemia Lymphoma Study Group (PPLLSG) and financially by National Science Centre, Poland (grants:NN407311839, NN407531438)

P-009

ACUTE LYMPHOCYTIC LEUKEMIA (ALL) WITH NORMAL HEMATIMETRIC VALUES AT TIME OF DIAGNOSIS

M.F. Mininni[1], M. Guitter[1], J. Rossi[1], P. Zubizarreta[1], M. Felice[1]

[1]Hematology - Oncology, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina

Objectives: ALL is the most frequent hematologic malignacy in childhood. Clinical suspicion allows diagnosis and opportune treatment. Abnormal blood count values are observed in 90% of cases. However, normal hematimetric values are detected in rare cases. Our aim was to analyze the cause of consultation, signs and symptoms at time of diagnosis and time elapsed between the first symptom and ALL diagnosis and outcome in patients presenting normal blood count values.
Methods: Clinical records and laboratory data of patients with diagnosis of ALL who disclosed normal hematrimetric values at diagnosis. Blood counts were considered normal when WBC count was between 5,000-10,000/mm^3 (without neutropenia or blasts), appropriate haemoglobin levels for age and platelet count >150.000/mm^3. Reason for consultation, signs and symptoms, time elapsed since first symptom until diagnosis, ALL biologic characteristics and outcome of these cases were analyzed.
Results: From January-1990 to October-2013, 1572 cases of ALL were diagnosed and, 42 (2.7%) of them presented with an initial normal blood count. The average age was: 8.3 (range: 1-17) years. The average time elapsed between symptoms and diagnosis was 2 months (range: 15 days- 8 months). The signs and symptoms observed were: fever: 37%, bone pain: 34%, asthenia: 16%, weight loss: 16%, joint compromise: 13%, respiratory involvement: 16%, abdominal mass: 11%, pericardial compromise: 5%, testicular-ovarial compromise: 5%, renal compromise: 8%, skin: 3%, CNS: 10%. Immunophenotype was B-cell precursor in 79% of cases and T-ALL in 18%. Complete remission was achieved in 86% of cases and 4% relapsed.
Conclusions: Normal blood count values were observed in 2.7% of ALL patients. Fever and bone compromise were the most frequent clinical findings, showing extramedullar compromise of several localizations in >50% of cases. Thus, normal hematimetric values do not rule-out ALL diagnosis and thorough clinical examination is essential for reaching an accurate diagnosis.

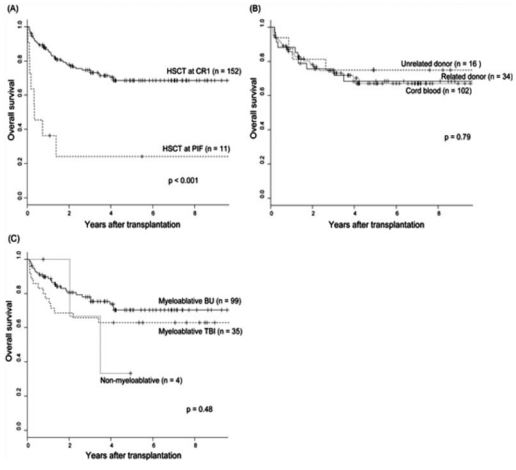
P-010

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR INFANTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A RETROSPECTIVE STUDY FROM THE PEDIATRIC ALL WORKING GROUP OF THE JSHCT

M. Kato[1], D. Hasegawa[2], K. Koh[3], J. Inagaki[4], K. Kato[5], H. Goto[6], J. Takita[1], H. Yabe[7], A. Sawada[8], Y. Atsuta[9], K. Kato[10]

[1]Department of Pediatrics, University of Tokyo, Tokyo, Japan; [2]Department of Hematology Oncology, Hyogo Children's Hospital, Hyogo, Japan; [3]Department of Hematology/Oncology, Saitama Children's Medical Center, Saitama, Japan; [4]Department of Pediatrics, National Kyushu Cancer Center, Fukuoka, Japan; [5]Department of Hematology/Oncology, Ibaraki Children's Hospital, Ibaraki, Japan; [6]Division of Hemato-oncology/Regeneration Medicine, Kanagawa Children's Medical Center, Kanagawa, Japan; [7]Department of Cell Transplantation and Regenerative Medicine, Tokai University, Isehara, Japan; [8]Department of Hematology/Oncology, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan; [9]Department of HSCT Data Management and Biostatistics, Nagoya University, Nagoya, Japan; [10]Department of Hematology and Oncology Children's Medical Center, Japanese Red Cross Nagoya First Hospital, Nagoya, Japan

Objectives: Infants with acute lymphoblastic leukemia (ALL) have worse outcomes than do older children, and recent clinical studies report improving results for infant ALL using intensified chemotherapy followed by hematopoietic stem cell transplantation (HSCT); however, the optimal role of HSCT as first line therapy for infant ALL is not defined. In this study, to obtain fundamental information for establishing a standard approach for infants with ALL, we retrospectively analyzed HSCT for infants ALL based which were reported to the Japan Society for Hematopoietic Cell Transplantation (JSHCT) registry.
Methods: A total of 163 infants with ALL were analyzed. The patients were selected according to the following criteria: (1) diagnosed as ALL at younger than 1 year old; (2) allogeneic HSCT was performed in first complete remission (1CR, $n = 152$); (3) HSCT was performed between 1996 and 2011. As a comparator, 11 infant ALL who undertook allogeneic HSCT in primary induction failure (PIF) during this period were also analyzed.
Results: Overall survival (OS) at 4 years was $70.5 \pm 3.9\%$ for 1CR group, and $24.2 \pm 13.8\%$ for those who received HSCT for PIF (Figure 1A, $p < 0.001$). There was no significant correlation between the outcomes and each factors including donor type (Figure 1B), conditioning of HSCT (Figure 1C), age at HSCT, initial leukocyte count, and cytogenetics.



Conclusions: Our results confirmed that HSCT was a valuable option for infants with ALL during the first CR, although it should be compared to the outcomes of chemotherapy and late complications should be assessed.

P-011

IN PATIENT INDUCTION MORTALITY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA: CAN WE COMBAT INFECTION? EXPERIENCE AT A TERTIARY CARE CENTRE

S. Anwar[1], M. faizan[1], N.Y.L.A. Asghar[1], N. Zia[1], A. Ali[2], M.A.R.Y. in collaboration with Taj[3]

[1]Paeds Hematology/Oncology, Children Hospital, Lahore, Pakistan; [2]Paeds Hematology/Oncology, Lahore General Hospital, Lahore, Pakistan; [3]Paeds Oncology, Royal Marsedan The Cclg Podc Group UK, London, United Kingdom

Objectives: The main objective of the study is to determine the common causes of mortality during the treatment of acute lymphoblastic leukaemia (ALL) in children especially during induction remission.
Methods: We present a retrospective descriptive study conducted at in patient unit of Haematology/Oncology Department at the Children's Hospital Lahore between November 2012 and October 2013. All newly registered patients of ALL between 1-15 years of age who expired over the one year period were included. Mortality data was collected and analyzed regarding age, gender, WBC count, risk categorization, timing of death with respect to treatment phase and cause of death. Lahore Group Protocol for acute lymphoblastic Leukemia LALL01 (Modified BFM and UKALLXI) was used for treatment.
Results: Out of 222 new patients of ALL registered in the study period, 40 (18%) died during treatment. Majority 19/40 (47.5%) were between1-5 years of age. Thirty (75%) patients belong to high risk group. During induction 11/40 (27.5%) died, 10/40 (25%) just after remission and 9/40 (22.5%) died before initiation of therapy. Infection alone or in combination with other factors was responsible for deaths in 25/40 (62.5%) patients. Septicemia and pneumonia were documented in 14/40 (35%) and 11/40 (27.5%) patients respectively. Ten (25%) died due to hemorrhage and 5 (12.5%) due to progressive and resistant disease.
Conclusions: Infection is the leading cause of mortality in ALL patients in our study population. The only key to the solution is better supportive care and which can be improved by decreasing the patient load, increasing the no of nursing staff and educating the families regarding infection prevention and control measures.

P-012

ACUTE INFECTION OF CENTRAL NERVOUS SYSTEM (CNS) IN CHILDREN WITH ACUTE LEUKEMIA

C. Ruiz[1], S. Gomez[2], J. Rossi[1], M. Guitter[1], C. Sánchez La Rosa[1], E. Alfaro[1], P. Zubizarreta[1], M. Felice[1]

[1]Hematology- Oncology, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [2]Infectology, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina

Objectives: Infections are the most frequent cause of morbidity in childhood acute leukemia (AL). However, CNS is a rare localization, with high mortality.
Our aim was to analyze cases with acute infection in CNS in patients with AL and to evaluate the causes of co-morbidity and immunocompromise status at the moment of this complication.
Methods: From January-1990 to February-2014, 2107 AL cases were diagnosed. Infection with CNS localization was detected in 20 cases (0.95%). We reviewed clinical records, biological-laboratory features and images of these patients.
Results: From the 20 observed cases, 17 (1.06%) were ALL (11 newly-diagnosed, 4 relapsed-ALL and 2 infants) and 3 (0.59%) AML. Etiology of infections was: **Bacterial** ($n = 10$), fungal ($n = 6$), parasitic ($n = 2$), viral ($n = 1$) and without germ isolation, but highly suspected bacterial ($n = 1$). Patients disclosed neutropenia at the moment of this event in 67% ($n = 14$) and 38% ($n = 8$) did not have cause of co-morbidity. The infection occurred during induction in 7 patients (35%), 6 (30%) during high-risk blocks, 1 following HSCT, 3 receiving late-reinduction and 3 during maintenance or off therapy. Nine patients (45%) presented seizures and 45% also neurologic impairment. Only 20% presented showed meningeal syndrome. CSF cultures confirmed diagnosis in 62% of cases, 28% required a biopsy of lesions and 10% were confirmed by pathognomonic images and laboratory tests. Eight patients (40%) died due to CNS infection, 5 (20%) presented sequelae (2 severe) and 7 (35%) remained alive without sequelae.
Conclusions: 1-CNS infections occurred with a low incidence (<1%) in AL. 2-Initial symptoms were mainly seizures and neurologic impairment. 3-Bacterial and fungal infections were the most frequent cause. 4- An increased risk was found during induction and consolidation phases. 5-Etiology was confirmed mainly by CSF culture or biopsy. 6-Most of patients either died or survived with sequelae. However, one third is alive with good performance status.

P-013

PREVALENCE OF INVASIVE FUNGAL INFECTIONS (IFI) IN CHILDREN WITH FEBRILE NEUTROPENIA BETWEEN 1- 12 YEARS TREATED FOR ACUTE LEUKEMIA- A PROSPECTIVE STUDY

J. Yadav[1], S. Amitabh[2], R. Seth[2], S.k. Kabra[2], I.M.A. Xess[3], M. Jana[4]

[1]Pediatrics, All India Institute of Medical Sciences, Delhi, India; [2]Pediatrics, All India Institute of Medical Sciences, Delhi, India; [3]Microbiology, All India Institute of Medical Sciences, Delhi, India; [4]Radiology, All India Institute of Medical Sciences, Delhi, India

Objectives: The objective of our study was to ascertain the prevalence, determinants, etiological species of invasive fungal infections (IFI) and outcome (discharge/death) during febrile neutropenic episodes in children with acute leukemia between 1-12 years age group during chemotherapy.
Methods: Episodes of febrile neutropenia of duration $\geq$96 hrs were enrolled and investigated for fungal infection. Blood investigations including Galactomannan antigen, aspergillus serology, Bactac fungal culture and radiological investigations were done. Serial monitoring of Galactomannan Ag was done to assess treatment response. Revised definitions of IFI from the European Organization for Research and Treatment of Cancer (EORTC) were used for analysis.
Results: Total 254 febrile neutropenic episodes were screened and 60 patients fulfilled the enrollment criteria. Out of 60, thirteen (21%) had IFI. As per EORTC out of thirteen, three (23%) classified as proven, seven (54%) probable and three (23%) as possible. Two (3%) patients died during same admission. Most common fungal isolate ($n = 3$) from blood was Candida (67%) and one patient had trichosporon. Radiological findings suggestive of IFI was present in ten patients, nodular opacity in lung was most consistent findings. Galactomannan Antigen was positive in thirty patients.
Conclusions: This study is ongoing and preliminary analysis showed Candida is most common fungal agent causing proven IFI. Aspergillus was most commonly associated with radiological abnormalities. Galactomannan Ag was found to be useful in early diagnosis and monitoring of response to antifungal therapy. Prolonged neutropenia (> 14 days) was most consistently associated risk factor for IFI. EORTC guidelines for IFI has limitations as children with nasal/Oral swab or urine culture showing fungal growth, CT showing fungal ball in solid organs (Kidney) with positive Galactomannan Ag test also benefited with antifungal therapy suggesting likely systemic fungal infection although these were not included in criteria of IFI.

P-014

WHAT PLATELET COUNT AVOIDS A TRAUMATIC LUMBAR PUNCTURE?

S. Totadri[1], A. Trehan[1], R. Srinivasan[2], D. Bansal[1], R.K. Marwaha[1]

[1]Pediatric Hematology and Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [2]Cytology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objectives: The first diagnostic lumbar puncture has immense prognostic significance in acute lymphoblastic leukemia (ALL). This study assesses whether thrombocytopenia is associated with increased risk of traumatic lumbar puncture (TLP) in newly diagnosed ALL patients.
Methods: Children diagnosed with ALL between January 2010 and December 2012 were evaluated. Platelet count on the day of diagnostic lumbar puncture (LP) and cerebrospinal (CSF) status were noted. It is not our routine practice to transfuse platelets in otherwise well children prior to LP. Procedure is done under short sedation with Midazolam and Ketamine.
Results: 310 children with ALL, median age 5 years (range 1-13 years), diagnosed to have ALL were evaluated. CSF status at the first diagnostic lumbar puncture (LP) was- 274: CNS1; 8: CNS3 and 28: TLP. Mean platelet count in patients with TLP was significantly lower than those with a non-traumatic LP (NTLP) ($p = 0.001$). A platelet count (PC) of <50,000/(L was observed in 93% of patients with a TLP, which was significantly higher than those who had a NTLP and a PC <50,000 ($p = 0.01$). A platelet count of <10,000/(L was seen in 43% of patients with TLP and 13% with a NTLP ($p = 0.001$). A receiver operator curve was constructed for predicting risk of TLP based on platelet count. Area under the curve was 0.74 ± 0.05 [95% CI 0.64-0.85]. Platelet count <50,500/(L at the time of LP had 93% sensitivity and 73% specificity in predicting a TLP.
Conclusions: Low platelet counts are significantly associated with risk of TLP. In a developing country with a high patient load and occasional inadequate infrastructure, platelet transfusions are not always given prior to performing a LP. Ensuring an adequate platelet count prior to the first LP in newly diagnosed ALL patients is necessary to avoid a TLP and subsequent associated morbidity and possible increased risk of relapse.

P-015

FEASIBILITY AND SAFETY OF FULL DOSE ANTICOAGULATION THERAPY (ACT) IN CHILDREN TREATED ACCORDING TO DANA-FARBER CANCER INSTITUTE (DFCI) ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) CONSORTIUM THERAPY PROTOCOLS

M.D. Bhatt[1], J. Fowler[1], A.K. Chan[1], U. Athale[1]

[1]Pediatric Hematology/Oncology, McMaster Children's Hospital, Hamilton, Canada

Objectives: There are no evidence-based guidelines for ACT with low molecular weight heparin (LMWH) in relation to platelet count. We examined the impact of thrombocytopenia on LMWH dosing and incidence of bleeding in children with ALL or lymphoblastic lymphoma (LL) who develop thromboembolism (TE) during therapy according to DFCI ALL protocols.
Methods: Patient records were reviewed for demographics, details of ALL/LL and TE diagnoses and therapy, platelet counts during ACT, LMWH dosing, and bleeding episodes. Institutional ACT policy is full dose LMWH for platelets $>30 \times 10^9$/L, half-dose between 20-30 $\times 10^9$/L and hold LMWH for platelets $<20 \times 10^9$/L. Also, we hold LMWH for 24 hours prior to an invasive procedure.
Results: Twenty-two TEs (5 DVT, 2 PE, 4 CSVT and 11 Cardiac) were diagnosed in 19 patients (Mean age 6 years; M:F 9:10; Diagnosis: 17 ALL and 2 LL) over 4 years. One patient was diagnosed with TE during induction phase and 18 (95%) in consolidation II with mean time to TE 5.5 months from ALL/LL diagnosis. All patients received LMWH and mean duration of ACT was 5.8 months (range 3-11 months). Platelets were measured weekly with a mean count of 292X10^9/L. On 26 occasions, platelet nadir was $<100 \times 10^9$/L and none $<30 \times 10^9$/L. Hence no patient required LMWH dose adjustment for thrombocytopenia. Fifty-four procedures (49 LPs, 5 CVL insertion/revision) required withholding of LMWH. There were no bleeding episodes. Although asparaginase was held with TE diagnosis, all 19 patients completed all scheduled doses as per protocol.
Conclusions: In our cohort, thrombocytopenia did not interfere with LMWH dosing. The timing of TE diagnosis could be the likely explanation. Ability to administer full dose LMWH, lack of bleeding and completion of all asparaginase doses while on ACT suggest full-dose ACT is feasible and safe in children with ALL/LL who develop TE during DFCI ALL Consortium therapy protocols.

P-016

SIGNIFICANTLY HIGHER INCIDENCE OF ALLERGIC REACTIONS FOR INTRAVENOUS PEG-ASPARAGINASE AS COMPARED TO INTRAMUSCULAR PEG-ASPARAGINASE IN CHILDREN WITH HIGH RISK ACUTE LYMPHOBLASTIC LEUKEMIA

T. MacDonald[1], K. Kulkarni[2], M. Bernstein[2], C. Fernandez[2], M. Yhap[2]

[1]Pharmacy and Pediatric Hematology/Oncology, IWK Health Centre and Dalhousie University, Halifax, Canada; [2]Pediatric Hematology/Oncology, IWK Health Centre and Dalhousie University, Halifax, Canada

Objectives: Peg-asparaginase (PEG-Asp) is a quintessential part of the treatment for Acute Lymphoblastic Leukemia (ALL). Historically PEG-Asp has been administered intramuscularly (IM) but Children's Oncology Group has introduced the intravenous (IV) administration of PEG-Asp in an effort to improve quality of life of ALL patients, and perhaps anti-leukemic efficacy. Those patients who experience an allergy require administration of IM Erwinase. However, there is paucity of published data on allergic reactions to IV PEG-Asp. The objective of this study was to determine the incidence of allergic reactions to IV compared to IM PEG-Asp in ALL patients.
Methods: The number of ALL patients who received IM PEG-Asp from January 2005 to May 2011 and those who received IV PEG-Asp from June 2011 to December 2013 was determined through the hospital database after ethics approval. The numbers of high risk (HR) and standard risk (SR) ALL patients were computed. The hospital drug database was utilized to determine the number of patients who received Erwinase, which was given to children who reacted to PEG. Comparison of incidence of allergic reactions in various patient groups was performed with Fisher's exact test.
Results: 128 ALL patients (SR-ALL: 89, HR-ALL: 39) were managed at the authors' institution during the study period. Allergic reactions were seen in 3% (2/77) of ALL patients receiving IM PEG and 14% (7/51) receiving IV PEG-Asp ($p = 0.029$). Allergic reactions occurred significantly more frequently in HR-ALL patients [24% (9/38)] versus SR-ALL [0%]; $p = 0.0001$. Allergic reactions to IV versus IM PEG occurred significantly more frequently in HR-ALL patients 44% (7/16) and 9% (2/22) respectively; $p = 0.021$.
Conclusions: The present study demonstrates significantly increased incidence of allergic reactions in HR-ALL patients receiving IV PEG compared with IM PEG. Further studies are needed to confirm this observation and to consider change to the drug administration policy.

P-017

ANTI-CANCER NON STEROIDAL ANTI-INFLAMMATORY DRUG, TOLFENAMIC ACID ENHANCES THE EFFICACY OF CHEMOTHERAPEUTIC AGENTS IN LEUKEMIA CELL LINES

R. Sutphin[1], D. Eslin[1], S. Connelly[1], U. Sankpal[2], P. Bowman[2], R. Basha[2]

[1]Pediatric Hematology and Oncology, UF Health Cancer Center, Orlando, USA; [2]Pediatrics, University of North Texas Health Science Center, Fort Worth, USA

Objectives: Leukemia is the most common malignancy affecting children. Current chemotherapy is effective but associated with many deleterious effects. The objective of this pre-clinical study was to test novel strategies to enhance the response of chemotherapy without additional morbidity. Recently, we demonstrated for the first time that Tolfenamic acid (TA), an anti-cancer NSAID inhibits leukemia cell proliferation by targeting Specificity protein (Sp) transcription factors, Sp1 and Sp3. Now, we evaluated the efficacy of TA in enhancing the chemotherapeutic response of Doxorubcin (DOX) and vincristine (VIN) in leukemia cells.
Methods: Jurkat, Reh, Molt and Nalm-6 cells were grown in the presence of TA (10-100(M) or DOX (10-100nM) or VIN (10-500nM) or TA (25(M) and DOX/VIN (25nM) and cell viability was measured at 24-72 h post-treatment using CellTiter Glo. The expression of Sp1, survivin was determined by Western blot analysis, Apoptosis was monitored by determining the expression of c-PARP by Western blot, caspase-3/7 activity by caspase-Glo kit and apoptotic cell population (Annexin-V staining) using flow cytometry.
Results: The combination of TA and DOX or VIN caused significantly higher cell growth inhibition when compared to individual agents. TA inhibited the expression of Sp1, survivin and up-regulated c-PARP. The chemotherapeutic agents had no effect on Sp1 and survivin. Confirmatory results show apoptotic markers (c-PARP expression, caspase-3/7 activity and Annexin V positive cells) were increased at 48 h post-treatment. The effect of proposed combinations on cell cycle phase distribution and markers of DNA damage and repair is under evaluation.
Conclusions: These results confirm that TA combined with Doxorubicin or Vincristine effectively inhibits leukemia cell growth. Further studies evaluating the mechanism of action of proposed combinations and in vivo assays are currently under investigation. This pre-clinical study suggests that by targeting Sp proteins, TA may enhance the anti-leukemic effect of standard chemotherapeutic agents.

P-018

IN VITRO DEXAMETHASONE SENSITIVITY OF ACUTE LYMPHOBLASTIC LEUKEMIA CELLS IS NOT INFLUENCED BY INTERVENING WITH HYDROCORTISONE

L. Warris[1], M.M. van den Heuvel - Eibrink[1], I.M. Aries[1], R. Pieters[1], E.L.T. van den Akker[2], M.L. den Boer[1]

[1]Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Pediatric Endocrinology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands

Objectives: Based on recent studies, we hypothesized that dexamethasone induced neuropsychological side effects on mood, behavior and cognition in children with acute lymphoblastic leukemia (ALL) are caused by dexamethasone induced cortisol depletion of the mineralocorticoid receptor (MR) in the brain. Therefore it is feasible that these side effects could be ameliorated by an intervention with hydrocortisone. To exclude interference with the efficacy of glucocorticoids on ALL cells, we performed the current study.
Methods: To investigate responsiveness of leukemic cell lines and fresh patients' leukemic cells to dexamethasone and prednisolone in the presence of physiologic doses of hydrocortisone, a MTT-assay was performed. In addition the expression of the MR and the glucocorticoid receptor (GR) on leukemic cells of different ALL subtypes was studied with a microarray-based gene expression profiling and validated by quantitative real-time PCR.
Results: *In vitro* glucocorticoid sensitivity of both glucocorticoid resistant and sensitive leukemic cell lines and ALL patients' cells was independent of the added dose of hydrocortisone. MR expression levels on leukemic patient cells were very low compared to GR expression levels. MR expression had a wide variation between patients and was relatively higher in the TEL/AML-1 subtype. No difference in sensitivity to prednisolone or dexamethasone was found with addition of hydrocortisone between the TEL/AML-1 subtype patient cells and the other ALL subtypes.
Conclusions: This present study shows that it is not likely that MR activation with hydrocortisone interferes with the efficacy of glucocorticoids on ALL cells. These findings enable the currently ongoing clinical randomized study hypothesizing that hydrocortisone decreases neuropsychological side effects of dexamethasone in children with ALL.

P-019

FUNCTIONAL GENOME WIDE ENRICHMENT ASSOCIATION ANALYSIS OF VINCRISTINE NEUROPATHY

J.L. Renbarger[1], C.H. Li[2], J. Skiles[1], L. Li[2]

[1]Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [2]Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, USA

Objectives: Vincristine is among the most commonly used anticancer agents, but little is known regarding its disposition and optimal dosing. Vincristine is associated with highly variable cumulative dose-dependent peripheral neuropathy (VIPN), which is often treated with pain medications and/or dose reductions which may compromise efficacy. In this study, we carried out a functional enrichment analysis using data from across the human genome to evaluate the association between genomic variation and VIPN in children with acute lymphoblastic leukemia.

Methods: Germline DNA from subjects enrolled to POG 9004 and 9005 was genotyped using the Affymetrix GeneChip Human Mapping 6 set. VIPN was captured using NCI CTCAE v3.0 and grade ≥ 2 was used as a cutoff for VIPN. GWAS analysis was completed and reported separately. Three functional analyses were conducted on GWAS results. The first focused on 101 genes targeted by 23 drugs, which treat pain as a manifestation of neuropathy. The second analysis focused on SNPs from gene regions that are differentially expressed in the fibrosarcoma cell line after vincristine treatment. The third analysis focused on SNPs from reported expression quantified trait loci (eQTLs) in cerebellar tissue from the Genotype Tissue Expression database.
Results: In the drug target analysis, SNPs were enriched in 8 genes: *CACNA1D, SLC29A4, CACNA1C, GRIK1, SCN8A, CACNB1, GRIN3A* and *SLC22A1* (p-value < 0.05). From the fibrosarcoma cell line expression experiments, 14 SNPs were associated with neuropathy ($p < 1 \times 10^{-4}$), including SNPs in: *MICAL3, ERCC8*, (both identified in original GWAS) and *CANA1C*. The eQTL analysis from cerebellar tissue identified two additional SNPs associated with VIPN.
Conclusions: Functional enrichment analysis identified a number of genes across the human genome that may be associated with VIPN. This information has significant potential clinical relevance given the widespread use of this important drug in treating childhood cancers.

P-020

GENETIC DETERMINANTS OF VINCRISTINE NEUROPATHY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

J.L. Skiles[1], C.H. Li[2], L. Li[2], J.L. Renbarger[1]

[1]Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [2]Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, USA

Objectives: Vincristine is among the most commonly used anticancer agents, however little is known regarding its disposition and optimal dosing. This gap in knowledge can lead to negative clinical outcomes such as toxicity due to drug overdosing or lack of efficacy due to sub-therapeutic dosing. Vincristine is associated with highly variable cumulative dose-dependent peripheral neuropathy (VIPN). We carried out a genome-wide association analysis to explore the association between germline variants and VIPN in pediatric acute lymphoblastic leukemia patients.
Methods: Germline DNA from ($n = 1098$) subjects enrolled to POG 9004 and 9005 was genotyped using the Affymetrix GeneChip Human Mapping 6 set. Quality control (QC) was performed to remove unreliable samples and markers. A population stratification approach was applied to adjust for potential ethnicity effects. VIPN was captured using CTCAE v3.0 for sensory and motor neuropathy. The primary outcome was defined as development of neuropathy ($\geq$ grade 2); and secondary outcome was time to development of neuropathy or neuropathic pain. Each SNP association was evaluated in three genetic models: additive, dominant, and recessive. The SNP effect on VIPN was further adjusted by the clinical, demographic, and population stratification variables in the Cox regression analyses.
Results: After QC, a total of 587,014 SNPs and 1068 individuals remained in the analysis. Using COX model for association analysis, a total of 56 SNPs in 23 genes were identified across both primary and secondary outcomes (p-value $< 1 \times 10^{-4}$). Genes of most potential biologic relevance include, *CSNK1G3, Nek6, MICAL3*, and *ERCC8*. Validation in an independent cohort is ongoing.
Conclusions: A number of genes across the human genome may be associated with VIPN. This information has significant potential clinical relevance given the widespread use of this important drug in treating childhood cancers.

P-021

GENETIC VARIANTS IN VINCRISTINE TRANSPORTERS AS NEUROTOXICITY MARKERS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

M. Pombar-Gomez[1], A. Echebarria[2], N. Bilbao-Aldaiturriaga[3], M.A. Piñán[4], J. Uriz[5], P. García-Miguel[6], A. Navajas[2], A. Garcia-Orad[1]

[1]Genetics Physical Anthropology and Animal Physiology, University of the Basque Country, Leioa, Spain; [2]University Hospital Cruces, Unit of Pediatric Hematology/Oncology, Bilbao, Spain; [3]University of the Basque Country, Department of Genetics Physic Anthropology and Animal Physiology, Leioa, Spain; [4]Service of Hematology and Hemotherapy, University Hospital Cruces, Bilbao, Spain; [5]Department of Pediatrics, University Hospital Donostia, San Sebastian, Spain; [6]Department of Oncohematology, University Hospital La Paz, Madrid, Spain

Objectives: Acute lymphoblastic leukemia (B-ALL) is the most common pediatric malignancy. Therapeutic advances have increased survival, due in part to standardized treatment protocols. Vincristine is used in different phases of treatment (induction, intensification and reinductions). However, some individuals experience neurotoxicity and there are no markers to predict it. As vincristine has a narrow therapeutic range, pharmacogenetic studies may be useful for predicting toxicity. Only few studies have been performed to date with conflicting results for CYP3A5 gene ABCB1 and MAPT. Recently, our group found new methotrexate toxicity markers, analyzing in depth genes involved in methotrexate transport. So, genes involved in vincristine transport, could also have a role in vincristine toxicity. The aim of the present study was to analyze in depth the role of genetic variations in genes involved in vincristine transport as markers of neurotoxicity in a large cohort of children with B-ALL homogeneously treated.
Methods: DNA was extracted from remission blood samples of 200 pediatric ALL patients, all of them homogeneously treated with LAL/SHOP protocol. We studied 172 SNPs that cover 11 genes involved in vincristine transport with Illumina GoldenGate platform. The association between SNPs and neurotoxicity was analyzed using the Fisher exact test.
Results: Our results suggest that pharmacogenetic studies may be useful for neurotoxicity prediction and adjustment of vincristine treatment in pediatric ALL patients.
Conclusions: In conclusion, polymorphisms in the vincristine pathway genes may be useful for neurotoxicity prediction and adjustment of vincristine treatment in pediatric ALL patients.
This project was supported by RETICS (RD/12/0036/0060) and Basque Government (IT661-13, S-PE13UN068 and 2012111053).

P-022

ASSOCIATION BETWEEN POLYMORPHISMS OF RFC1 GENE AND HIGH-DOSE METHOTREXATE THERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

J. Yang[1], H. Jiang[1], H. Li[1]

[1]Hematology/Oncology, Shanghai Children's Hospital, Shanghai, China

Objectives: To investigate the association of the gene polymorphism of RFC1G80A and high-dose MTX (HD-MTX) related toxicity.
Methods: 68 cases of ALL were enrolled in our department from February 2009 to January 2012. RFC1G80A gene polymorphism was detected before HD-MTX treatment. Plasma MTX concentration, liver and kidney function and peripheral blood cell count were detected on time after HD-MTX 24 to 42 hours. All data were analyzed by SPSS 16.0.
Results: RFC1 G80A gene polymorphism was associated with MTX toxicity. The risk of hepatotoxicity and myelosuppression in RFC1-AAgenotype were 7.28 and 2.8 times higher than RFC1-GG ($P = 0.000$, $p = 0.005$). There were no significant differences between gene polymorphism of RFC1G80A and elimination delay of MTX and prognosis ($P > 0.05$).
Conclusions: RFC1G80A genetic polymorphisms were associated with hepatotoxicity and myelosuppression after HDMTX chemotherapy and would be used as a risk indicators for HDMTX-related toxicity. No significant association was found among plasma MTX concentration, elimination delay and prognosis of childhood ALL with gene polymorphism of RFC1G80A.

P-023

THE EFFECT OF CRANIAL RADIATION THERAPY (CRT) ON BODY MASS INDEX (BMI) DURING TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN CHILDREN: AN EXPLORATORY ANALYSIS

A. Athale[1], T. Nayiager[2], J. Badhiwala[3], U. Athale[4]

[1]Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada; [2]McMaster Children's Hospital, Hamilton Health Sciences, Hamilton, Canada; [3]Department of Pediatrics, Michael DeGroote School of Medicine, Hamilton, Canada; [4]Department of Pediatrics, McMaster University, Hamilton, Canada

Objectives: CRT is shown to be associated with obesity in long-term survivors of childhood ALL. However, its impact on BMI during therapy is not well studied. The objective of this study was to determine the effects of CRT on BMI in children aged 2-18 receiving therapy according to Dana-Farber Cancer Institute ALL protocols from 1995-2010 at McMaster Children's Hospital.
Methods: Retrospective chart review was conducted to collect baseline demographic (age, gender, ALL risk category), therapy (steroid type and CRT) and anthropometric data at five time points during therapy (0,6,12,18 and 24 months). We studied the impact of above factors on BMI z scores (calculated according to the Centers for Disease Control and Prevention guidelines). Paired t-test and independent sample t-tests were used to compare BMI z-scores within and in-between groups respectively.
Results: A total of 159 children [mean age 78.4 months] were included. Of these 81 (50.9%) were male, 105 (66%) had standard-risk ALL, 91 (57.2%) received dexamethasone and 60 (37.7%) received CRT. There was a significant increase in BMI z-scores from 0 months to end of therapy (24 months) in the whole cohort (-0.076 (0.12) vs 0.67 (0.11) $p < 0.001$). Patients receiving CRT had significantly lower BMI z-scores at 6 months (the first time point following CRT), compared to those without CRT (-0.58 (0.29) vs.-0.06 (0.16), $p < 0.05$). Moreover, the rate of change in BMI z-scores from 0 to 6 months in these two groups (-0.54 (0.23) vs. -0.048 (0.15), $p = 0.06$) was different. No other covariates significantly impacted BMI z-scores at six months. There was no difference in the BMI z scores at 12, 18 and 24 months in patients with or without CRT.
Conclusions: Patients receiving CRT tend to have significant reduction in BMI soon after administration, but this effect is transient. This observation suggests the need of different nutritional strategies in patients receiving CRT. Further research is needed to confirm these findings.

P-024

OUTCOMES OF YOUNG CHILDREN WITH CNS POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH AND WITHOUT CRANIAL RADIOTHERAPY: A SINGLE-CENTRE EXPERIENCE

M. Wilejto[1], S. Gupta[1], G. Di Giuseppe[1], B. Spiegler[2], J. Hitzler[1], O. Abla[1]

[1]Hematology-Oncology, Hospital for Sick Children, Toronto, Canada; [2]Psychology, Hospital for Sick Children, Toronto, Canada

Objectives: Acute lymphoblastic leukemia (ALL) is the most common cancer in children and is treated with a combination of intra-thecal (IT) and systemic chemotherapy +/- cranial radiotherapy (CRT). With increasing recognition of the long-term sequela of CRT, modern trials have largely omitted prophylactic CRT. For patients with CNS disease at diagnosis however, the decision to omit CRT is less clear. Children < 5 years of age are a particularly challenging subgroup, in whom the neuro-cognitive and endocrine consequences of CRT can be exceptionally devastating. The primary aim of this study was to describe the outcome of young children (1-< 5years of age) with CNS positive ALL treated with and without CRT.
Methods: Retrospective cohort study of children age 1-<5years with ALL diagnosed between January 2000 - May 2013 at the Hospital for Sick Children. Data were abstracted through chart review. This study has been approved by the Institutional Review Board.
Results: 468 children met inclusion criteria, 19 (4%) of whom presented with CNS involvement at diagnosis. Of these, only one child was treated with upfront CRT as part of bone marrow transplant (BMT) conditioning. Other forms of therapy intensification in this cohort included triple IT chemotherapy (16/19, 84%), dexamethasone (11/19, 58%) and high dose methotrexate (14/19, 74%). 16/19 (84%) patients are alive at last follow-up. Three children died from treatment related toxicity and one child had an isolated CNS relapse that was salvaged with BMT.
Conclusions: CNS leukemia in young children can be effectively treated with intensified IT and systemic chemotherapy and without CRT while maintaining favorable outcomes. This study adds to the growing body of literature supporting the omission of CRT from modern ALL protocols in an attempt to minimize acute and long term toxicities.

P-025

UNDERWEIGHT AND WEIGHT LOSS NEGATIVELY INFLUENCES OUTCOME IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

M. den Hoed[1], S.M.F. Pluijm[1], H.A. de Groot-Kruseman[2], M.L. te Winkel[1], E.L.T. van den Akker[3], P. Hoogerbrugge[4], H. van den Berg[5], J.A. Leeuw[6], M.C.A. Bruin[7], D. Bresters[8], A.J.P. Veerman[9], R. Pieters[10], M.M. van den Heuvel-Eibrink[1]

[1]Pediatric Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Pediatric Oncology, Dutch Childhood Oncology Group, The Hague, Netherlands; [3]Endocrinology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [4]Pediatric Oncology, Radboud University Medical Center Nijmegen, Nijmegen, Netherlands; [5]Pediatric Oncology, Academic Medical Center, Amsterdam, Netherlands; [6]Pediatric Oncology, Beatrix Children's Hospital University Medical Centre Groningen, Groningen, Netherlands; [7]Pediatric Oncology, University Medical Center Utrecht, Utrecht, Netherlands; [8]Pediatric Oncology, Willem-Alexander Children's Hospital Leiden University Medical Center, Leiden, Netherlands; [9]Pediatric Oncology, VU University Medical Center, Amsterdam, Netherlands; [10]Pediatric Oncology, Princess Maxima Center, Utrecht, Netherlands

Purpose: To study the influence of (change in) body mass index (BMI;kg/m^2) on outcome in pediatric patients with ALL who were treated according to a dexamethasone-based protocol (Dutch Childhood Oncology Group [DCOG] ALL-9).
Patients and Methods: Data of body composition were prospectively selected from a national cohort of newly diagnosed Dutch pediatric ALL patients (n = 762, age 2-17 years), treated from 1997-2004. BMI was expressed as standard deviation scores (SDS) and categorized into overweight (>1.1 SDS ≈ >25 kg/m^2) normal weight (–1.8 to 1.1 SDS ≈ > 18.5 to 25 kg/m^2) and underweight (<–1.8 SDS ≈ < 18.5 kg/m^2). Dual X-ray Absorptiometry (DXA) scans were performed in a nested single center cohort to assess the contribution of%fat and lean body mass to BMI. Body composition was reassessed after 32 weeks of treatment. Outcome measures were defined as 10-year event free survival (EFS), cumulative incidence of relapse (CIR) and overall survival (OS). Uni- and multivariable Cox-regression analysis were performed to examine the association between BMI and survival.
Results: Underweight patients (8%) at diagnosis had an increased risk of relapse (Hazard Ratio (HR) 1.86, 95% CI:[1.08-3.21] but not an increased mortality rate (HR 1.17 [0.61-2.24]). A BMI decrease during the first 32 weeks of treatment was associated with a higher mortality rate (HR 1.93 [1.04-3.58]), but not with a higher relapse rate (HR 1.18 [0.65-2.15]). DXA revealed that a BMI decrease consisted of a loss of lean body mass, while these patients showed an increase in their%fat.
Conclusion: Underweight at diagnosis influences the likelihood of relapse. A BMI decrease, which seems to consist of mainly muscle loss, is associated with a decreased overall survival in children with ALL.

P-026

OESTRADIOL AND DHEA BUT NOT TESTOSTERONE MODULATE OSTEOCYTE VEGF SECRETION IN VITRO: IMPLICATIONS FOR THE PATHOGENESIS OF CORTICOSTEROID-INDUCED OSTEONECROSIS

M. Adams[1], M. Jenney[2], S. Hiscox[1], J. Gregory[1], B. Evans[1]

[1]Institute of Molecular and Experimental medicine, Cardiff University, Cardiff, United Kingdom; [2]Paediatric Oncology, Children's Hospital for Wales, Cardiff, United Kingdom

Objectives: Interruption to VEGF signalling is a major pathological mechanism of corticosteroid-induced osteonecrosis, a disabling side effect of therapy for acute lymphoblastic leukaemia. Adolescent females are at greatest risk but any relationship between sex steroids, puberty and VEGF signalling in osteocytes has not been previously documented. We have previously demonstrated that dexamethasone reduces osteocyte VEGFsecretion and now hypothesise that sex steroids may influence osteocyte proliferation and/or VEGF secretion either via nuclear steroid receptors or via a non-genomic pathway.
Methods: MLO-Y4 osteocytes were incubated (24-72 hours) with oestradiol, DHEA or testosterone (10^{-11} – 10^{-8}M) in the presence or absence of dexamethasone (10^{-7}M). Cell number (MTS) and VEGFsecretion (ELISA) were measured. Mechanisms were investigated by blockade of oestrogen receptors (ERs) with selective oestrogen receptor modulators (SERMs) tamoxifen and fulvestrant (both 10^{-7}M) and inhibition of the conversion of DHEA to oestradiol with the aromatase inhibitor anastrozole (10^{-7}M). The effect of dexamethasone on ER as well as the non-genomic G-coupled protein receptor 30 expression was also measured (qRTPCR).
Results: Oestradiol and DHEA significantly reduced osteocyte cell number (8-13% and 12-16% reduction respectively, $p < 0.001$). When SERMS were co-incubated with oestradiol and anastrozole with DHEA, these effects were abolished. Both oestradiol significantly increased VEGF secretion (by 24%; $P = 0.002$ and 43%; $p < 0.001$ respectively). Co-incubation with SERMs or anastrozole did not ameliorate this increase suggesting firstly that oestradiol acts via a non- genomic pathway and secondly that DHEA exerts independent activity rather than by conversion to oestradiol. Dexamethasone prevented the oestradiol-induced increase in VEGFsecretion and caused a 2.3 fold reduction ($p < 0.001$) in ER alpha gene expression. No effect of testosterone on cell number or VEGF secretion was demonstrated.
Conclusions: This study reveals novel interactions between sex steroids and dexamethasone on osteocyte angiogenesis which may contribute to the understanding of the high incidence of osteonecrosis in adolescent patients.

P-027

DO PARENTAL OCCUPATION AND AREA REMOTENESS LEAD TO SOCIAL DISPARITIES IN SURVIVAL FROM CHILDHOOD LEUKEMIA? RE-ANALYSIS OF DATABASES AND A META-ANALYSIS

M. Kourti[1], T. Sergentanis[2], C. Perlepe[2], E. Papathoma[2], G. Tsilimidos[2], E. Kontogeorgi[2], M. Baka[3], M. Moschovi[4], S. Polychronopoulou[5], V. Sidi[1], E. Hatzipantelis[6], E. Stiakaki[7], E. Petridou[2]

[1]Pediatric Hematology Oncology Unit 2nd Department of Pediatrics, Hippokration General Hospital, Thessaloniki, Greece; [2]Dept of Hygiene Epidemiology and Medical Statistics, University of Athens Medical School, Athens, Greece; [3]Department of Pediatric Hematology-Oncology, 'Pan.&Agl. Kyriakou' Children's Hospital, Athens, Greece; [4]Hematology-Oncology Unit First Department of Pediatrics Athens University Medical School, 'Aghia Sophia' General Children's Hospital, Athens, Greece; [5]Department of Pediatric Hematology-Oncology Athens University Medical School, 'Aghia Sophia' General Children's Hospital, Athens, Greece; [6]Pediatric Hematology Oncology Unit 2nd Department of Pediatrics, Aristotle University School of Medicine AHEPA General Hospital, Thessaloniki, Greece; [7]Department of Pediatric Hematology-Oncology, University Hospital of Heraklion, Thessaloniki, Greece

Objectives: Advances in treatment have greatly improved survival of children suffering leukemia during the last decades. Concerns have been raised, however, regarding social disparities in survival due to potential interference of socio-economic status (SES) and health care access components with treatment. This re-analysis of available primary data in two databases along with meta-analyses following a systematic review of the literatures aims to shed light into the effects of parental occupation and area remoteness in terms of rural/urban status upon survival from childhood leukemia.
Methods: The National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER) 1973-2010 data were critically re-analyzed along with the Greek Nationwide Registry of Childhood Hematological Malignancies (NARECHEM, 1996-2011) data, whereas a systematic review of the literature contributed to the subsequent meta-analyses additional study arms from published evidence. Overall survival was the main outcome; random-effects (DerSimonian-Laird) models were appropriately used to calculate pooled effect estimates.
Results: In the largest ever analyses (>27,000 acute lymphoblastic leukemia, ALL and >3,000 acute myeloid leukemia, AML cases), less privileged parental occupation predicted considerably poorer survival from ALL (pooled RR = 1.51, 95%CI: 1.22-1.87), whereas the respective finding for childhood AML did not reach significance. No statistically significant association was observed regarding rural vs. urban place of residence with survival from either ALL (pooled RR = 1.06, 95%CI: 0.89-1.26) or AML (pooled RR = 1.19, 95%CI: 0.92-1.55).

Conclusions: Lower occupation related SES may unfavorably impact on survival, at least from the less aggressive ALL, through a variety of functions, such as poor compliance, refusal or abandonment of treatment, modified attitudes by health care providers, inadequate health insurance and access to quality health care. Contemporary satisfactory transport infrastructure, may underlie, the minimal, non significant association with residence remoteness.

P-028

COMPARISON OF THE EFFICACY, SAFETY AND ECONOMIC COST OF VINDESINE AND VINCRISTINE FOR NEWLY DIAGNOSED PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A RETROSPECTIVE ANALYSIS

J. Zhang[1], Y. Zhang[1], X. Li[1], R.M. Jin[1]

[1]Pediatrics, Union Hospital Tongji Medical College Huazhong University of Science and Techn, Wuhan, China

Objectives: The anti-tumor botanicals Vincaal kaloidsm, vindesine (VDS) and vincristine (VCR), are worldwide used components of chemotherapy, although associated with serious adverse effects. We compared the efficacy, toxicity and economic cost of VDS to VCR during induction and intensification in children with newly diagnosed acute lymphoblastic leukemia (ALL) on the Chinese Children's Leukemia Group (CCLG) - ALL 2008 protocol in a hospital.
Methods: Archived medical records were reviewed for 105 children diagnosed in our hospital in the trial CCLG-2008 who had received VDS administered as 3 mg/m2 or VCR 1.5 mg/m2 per week during induction and Intensification.
Results: Between May 2009 and October 2013,105 children (1 to 18 years of age, 48 VDS vs. 57 VCR) with newly diagnosed ALL (excluding mature B-cell ALL) were included. Complete-remission (CR) rates were similar with VDS and VCR (91.7% and 94.7%, respectively; $P = 0.53$). Three-year results in both treatment groups were similar (overall survival $91.7\% \pm 4.4\%$ for VDS vs. $91.2\% \pm 4.3$ for VCR, $P = 0.94$, event-free survival $89.6\% \pm 4\%$ vs. $82.5\% \pm 4\%$, $P = 0.14$). Treatment-related mortality (TRM) in continuous complete remission children was lower in the presence of VDS than VCR (2.2% vs. 14.2%, $P = 0.04$). A total of 199 cases (including 113 cases/times for VDS group, 86 cases/times for VCR group), were recorded for adverse events' statistics. VDS had lower rates of Grade 3/4 decreased hemoglobin ($P < 0.001$) and thrombocytopenia ($P = 0.01$) than VCR, and total neurotoxicity ($P = 0.008$). Three cases of VCR group occurred unbearable paresthesia or significant movement disorders, which disappeared with VDS. The expenses of hospitalization were lower with VDS than VCR (25,996 RMB vs. 34,244 RMB, $P = 0.002$).
Conclusions: At the given dose, VDS has similar antileukemic activity compared to VCR, causes less treatment-related mortality in continuous complete remission children, decreases the rates of neurotoxicity and hematotoxicity and reduces the expenses of hospitalization, worthy of further clinical studies and use.

P-029

CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN THE MIDDLE EAST AND NEIGHBORING COUNTRIES: A PROSPECTIVE MULTI-INSTITUTIONAL INTERNATIONAL COLLABORATIVE STUDY BY THE MIDDLE EAST CHILDHOOD CANCER ALLIANCE (MECCA)

A. ALNasser[1], N. AlMulla[1], P. Chandra[1], M. Khattab[1], F. Madanat[1], M. Farranoush[1], E. Torfa[1], Z. Al-Lamki[1], G. Zain[1], S. Muwakkit[1], S. Mahmoud[1], A. Al-Jassmi[1], M. Tuncer[1], H. Al-Mukharraq[1], S. Barsaoui[1], R. Arceci[1], S. Howard[1], A. Kulozik[1], Y. Ravindranath[1], G. Reaman[1]

[1]MECCA, Middle East Childhood Cancer Alliance, Doha, Qatar

Objectives: The Middle East Childhood Cancer Alliance (MECCA) was established in 2000 and is comprised of member institutions in 16 countries in the Middle East and surrounding area. Little is known about childhood ALL in the Middle East. This study, funded by Qatar National Research Fund, was undertaken by MECCA as initial efforts in collaborative data collection to provide clinical, laboratory, molecular genetic characterization, induction toxicity and outcome data on children with ALL in the Middle East.
Methods: Clinical, laboratory, molecular genetic characterization, induction toxicity and outcome for patients with ALL between January 2008-April 2012 were prospectively collected from institutions in 14 Middle East countries and entered into a custom-built-database during induction phase. All laboratory studies including cytogenetics were done at local institutions.
Results: The 1,171 voluntarily enrolled patients had a mean age of 6.1 ± 3.9 years and 59.2% were males. T-ALL represented 14.8% and 84.2% had B-precursor ALL. At diagnosis, 5.6% had CNS disease. The distribution of common genetic abnormalities reflected a similar percentage of hyperdiploidy (25.6%), but a lower percentage of *ETV6-RUNX1* translocation (14.7%) compared to large series reported from Western populations. By clinical criteria, 49.1% were low/standard risk, 16.9% were intermediate risk and 36% were high-risk. The majority of patients (96.9%) received care at their local or regional hospitals. Patients had excellent induction response to chemotherapy with an overall complete remission rate of 96%. Induction toxicities were acceptable.
Conclusions: In conclusion, we believe that this study provides proof of principle that collaborative clinical research with a centralized data repository is feasible in the Middle East. Despite the limitations of an incomplete population-based study, it provides the first comprehensive baseline data on clinical characteristics, laboratory evaluation, molecular genetic characterization, induction outcome and toxicity. Further work is planned to uncover possible biologic differences of ALL in the region and to improve diagnosis and management.

P-030

SURVIVAL OF CHILDREN WITH LEUKEMIA IN SOUTH AFRICA AND LESOTHO

D. Stefan[1], A. Van Zyl[1], D.K. Stones[2]

[1]Paediatrics & Child Health, Stellenbosch University, Cape Town, South Africa; [2]Paediatrics & Child Health, Free State University, Bloemfontein, South Africa

Objectives: Leukemia remains the most common childhood cancer in South Africa and Lesotho. The cure rates of acute lymphoblastic leukemia (ALL) in developed countries reach 90%. In Africa there is a paucity of data regarding the survival of children with leukemia. The aim of the study was to calculate the survival rates of children diagnosed and treated for ALL in South Africa and Lesotho.
Methods: This was a retrospective study including all children <15 years diagnosed and treated for ALL between 1 January 1995 to 31 December 2009 in 2 centres in South Africa (Tygerberg Hospital in Cape Town and Universitas Hospital in Bloemfontein) and and all the patients from Lesotho. All diagnoses were confirmed by the certified National Health Laboratory Services in South Africa.
Results: There were 307 patients treated for ALL (27 from Lesotho and 280 from SA)., males 55% and females 45%. The average age at diagnosis was 78.9 months (range 2 -181 months). The black children were the most 128, followed by the colored population, 100 patients and finally the white 79 patients. The overall survival for the group was 55% (the 2 South African centres 46.8% and 67.7%) and Lesotho 44.4%. The follow up time was 66 months. The survival of the black children was the lowest at 45.3% followed by the white children 59.5%. The colored children had the best survival rate at 64%. All patients were treated with the same protocols.
Conclusions: The survival rates of children diagnosed with ALL in South Africa and Lesotho are low and showed significant differences in corelation with the ethnic group. Further clinical and genetic research is required.

P-031

STANDARD RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN MOROCCO: EXPERIENCE OF 170 CASES TREATED IN A SINGLE CENTER

M. Khattab[1], M. Elkababri[1], A. Kili[1], L. Hessissen[1], M. Elkhorassani[1], U. Athale[2]

[1]Pediatrics, University Mohammed V-Souissi, Rabat, Morocco; [2]Pediatrics, McMaster University, Hamilton Ontario, Canada

Objectives: The event free survival of childhood acute lymphoblastic leukemia (ALL) was < 34% in Morocco. The main causes of failure were abandonment (15%) and non-availability of drugs for almost 80% of patients. A national therapy protocol (MARALL 2006) was developed based on the French protocol FRALLE 2000. Herein we report the results of the Standard Risk (SR) group.
Methods: Treatment included Induction, consolidation, intensification and interphase courses (11 months) followed by maintenance (2 years). Chemotherapy consisted of Vincristine, Doxorubicin, L-Asparaiginase, corticosteroids, high and low-dose Methotrexate, Cyclophosphamide, Cytarabine, 6-mercaptopurine, and 18 doses of triple intrathecal therapy. Children ($\geq$ 2and $\leq$9 yrs) diagnosed with *de novo* precursor-B ALL with WBC < 50,000/mm^3 and absence of central nervous system disease were categorized as SR. A dedicated team of physicians, nurses, social worker and data manager supervised the ambulatory ALL therapy. All patients had free access to medication through NGOs, Hospital and health insurance. Weekly team meetings reviewed patient management, data, problems and arrangement for aid to patients.
Results: From 2006 to 2013, a total of 389 patients were diagnosed with ALL; 170 (44%) were SR. The median age was 4 years and M:F ratio was 1.29. FAB classification was L1 in 74% and L2 in 26% of cases. Remission rate was 97% and 1% had refractory ALL. Therapy abandonment rate was 2%. Overall mortality was 2% and 11% patients relapsed with a median time of 18 months from diagnosis. With a median follow-up of 49 months, the event free and overall survivals were 66% and 72% respectively.
Conclusions: Compared to historical data, MARALL 2006 protocol resulted 50% increase in survival of children with SR ALL and low abandonment rate. This was achieved with a close follow-up by a dedicated ALL team, commitment to drug procurement and social support for patients.

P-032

DEVELOPMENT OF THE EVALUATING QUALITY OF LIFE IN ACUTE LYMPHOBLASTIC LEUKAEMIA (EQUALL) QUESTIONNAIRE: A TREATMENT-SPECIFIC MEASURE FOR THE EFFECTS OF CORTICOSTEROIDS ON QUALITY OF LIFE

M. Adams[1], S. Sherratt[1], A. Johnson[1], J. Tomlins[2], J. Grainger[3], M. Jenney[1]

[1]*Paediatric Oncology, Children's Hospital for Wales, Cardiff, United Kingdom;* [2]*TYA Haematology, Christie Hospital, Manchester, United Kingdom;* [3]*Paediatric Haematology, Manchester Children's Hospital, Manchester, United Kingdom*

Objectives: The use of corticosteroids (particularly dexamethasone) within acute lymphoblastic leukaemia (ALL) protocols has contributed greatly to the excellent survival rates. However this is not without cost – in addition to physical side effects, corticosteroids influence behaviour, mood and cognitive functioning leading to an impaired quality of life (QoL) for patients. The UKALL 2011 randomisation to maintenance therapy with or without dexamethasone pulses has both survival and QoL as primary outcome measures. The aim of this study was to develop a QoL measure sensitive to the effects of corticosteroids that may detect potential differences in QoL in patients receiving dexamethasone.
Methods: Patients aged 8-24 years and parents of children aged 1-15 years receiving maintenance therapy for ALL from 4 UK centres, were invited to participate. The study comprised 3 stages: A) focus groups and interviews asked participants to describe their experience of dexamethasone, and the themes identified formulated Version 1 of EQuALL. B) Version 1 was emailed electronically to healthcare professionals and patients to evaluate the importance and relevance of questions. Amendments were made to create Version 2. C) Cognitive interviewing confirmed face validity and explored question interpretation. Further modifications were made to define Version 3.
Results: Six parents and eight patients attended focus groups/interviews. Interpretative phenomenological analysis of transcripts identified that patients feel dexamethasone has adverse effects on behaviour, appetite, body image, mood and family relationships. 121 healthcare professionals and 36 patients/parents completed the electronic survey leading to further amendment of the questions. Face validity was confirmed by cognitive interviewing of 21 patients. EQuALL comprises 35 questions within 4 domains and has age-specific versions.
Conclusions: EQuALL is the first treatment-specific QoL measure for corticosteroids. It can be completed in 10-15 minutes by children aged 8 years and above. Further validity and reliability testing will be undertaken within UKALL 2011.

P-033

OUTCOME OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS UNDERGOING CHEMOTHERAPY USING LOW-INCOME-COUNTRY REGIMEN 1 PROTOCOL AT THE UNIVERSITY OF THE PHILIPPINES - PHILIPPINE GENERAL HOSPITAL (2009-2013)

D. Arca[1], E. Melendres[1], A. Goletea-Dy[1], A. Goleta-Dy[1], A. Alcasabas[1], P. Fajardo[1], Y. Medina[1]

[1]*Pediatric Hematology-Oncology, University of the Philippines, Manila, Philippines*

Purpose: To determine the impact on survival rate, toxicity and abandonment of treatment among childhood Acute Lymphoblastic Leukemia (ALL) patients using the Low Income Country (LIC) Regimen 1 Chemotherapy Protocol at the University of the Philippines - Philippine General Hospital (UP-PGH).
Methods: Medical records of newly diagnosed ALL patients from June 2009 to September 2011, ages 0-18 years, were reviewed. Demographic data were collected. Treatment outcome was evaluated at study endpoint, December 31, 2013, and included death, treatment refusal, abandonment, relapse, and phase of treatment.
Results: 173 patients were diagnosed from June 2009 to September 2011. Diagnosis was by immunophenotyping in 86% and morphology in 14%. Seventy-five patients (43.40%) refused treatment; while 86 patients underwent LIC regimen 1 (without radiation). Male to Female ratio was 2.4:1. Age ranged from 17 months-18 years (mean = 6 years). 60% were NCI standard risk, and 40% high risk. One had CNS involvement at diagnosis. None had testicular involvement at start of therapy. Remission induction was 75.58% (n = 65). Ten patients (10.47%) died during Induction. At study endpoint, 20 (23.5%) completed therapy, 9 (10.6%) were on maintenance. Relapses occurred in 18 patients: CNS (n = 10; 11.8%) and bone marrow (n = 8; 9.4%). Fifteen (17.6%) abandoned treatment. Seventeen patients died during treatment (19.77) due to sepsis and intracranial bleeding. At end of study period, 39.53% of the patients were alive (n = 34) and 30.23% (n = 26) were in remission.
Conclusion: In LIC, the choice of ALL therapy should consider available supportive care. Aside from good infection control, accessibility of blood products, database, financial and social work support are imperative. The survival rate among our ALL patients is still low, however the use of LIC Regimen 1, was associated with an improvement in the survival rate and reduction in toxic death and abandonment.

P-034

BIOIMPEDANCE ANALYSIS (BIA) AND ANTHROPOMETRY IN PROGNOSIS OF COMPLICATIONS AND GRAFT FUNCTION AFTER HEMATOPOIETIC STEM CELLS TRANSPLANTATION (HSCT) IN CANCER CHILDREN

G. Tseitlin[1], A. Vashura[1], M. Konovalova[1], D. Balashov[2], M. Maschan[2]

[1]*Rehabilitation, Dmitry Rogachev Federal Research Centre of Pediatric Hematology Oncology and Immunology, Moscow, Russia;* [2]*Transplantation, Dmitry Rogachev Federal Research Centre of Pediatric Hematology Oncology and Immunology, Moscow, Russia*

Objectives: HSCT has become an established treatment for malignant hematological diseases, solid malignancies and autoimmune diseases. Our goal is to assess the value of some BIA and anthropometric indicators as prognostic factors for severe complications (steroid diabetes; erosive or ulcerative duodenitis/enterocolitis with bleeding; gastro/enterocolitis more than 30 days; destructive pancreatitis (pancreanecrosis); veno-occlusive disease; hemorrhagic cystitis more than 14 days; renal insufficiency; toxicodermia more than 30 days; toxic or infectious encephalopathy; heavy toxic polyneuropathy; mukositis 2nd or higher degree; septic shock) after HSCT.
Methods: There were 101 patients examined at a period started before conditioning till day +100 after HSCT. Both BIA and anthropometry were used in 50 children aged 5 to 17; anthropometry without BIA was used in 61 children aged 6 months to 4 years old.
Results: In patients with the following indexes before conditioning: phase angle (PA) $\leq 4^{\circ}$, the ratio of active cell mass/lean body mass (ACM/LBM) < 0.45 and shoulder muscles circumference (SMC) ≤ 10 percentiles the risk of severe complications was significantly higher in the early period after HSCT ($P < 0.05$). Similarly, in patients with PA ≤ 4 and ACM/LBM < 0.45 the risk of graft hypofunction was considerably higher in compare with patients with PA>4 and ACM/LBM≥ 0.45 ($P < 0.05$).
Conclusions: Low PA, ACM/LBM and SMC before conditioning are prognostic factors of severe complications and graft hypofunction after HSCT. Low PA, ACM/LBM and SMC are symptoms of malnutrition, so malnutrition before conditioning is a significant factor of high risks of severe complications and graft hypofunction after HSCT. Thus, nutritional status correction should be included as a mandatory component of children preparation for HSCT. BIA is a good method to assess the nutritional status and prognose risks of severe complications and graft hypofunction after HSCT.

BONE TUMOURS

P-035

QUANTIFICATION OF CIRCULATING TUMOR DNA FROM PLASMA OF SARCOMA PATIENTS

M. Krumbholz[1], B. Steif[1], S. Semper[1], G. Koehler[2], U. Dirksen[3], M. Metzler[4]

[1]*Department of Pediatrics, University Hospital Erlangen, Erlangen, Germany;* [2]*Department of Pathology, University Hospital Muenster, Muenster, Germany;* [3]*Department of Pediatric Hematology and Oncology, University Hospital Muenster, Muenster, Germany;* [4]*Department of Pediatrics, University Hospital Erlangen, Erlangen, Germany*

Objectives: Quantification of tumor specific molecular markers is a well-established diagnostic tool for therapy monitoring in acute and chronic leukemia. Response assessment in solid tumors is mainly based on imaging studies, particularly in sarcomas, lacking secretion of tumor associated protein markers or release of metabolites to the blood stream. However, the majority of sarcomas is characterized by specific chromosomal translocations, representing a potential marker not only for diagnostic purposes but also for assessment of therapy response by the quantification of circulating tumor DNA (ctDNA) from patient's blood samples.
Methods: Correlation of ctDNA-quantity and Ewing sarcoma (ES) volume was evaluated in a NOD scid gamma mouse xenotransplantation model. ES cells were injected intravenously and blood samples were taken once a week during tumor growth. ctDNA was quantified in plasma with *EWS-FLI1* fusion sequence spanning probe sets using high sensitivity droplet digital PCR. After optimization of the assay, plasma samples from ES patients under treatment were collected and analyzed in comparison to the tumor regression assessed by MRT and PET-CT.
Results: We were able to document the tumor growth by quantification of tumor-specific *EWS-FLI1* fusion sequences in the plasma of xenotransplanted mice. Tumor growth was correlated with increasing ctDNA levels. The percentage of fusion gene-specific DNA fragments of all circulating DNA molecules reached up to 10%. In serum samples of patients under ES treatment, initial tumor size and regression during induction therapy could be monitored with ctDNA copy numbers.
Conclusions: Chromosomal translocations represent genomic markers enabling highly sensitive DNA quantification. Their unique sequence composition at the fusion sites enabled a superior specificity compared to single nucleotide mutations predominantly identified in common epithelial cancers. Conventional blood sample volumes are sufficient to allow the detection and quantification of circulating tumor DNA both in experimental xenotransplant mouse models and ES patients under treatment.

P-036

IS THE MONITORING OF ANGIOGENIC FACTORS RELEVANT IN PATIENTS WITH OSTEOSARCOMA?

M.-D. Tabone[1], L. Brugiéres[2], S. Piperno-Neumann[3], M.A. Selva[4], P. Marec-Berard[5], H. Pacquement[6], C. Mahier-Ait Oukhatar[7], A. Chevance[8], N. Entz-Werle[9], M.C. Le Deley[8]

[1]*Paediatric Onco-haemalogy, Armand Trousseau Hospital, Paris, France;* [2]*Paediatric Oncology, Gustave Roussy Institute, Villejuif, France;* [3]*Medical Oncology, Curie Institute, Paris, France;* [4]*Biochemistry, Armand Trousseau Hospital, Paris, France;* [5]*Institute for Paediatric Haematology and Oncology, Leon Bérard Cancer Centre, Lyon, France;* [6]*Paediatric Oncology, Curie Institute, Paris, France;* [7]*Clinical Studies, Unicancer, Paris,*

France; [8]Biostatistics, Gustave Roussy Institute, Villejuif, France; [9]Paediatric Oncology, Hautepierre Hospital, Strasbourg, France

Objectives: Osteosarcoma is the most common malignant bone tumour in adolescents and young adults. Angiogenesis is essential for the progression and metastasis of solid tumors, but the relevance of monitoring angiogenic factors in patients with osteosarcoma still needs to be addressed. The aim of this study was to determine the levels of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in patients with osteosarcoma and to investigate whether these biomarkers at diagnosis as well as their kinetic under treatment were associated with disease characteristics and provide prognostic information.
Methods: Patients with localized or metastatic osteosarcoma registered between 2005 and 2011 in OS 2005/2006 clinical trials were prospectively included. Levels of VEGF and bFGF in serum and plasma, and of bFGF in urine were measured by ELISA at diagnosis, before surgery and at the end of treatment.
Results: Samples at diagnosis were available in 269 patients (54% males; 73% $\leq$18 years; 68% with a localized disease, 17% with lung doubtful lesions and 15% with metastases). Median follow-up was 3.3 years, 3-year progression-free survival was 62% (se = 3%). High values of serum (>402 pg/ml) and plasma (>115 pg/ml) VEGF were observed in 55% and 39% of patients respectively. Serum and plasma VEGF levels correlated ($r = 0.53$; $p < 0.0001$). High VEGF levels were more frequent in large tumors ($\geq$10 cm, $p = 0.003$). We observed a significant VEGF decreased during pre-operative chemotherapy ($p < 0.0001$), but the variation was not associated with the histological response, nor with the outcome. No significant association was found between blood or urine levels of bFGF and clinical characteristics, histological response or outcome.
Conclusions: High levels of angiogenic factors can be detected in body fluids of osteosarcoma patients, but the clinical utility of these measurements was not demonstrated.

P-037

THE RECEPTOR TYROSINE KINASE RON: A THERAPEUTIC TARGET IN METASTATIC EWING SARCOMA?

C. Schleithoff[1], A. Tillmanns[1], B. Lechtape[1], C. Schaefer[1], H. Jürgens[1], G. Hempel[2], U. Dirksen[1], J. Potratz[3]

[1]Paediatric Haematology/Oncology, University Children's Hospital Münster, Münster, Germany; [2]Institute of Pharmaceutical and Medical Chemistry, Westfälische Wilhelms-Universität Münster, Münster, Germany; [3]General Paediatrics, University Children's Hospital Münster, Münster, Germany

Objectives: Novel treatment options for Ewing sarcoma patients with metastatic disease are urgently needed. Yet, while therapeutic targeting of receptor tyrosine kinases (RTK) in cell proliferation has improved prognosis in many cancers, and a role for RTKs in cell migration and metastasis is undisputed, it remains less well understood. Also, the emerging RTK networks by-passing targeted inhibition remain to be elucidated. Our previous work suggested the "pro-metastatic" RTK RON as possible resistance factor in IGF1R-targeted therapies in paediatric sarcomas. Objective therefore is to elucidate and target RON function in paediatric sarcoma metastases.
Methods: See below.
Results: RON is expressed in Ewing sarcomas and mRNA expression levels (TaqMan-PCR) in primary tumours of 6 patients with metastases were significantly higher than in 15 patients with localized disease, supporting a role in metastasis. RON protein was phosphorylated (i.e. activated) in the presence of serum or specific MSP ligand, as were downstream signalling elements AKT and ERK. Also, RON knockdown impaired cellular migration in wound-healing assays. 3D-spheroid formation is being investigated.
To evaluate RON as therapeutic target, sarcoma cell lines were treated with anti-RON antibody in monolayer and 3D cultures. Surprisingly, no activity was observed, either alone or in addition to an IGF1R antibody, and independent of baseline IGF1R antibody sensitivity. This prompted us to investigate for RON variants, including a short-form (sfRON) lacking the extracellular (antibody binding) domain. First experiments found sfRON in Ewing sarcoma cell lines; and in keeping, some activity for the BMS-777607 inhibitor targeting the RON tyrosine kinase domain.
Conclusions: RON is expressed and activated in Ewing sarcomas, with evidence for pro-metastatic cellular functions. Experimental and therapeutic targeting is challenging, possibly due to RON short-form or splicing variants. Given the clinical impact of metastasis and an ongoing development of multi-tyrosine kinase inhibitors, further studies are warranted.
Acknowledgements: The project is supported by Deutsche Krebshilfe.

P-038

THE ROLE OF MEGATHERAPY (MGT) AND STEM CELL TRANSPLANTATION (SCT) IN HIGH RISK EWING TUMORS (ET): MORE THAN 30 YEARS OF EBMT ACTIVITY

R. Ladenstein[1], D. Valteau-Couanet[2], E. Glogova[3], H. Juergens[4], S. Burdach[5], J. Michon[6], H. van den Berg[7], I. Lewis[8], I. Yaniv[9], C. Peters[10]

[1]Studies and Statistics on Integrated Research, Children's Cancer Research Institute, Vienna, Austria; [2]Paediatric Oncology Haematology, Institut Gustave Roussy, Villejuif, France; [3]Studies and Statistics on Integrated Research and Projects, Children's Cancer Research Institute, Vienna, Austria; [4]Paediatric Oncology Haematology, University Children's Hospital Münster, Münster, Germany; [5]Paediatric Oncology Haematology, Children's Hospital München Schwabing, München, Germany; [6]Paediatric Oncology Haematology, Institut Curie, Paris, France; [7]Paediatric Oncology Haematology, Emma Children Hospital AMC University of Amsterdam, Amsterdam, Netherlands; [8]Paediatric Oncology Haematology, St. James University Hospital, Leeds, United Kingdom; [9]Paediatric Oncology Haematology, Schneider Children's Medical Center of Israel, Petach Tikvah, Israel; [10]Paediatric Oncology Haematology SCT, St. Anna Children's Hospital, Vienna, Austria

Objectives: Registry data of the European Group for Blood and Marrow Transplantation (EBMT) on ET helps to explore indications and outcomes.
Methods: Since 1980, 3,695 patients (pts) with ET (2186 males) were registered (142 centers/24 countries). MGT indications were primary multifocal &high-risk local disease (2411pts) or relapse (719pts). Median age is 15 years (yrs); range, 1 to 65; 2,568pts <18yrs. The median survival time is 0.5 yrs after allogeneic (70 pts) and 2.8yrs after autologous (A) SCTs. Peripheral blood stem cells were used in 3143 pts.
Results: The 5-year overall survival rates (%) are: 44% with ASCT (3,521pts) (49% for primary treatments [for localized disease: 53%; for multifocal 41%]; 31% after relapse) and 12% for alloSCT ($p < 0.001$). Age has significant impact: 48% for $\leq$10yrs, 43% for >10 to $\leq$ 18yrs and 38% >18yrs ($p < 0.001$). The preSCT remission status is of importance (ASCT only): 58% in first complete remission (CR1) (1,343pts), 40% in partial remission (836pts), only 20% in stable disease (144pts) or primary refractory (146pts); ($p < 0.001$). The second complete remission (CR2) results in 46%; all others do significantly worse with< 20% ($p <$ .000). During primary treatment total body irradiation (TBI) regimens are inferior to non-TBI MGT with 38% vs. 50% ($p < 0.026$). A significant influence of MGT type > year 2000 is observed: busulphan based (684 pts) 60%, melphalan based (148 pts) 37%, treosulfan based (95pts) 19% and others (133pts): 55% ($p < 0.01$). A Cox proportional hazards regression model identified age, response status, stem cell source and MGT regimens as independent risk factors.
Conclusions: EBMT Ewing data shows improved results in high-risk pts and favours busulphan based MGT and suggests exploring in more depth the results and roles of Busulphan versus Treosulfan in front line trials.

P-039

RISK STRATIFICATION BY NUMBER OF METASTATIC SITES IN NON-LOCALIZED EWING SARCOMAS

A. Ranft[1], U. Dirksen[1], H. Juergens[1]

[1]Pediatric Hematology and Oncology, University Children's Hospital, Muenster, Germany

Objectives: The outcome variation in subgroups of Ewing sarcoma patients with metastases at initial diagnosis is high. A major current criterion is to stratify Ewing sarcoma patients according to the site of metastases, e.g., patients with pulmonary metastases only are distinguished from patients with bone metastases and other metastatic sites. In this project outcome in non-localized Ewing sarcomas was analyzed according to the number of metastatic sites.
Methods: Five-hundred patients with Ewing sarcoma with metastases at diagnosis were retrospectively analyzed. All patients were included in the GPOH (German Society of Pediatric Oncology and Hematology) Ewing sarcoma registry from 1998-2009 and received similar treatment strategies with standard and/or high-dose chemotherapy in accordance with the appropriate GPOH protocols*. The median follow-up was 2.62 years (range 0.20-14). Outcome by event-free-survival (EFS) was analyzed by univariate and multivariate analyses.
Results: 3y-EFS in patients with isolated pulmonary metastatic disease was 0.46 (SE = .03; n = 268), compared to 0.27 (SE = .03; n = 232) in patients with dissemination to sites other than lung alone, primarily bone metastases (R3) ($p < .001$). In R3 patients, 3y-EFS with one metastatic site was 0.39 (SE = .07; n = 52), compared to 0.28 (SE = .04; n = 120) with two, and 0.14 (SE = .05; n = 60) with three or more metastatic sites ($p < .001$). Overall outcome in non-localized patients with one metastatic site, also including patients with isolated pulmonary metastatic disease, was 0.45 (SE = .03; n = 320). In multivariate analysis, the number of metastatic sites persisted as the major significant risk factor (Hazard ratio (HR): 1.45 (2 vs. 1); 2.38 (>2 vs. 1); $p < .001$), whereas the risk group affiliation did not (HR: 1.21; $p = .302$), even if the model was controlled for treatment intensification with high-dose chemotherapy (HR: 1.82-2.70; $p < .001$ vs. 1.63; $p = .025$; n = 432).
Conclusions: Stratification by virtue of the quantity of metastatic sites appears to discriminate for prognosis in non-localized Ewing sarcoma patients.
*supported by Deutsche Krebshilfe

P-040

MAINTENANCE THERAPY WITH ORAL CYCLOPHOSPHAMIDE + CELECOXIB IN PATIENTS WITH METASTATIC EWING SARCOMA: PRELIMINARY RESULTS OF THE ITALIAN SARCOMA GROUP/AIEOP EW-2 STUDY

R. Luksch[1], M. Abate[2], A. Tamburini[3], F. Fagioli[4], C. Manzitti[5], N. Puma[1], M. Podda[1], S. Asaftei[4], G. Bisogno[6], S. Ferrari[2]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [2]Department of Chemotherapy, Istituto Ortopedico Rizzoli, Bologna, Italy; [3]Department of

Pediatric Onco-Hematology, Ospedale Pediatrico Meyer, Firenze, Italy; [4]Department of Pediatric Onco-Hematology, Ospedale Infantile Regina Margherita-Sant'Anna, Torino, Italy; [5]Department of Pediatric Onco-Hematology, Ospedale Giannina Gaslini, Genova, Italy; [6]Hematology-Oncology Division, Clinica di Oncoematologia Pediatrica - Università di Padova, Padova, Italy

Objectives: To ameliorate the prognosis of patients with metastatic Ewing sarcoma at onset, ISG and AIEOP designed a phase II treatment protocol including a maintenance phase with oral low-dose cyclophosphamide + celecoxib (ISG/AIEOP EW-2, Eudract 2009-011197-15).
Methods: ISG/AIEOP EW-2 was opened on April 2009. Inclusion criteria are: histologically proven previously untreated Ewing sarcoma, synchronous metastases at lungs or solitary skeletal metastasis, age < 40 years. ISG/AIEOP EW-2 consists of 8 courses chemotherapy, radiotherapy and/or surgery on the primary tumor, high-dose busulphan/melphalan+autologous stem cell rescue, radiotherapy on the lungs; responsive patients receive a continuous 180-days maintenance phase with cyclophosphamide 50 mg/d + celecoxib 400 mgx2/d (200 mgx2/d for pts <14 years of age). Exclusion criteria from the maintenance phase are progression of the disease, cardiovascular or gastrointestinal co-morbidity. Aims of the study were to evaluate the feasibility of the maintenance phase and the 3-year survival probability.
Results: From 1 April 2009, 47 consecutive patients (36 males, 11 females; median age 15 years, range 1-37) have been enrolled. 16/47 concluded the maintenance phase, 14/47 were ineligible for previous progression of the disease (n = 11) or for concomitant co-morbidities (n = 3), 17/47 are on treatment. One pt interrupted the maintenance at day 101 for progression of the disease. A temporary suspension of maintenance occurred in 9% of days of maintenance scheduled up to now and occurred in 6 patients, with a range of 1-20 days suspension (median 9 days), due to the following reasons: HZV infection-2, grade 3 hematological toxicity-2, fluid retention-2, diarrhoea-1, pulmonitis-1, febrile episode-3. The 3-year EFS probability for patients who entered the maintenance phase is 0.63 (± 0.11).
Conclusions: This schedule of maintenance phase is feasible, with encouraging results. The enrolment is ongoing, and a longer follow-up is needed to evaluate efficacy and to monitor side effects and late sequelae.

P-041

LOCAL CONTROL IN EWING SARCOMA OF THE CHEST WALL- THE VALUE OF COMBINED MODALITY LOCAL TREATMENT

B. Bedetti[1], A. Ranft[2], H. Jurgens[3], K. Wiebe[4], U. Dirksen[3]

[1]Thoracic Surgery and Lung Transplantation, University Hospital, Muenster, Germany; [2]Pediatric Hematology and Oncology, University Hospital, Muenster, Germany; [3]Pediatric Hematology and Oncology, University Hospital, Muenster, Germany; [4]Thoracic Surgery and Lung Transplantation, University Hospital, Muenster, Germany

Objectives: Primary Ewing sarcoma (ES) may present as chest-wall tumor. Multidisciplinary management including systemic treatment and local treatment consisting of surgery, radiotherapy, or both has improved the survival of patients with localized ES. The best approach to achieve local control, however, remains controversial.
Methods: We retrospectively analyzed data from 198 patients registered in the database of the German Society of Pediatric Hematology and Oncology who had histologically confirmed non-metastatic ES of the chest wall and were treated between July 1998 and April 2009. Median age was 13,9 (0.5-60) years. 119 patients were male. Surgical resection was performed in 191 patients. 85 patients underwent only surgery (group 1) and 106 patients were treated with surgery in combination with radiotherapy (group 2). Seven patients received only radiotherapy (group 3).
Results: Overall survival (OS) for all patients was 78% and 71% at 3 and 5 years. The event-free survival (EFS) at 5 years was 73% in group 1, 63% in group 2 and 57% in group 3. Multivariate analysis including tumor size (</> = 200ml), local therapy modality (OP vs OP&RT), surgical margins (R0 vs R1&R2) and pleural effusion (no vs yes) showed that poor histological response (HR = 2.74; 95%CI 1.54-4.89) and initial pleural effusion (HR = 1.87; 95%CI 1.02-3.44) remained as significant risk factors. Seventeen patients showed late complications (3 secondary malignancy, 3 thoracic bone hypoplasia, 1 myelopathy, 3 valvular disease, 7 lung function reduction).
Conclusions: An additional benefit of radiotherapy in terms of survival could not be demonstrated. This was also true for patients with additional risk factors such as large tumors, inadequate surgical margins, poor histological response. The main limitation of the current analysis consists in the very nature of a retrospective analysis. A prospective evaluation on the role of radiotherapy in chest wall Ewing sarcomas is warranted.

P-042

IS NON-HIGH DOSE–METHOTREXATE (HD-MTX) BASED, DOSE-DENSE, COMBINATION CHEMOTHERAPY (CT) A VALID CHOICE IN HIGH TUMOR BURDEN AND NUTRITIONALLY CHALLENGED OSTEOSARCOMA?

J. Bajpai[1], M.V. Chandrakanth[1], V. Agarwala[1], S. D'souza[1], A.J.A.Y. Puri[2], B. Rekhi[3], G. Chinnaswamy[1], S. Laskar[4], S. Banavali[1], S. Gupta[1]

[1]Medical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [3]Pathology, Tata Memorial Hospital, Mumbai, India; [4]Radiation Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Standard treatment of osteosarcoma includes HD-MTX; however considering significant toxicity, and need of complex pharmacokinetic monitoring, other non HD-MTX based CT regimens are worth exploring.
Methods: This prospective study evaluated the efficacy & toxicity of dose-dense CT regimen comprising Doxorubicin, Ifosfamide, & Cisplatin. CT response was evaluated with histological-necrosis (HN) grading. Good responders (GR) were defined as those with ≥ 90% HN. Baseline tumor burden and nutritional parameters were correlated with outcomes and toxicity. Survival analysis was performed using the Kaplan–Meier method and compared with Log-rank test.
Results: 239 eligible patients were enrolled (median age 17yrs) between December 2011 and December 2013. At presentation, 48% were malnourished, 31% anemic, 50% iron deficient, and 39% were B12 deficient. Mean lesion size was 11 cm, 24% had metastasis, 46% had high LDH and 85% had high SAP. Post CT, 194 underwent surgery till analysis; 56% had GR. At a mean follow-up of 16 months, median overall survival (OS) is not reached in nonmetastatic (NM) patients while in metastatic patients it was 25.36 months (p = 0.008). Estimated 2-year-OS is 87% in NM and 67% in metastatic patients. Grade III/IV chemotoxicity like febrile-neutropenia (FN) (20%), thrombocytopenia (7%) & GI-toxicity (11%) were managed successfully. Compliance to chemotherapy was 81%. In multivariate analysis HN, low albumin & FN were identified as independent variables for OS; ECOG-PS and transferrin-saturation (TS) were identified as independent variables for FN.
Conclusions: Non-HD-MTX based dose-dense CT regimen produces outcomes comparable to those of HDMTX-containing regimens with acceptable toxicity and compliance even in nurtitionally challanged and high tumor burden osteosarcoma cases.
Albumin & FN are identified as nonconventional potential prognostic markers while ECOG-PS and transferrin-saturation as noval markers for toxicity prediction at baseline, and merits further exploration.

P-043

SELF-REPORTED FUNCTIONAL OUTCOMES AND QUALITY OF LIFE ASSESSMENTS IN LONG-TERM SURVIVORS OF PEDIATRIC EWING SARCOMA

B. Stish[1], S.K. Ahmed[1], P.S. Rose[2], N.N. Laack[1]

[1]Radiation Oncology, Mayo Clinic, Rochester, USA; [2]Orthopedic Surgery, Mayo Clinic, Rochester, USA

Objectives: To collect long-term patient-reported functional outcomes and quality of life assessments from pediatric patients treated for Ewing Sarcoma at Mayo Clinic and assess the impact of disease characteristics and primary tumor treatment modality.
Methods: Surviving patients treated at Mayo Clinic for Ewing Sarcoma between 1977 and 2009 were eligible to complete a self-reported quality of life questionnaire. Assessment tools included the Toronto Extremity Salvage Score (TESS) and the age appropriate PEDSQL™4.0 Generic Core instruments. Inventory scores were calculated according to the published TESS and PEDSQL guidelines, with higher scores indicating better outcomes for each instrument (range 0-100). Univariate analysis of TESS and PEDSQL score with patient clinical characteristics was assessed using a Chi square for discrete variables and the ANOVA method for continuous variables.
Results: Thirty-three patients (20 male) completed the self-assessment. Median age at diagnosis was 14.9 years (range 3.5-17.9) and median age at survey completion was 31.5 years (range 12.2-52.8). The median TESS scores and PEDSQL total scores for all patients were 99.2 (IQR = 96.9-100) and 89.1 (IQR = 78.4-98.4), respectively. Within the PEDSQL instrument, scores were highest in the social domain (median = 100) and lowest in the physical domain (median = 87.5). PEDSQL total scores correlated strongly with TESS scores with a Pearson correlation coefficient of 0.72. Median TESS scores did not differ significantly based on primary tumor location (axial = 100, extremity = 98.8, pelvis = 97.9, p = 0.84). Local therapy did not affect TESS scores significantly, with mean scores of 99.2 (RT), 100.0 (S), and 98.3 (RT+S), p = 0.78.
Conclusions: This study is the largest single institutional assessment of quality of life in long-term survivors of pediatric Ewing Sarcoma. Self-reported functional outcomes in our series were excellent relative to published values for healthy subjects and do not appear to be influenced by tumor location or mode of local therapy. These data will provide a benchmark for comparison in future studies.

P-044

METHYLENE TETRAHYDROFOLATE REDUCTASE POLYMORPHISMS AND TOXIC EFFECTS AFTER HIGH-DOSE METHOTREXATE IN CHILDREN WITH OSTEOSARCOMA

V. Ilic[1], Z. Bekic[1], J. Bokun[1], M. Pudrlja Slovic[1], I. Tufegdzic[1], S. Radulovic[2], L. Paripovic[1]

[1]Paediatric Department, Institute of Oncology and Radiology of Serbia, Belgrade, Serbia; [2]Department of Experimental Oncology, Institute of Oncology and Radiology of Serbia, Belgrade, Serbia

Objectives: Methotrexate is a dihydrofolate reductase inhibitor. High-dose methotrexat (HD-MTX) is one of the most important agents in therapy of high-grade osteosarcoma in children.

The major side effects of HD-MTX include mucositis, nephrotoxicity and hepatotoxicity. Delayed MTX clearance followed by toxic effects (acute and delayed) still represent clinical problems. Methylene tetrahydrofolate reductase (MTHFR) has a key role in the folate cycle. Usual polymorphism of MTHFR gene is represented by replacement of citozin (C) with timine (T) on position 677. The result is C677T allele with 60% of enzyme activity or T677T allele with 30% of enzyme activity. Consequence of lower MTHFR enzyme activity is reduced folate pools witch may cause additional toxicity and delayed MTX clearance.
Methods: During 2010 we evaluated 15 patients (pts) with high-grade osteosarcoma, which had delayed MTX clearance and toxic effects after administration of HD-MTX in dose of 12g/m^2. The median age was 15 years (10,5 to 16,5 years). We used PCR-RFLP method and analyzed peripheral blood to detect polymorphism of 677 MTHFR allele. Prior to HD MTX infusion all pts had normal laboratory findings.
Results: All 15 evaluated pts had delayed MTX clereance from 144 to 192 hours and hepatotoxicity grade 3-4. Three pts had nausea and vomiting. Eight out of fifteen pts had C677T polymorphism with 60% of enzyme activity, one patient had 30% of enzyme activity (T677T). One patient with C677T allele had developed mucositis/stomatitis grade 3/4.
Conclusions: MTX toxicity and delayed MTX clearance can be explained by MTHFR polymorphism on position 677 and prolonged MTX exposure. Polymorphism C677T on MTHFR gene is related to lower level of folate pools caused by loss of catalitic function of MTHFR. Carriers of MTHFR polymorphism receving HD-MTX chemotherapy protocols could be in grater risk for toxic effects.

P-045

RESPONSE TO CHEMOTHERAPY ESTIMATED BY FDG PET AS AN IMPORTANT PROGNOSTIC FACTOR IN PATIENTS WITH EWING SARCOMA

A. Raciborska[1], K. Bilska[1], K. Drabko[2], R. Chaber[3], M. Pogorzala[4], K. Polczynska[5], G. Sobol[6], M. Wieczorek[7], K. Muszynska-Roslan[8], M. Dziuk[9]

[1]Surgical Oncology for Children and Youth, Mother and Child Institute, Warsaw, Poland; [2]Pediatric Hematology Oncology and Transplantology, Medical University, Lublin, Poland; [3]Pediatric Oncology Hematology and Bone Marrow Transplantation, Medical University, Wroclaw, Poland; [4]Pediatric Hematology and Oncology Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland; [5]Pediatric Hematology and Oncology, Medical University, Gdansk, Poland; [6]Pediatric Oncology Hematology and Chemotherapy, Medical University, Silesia, Poland; [7]Pediatrics and Oncology, Pediatric and Oncologicol Children's Centre, Chorzow, Poland; [8]Pediatric Oncology and Hematology, Medical University, Bialystok, Poland; [9]Nuclear Medicine PET-CT Department, Military Institute of Medicine Mazovian Medical Centre, Warsaw, Poland

Objectives: Response to the neoadiuvant chemotherapy is a prognostic factor in patients with Ewing sarcoma (ES). The role of FDG PET to predict response to neoadjuvant chemotherapy in these patients has not been thoroughly investigated. We evaluated the diagnostic accuracy and the potential of F-18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG PET) to compare chemotherapy (CHT) response with the degree of necrosis defined histologically.
Methods: We analyzed data of 50 patients with ES (median age 12,6 years). All patients were treated with neoadiuvant CHT, and underwent surgery excision. All patients had ^{18}F-FDG PET/CT at diagnosis and after induction CHT, prior to local control. We compared response assessed by histopathology with FDG PET using standard uptake values (SUV). We also analyzed FDG PET uptake with other diagnostic imaging studies.
Results: Forty-three patients (86%) are alive with a median follow-up of 25.63 months from diagnosis. Median SUV at diagnosis was 5 (range 0-17). Median SUV after initial chemotherapy was 1.95range 0-8.4). Histologically, 38 (76%) patients were classified as having good responses ($\geq$90% necrosis) and 12 (24%) as having poor responses (<90% necrosis). SUV after CHT was significantly lower in patients with good histological response than in patients with poor histological response (median 1.8 vs. 3.1). Additionally, FDG PET was more sensitive than bone scintigraphy to detect bone metastases; however, its sensitivity for detection of lung disease was low.
Conclusions: ^{18}F-FDG PET demonstrates high diagnostic accuracy for response to initial chemotherapy and it is more sensitive than bone scintigraphy for the detection of bone metastases. FDG PET may be a useful tool in the estimation of histological response in patients with ES.

BRAIN TUMOURS

P-046

OUTCOMES FOR PEDIATRIC MEDULLOBLASTOMA IN CANADA FROM 1990 TO 2010: A REPORT FROM THE CANADIAN PEDIATRIC BRAIN TUMOR CONSORTIUM.

L. Grimard[1], D. Johnston[2], D. Keene[3], D. Strother[4], A. Carret[5], V. Percy[6], C. Fryer[7], S. Afzal[8], V. Larouche[9], E.R.I.C. Bouffet[10]

[1]Radiation Oncology, The Ottawa Hospital, Ottawa, Canada; [2]Pediatric Oncology, The Children's Hospital of Eastern Ontario, Ottawa, Canada; [3]Pediatric Neurology, The Children's Hospital of Eastern Ontario, Ottawa, Canada; [4]Pediatric Oncology, University of Calgary, Calgary, Canada; [5]Pediatric Oncology, Hopital Sainte Justine, Montreal, Canada; [6]Pediatric Oncology, Cancer Care Manitoba, Winnipeg, Canada; [7]Pediatric Oncology, British Columbia Children's Hospital, Vancouver, Canada; [8]Pediatric Oncology, IWK Children's Hospital, Halifax, Canada; [9]Pediatric Oncology, Centre Hospitalier Universitaire de Quebec, Quebec, Canada; [10]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada

Objectives: The Canadian Pediatric Brain Tumor Consortium (CPBTC) examined the incidence of medulloblastoma from 1990 to 2010. The outcomes by treatment type, especially use of radiotherapy, are presented.
Methods: Treatment of children with brain tumors is centralised in 16 institutions in Canada forming the CPBTC. In order to assess if there was a change in incidence from 1990-2010, data was collected. The outcomes according to treatment, 5-year groups (1990-94, 95-99…) M status, gender, age, and use of radiotherapy in first line treatment are presented.
Results: There were 669 patients treated over 20 years, 406 male and 255 female. 443 patients had M0 disease and 226 had metastatic disease. There were 304 patients under age 5 with a greater proportion having M+ disease: 42% vs. 30% for those older. First line therapy was chemotherapy only in 9.6% of patients, radiotherapy only in 11.4%, with a decrease from 16.4% in the first decade to 6.8% in the latter decade, and combined chemotherapy and radiotherapy in 60.8% of patients. In the 2005-2010 period, high dose chemotherapy was used alone in 8.7% and with radiotherapy in 23.1%. Survival at 5 years was 80% for patients receiving radiotherapy and 40% for those not receiving radiotherapy ($p = 0.0001$). Stage M0 vs. M+, and age under 5 years were also significantly related to survival (both $p = 0.038$) in the COX Hazard model. There was no difference in survival by gender or 5-year periods.
Conclusions: There was no improvement in survival over the study time period, and the use of radiotherapy as first line was the most important prognostic factor. Younger children, under 5 years, presented with a worse stage. There was an independent effect of young age and stage on prognosis, but to a much lower extent than the use of radiotherapy as first line therapy.

P-047

LONG TERM FOLLOW UP OF INFANTS WITH MEDULLOBLASTOMA TREATED WITH SEQUENTIAL HIGH DOSE CHEMOTHERAPY

L. Lafay-Cousin[1], S. Chi[2], J. Madden[3], A. Smith[4], E. Wells[5], E. Owen[4], D. Strother[1], N. Foreman[3], R. Packer[5], E. Bouffet[6]

[1]Pediatric Oncology, Alberta Children's Hospital, Calgary, Canada; [2]Pediatric Oncology, Dana Farber Institute, Boston, USA; [3]Pediatric Oncology, Children's Hospital of Colorado, Denver, USA; [4]Pediatric Oncology, Arnold Palmer Hospital for Children, Orlando, USA; [5]Pediatric Oncology, Children's National Medical Center, Washington DC, USA; [6]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada

Objectives: High dose chemotherapy strategies were developed to avoid craniospinal irradiation and prevent unacceptable neurotoxicity in young children. However, long-term outcome, including neurocognitive outcome, of this approach has not been widely described.
Methods: This retrospective study collected data from 6 institutions, on young children with medulloblastoma who received high-dose Carboplatin, Thiotepa according to the protocol CCG99703 between 1998-2012. Data on pathology, molecular subgrouping, chemotherapeutic, radiation, ototoxicity, neurognitive evaluations and survival were collected.
Results: There were 47 (25 males) patients diagnosed at a median age of 24.5 months (2.9-63.2). Nineteen (39.6%) had metastatic disease and 30 (62.5%) underwent gross total resection (GTR). Fifteen (31.3%) had nodular desmoplastic (ND) subtype. Three patients received intrathecal chemotherapy, 6 received HD MTX during induction and 7 underwent maintenance chemotherapy post HDC. Fifteen patients received radiation, including 9 (18.7%) in an adjuvant setting. Complete continuous remission (CCR) rates after induction and consolidation were respectively 66.7% and 75%. Two patients died of treatment related toxicity. Thirty seven patients are alive at a median follow-up of 3.7 years from diagnosis with a projected 5-year PFS and OS of respectively 68.4% ($\pm$ 7.5) and 76.4% ($\pm$ 6.6). GTR, M0&M1 stage, ND histology, and CCR were significantly associated better PFS, but only CCR post consolidation and M0&M1 stage remained significant for better OS. Non irradiated children had a better PFS compare to those who received radiation (5y PFS 82.3% versus 45% $p = 0.017$). Outcome by molecular subgrouping is pending. Severe ototoxicity ($\geq$ Brock grade 3) was present in 23.3% of 30 evaluable patients. Nine required hearing support. Neurocognitive assessements were available in 19 patients (51%). Mean FSIQ for the cohort was 91 (range 67-119).
Conclusions: Young children with MB treated with this strategy have an encouraging OS (76.4%). Less than 20% of the patients received adjuvant radiation. Although the ototoxicity of this regimen was significant, neurocognitive profile of the survivors appears to be within normal range.

P-048

ACUTE TOXICITIES AND TREATMENT OUTCOMES FOR PEDIATRIC MEDULLOBLASTOMA PATIENTS TREATED WITH PROTON-BASED CRANIOSPINAL IRRADIATION

A. Hollander[1], R.A. Lustig[1], Z. Tochner[1], I. Paltin[2], S. Both[1], H. Zhai[1], M.J. Fisher[2], J.E. Minturn[2], P. Phillips[2], C.E. Hill-Kayser[1]

[1]Radiation Oncology, University of Pennsylvania, Philadelphia, USA; [2]Oncology, Children's Hospital of Philadelphia, Philadelphia, USA

Objectives: CSI was delivered using cranial photon fields and spinal posterior-anterior proton fields to allow for field size limitations at our institution. We report the acute toxicities and outcomes with this technique.
Methods: From September 2011-August 2013, 19 patients were treated. Standard-risk patients received 23.4Gy (RBE) CSI and tumor bed proton boost to 54Gy (RBE); high-risk (HR) 36Gy (RBE) and 55.8Gy (RBE), respectively (2 with spine boosts of 5.4Gy (RBE) and 12.6 Gy (RBE)). All patients received vincristine. 3 HR patients received additional daily carboplatin. Toxicities were documented according to CTCAEv4.
Results: Median age was 10.3 years (range 3.7-17.4). 11 were female, 11 required daily anesthesia during radiation, 14 were standard-risk. At baseline, mean neuropsychological abilities across a broad range of performance based measures and parent reported functioning were in the average range (Wechsler IQ Mean = 101.86, SD = 13.18, Range 76-115). Most toxicities were grade 1-2 (G1-2). The only G3+ toxicities were: nausea/vomiting (G3, n = 3), anorexia (G3, n = 9, max weight loss G2), decreased hemoglobin (G3, n = 3), leukopenia (G3, n = 3; G4, n = 1) and thrombocytopenia (G3, n = 1). The patient with G4 leukopenia also had G3 thrombocytopenia; she had high-risk medulloblastoma, treated with spine boost, vincristine and carboplatin. G3+ bone marrow toxicity occurred in 4/5 HR patients and all patients receiving carboplatin. Hepatic and renal toxicities were mild. Of 8 patients with available audiograms, at median 11.3 months from end of RT (range 6.6-26.6), 5 had mild-moderate hearing loss, 3 had none. Of 8 patients for whom detailed post-radiotherapy imaging was available, none had radiation necrosis. Follow-up data were available for 16 patients. At median follow up of 13.8 months (range 3.8-24.5), 14 are alive without disease, 1 is alive with cerebellar and thecal sac recurrences, and 1 is alive with ventricular recurrence.
Conclusions: This CSI technique is safe and well-tolerated. Proton CSI may decrease GI, bone marrow, hepatic, and renal toxicities depending on chemotherapy regimen.

P-049

CLINICAL OUTCOME BY REDUSED-DOSE IRRADIATION PLUS ADJUVANT CHEMOTHERAPY AND PROGNOSIS AFTER RECURRENCE IN MOLECULAR SUBGROUPING OF MEDULLOBLASTOMAS

N. Kagawa[1], R. Hirayama[1], M. Kijima[2], Y. Chiba[1], M. Kinoshita[3], K. Takano[1], D. Eino[1], S. Fukuya[1], F. Yamamoto[4], K. Nakanishi[1], Y. Hashii[5], N. Hashimoto[1], J. Hara[6], M.D. Tylor[2], T. Yoshimine[1]

[1]Department of Neurosurgery, Osaka University Graduate School of Medicine, Osaka, Japan; [2]Division of Neurosurgery, The Hospital for Sick Children University of Toronto, Toronto, Canada; [3]Department of Neurosurgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan; [4]Department of Neurosurgery, Suita Manucipal Hospital, Osaka, Japan; [5]Department of Developmental Midicine, Osaka University Graduate School of Medicine, Osaka, Japan; [6]Department of Pediatric Hematology/Oncology, Osaka City General Hospital, Osaka, Japan

Objectives: Therapeutic challenges against recurrence of medulloblastomas have difficult problems, although prognosis of medulloblastomas has been improved by craniospinal irradiation and adjuvant chemotherapy. We retrospectively analysed recurrent patterns and differences of clinical outcome based on molecular subgrouping for medulloblastomas treated by redused-dose irradiation and high-dose chemotherapy.
Methods: Twenty-one patients with medulloblastomas treated in our institution from 1994 to 2013 were classified into four subgroup by nanoStrings assay using frozen specimens. Age distribution was one to twenty-two years old. The subgroup distribution was four SHH, five group 3 and eleven group 4 without WNT case. In all cases older than 3 years old, redused-dose craniospinal or cranial irradiation (18 Gy) plus adjuvant chemotherapy was done after tumor removal. High-dose chemotherapy was performed in high-risk group.
Results: No recurrence was seen in SHH. Of five group 3 cases, four had recurrent medulloblastomas and the period between initial treatment and recurrence was within 16 months. 5 year progression-free survival (5y-PFS) was 20.0%. Recurrent cells were rapidly and extensively disseminated and progressive despite of many therapeutic chanllenges. The period between recurrence and death was 4 to 7 months and 5 year overall survival (5y-OS) was 26.6%. Of eleven group 4, slow-growing and asymptomatic recurrences were shown in four cases. The period between initial treatment and recurrence was 18 to 70 months. Both 5y-PFS and 5y-OS were 70%. Although high-dose chemotherapy or intrathecal injection of chemotherapeutic agents had little effect, the conditions of partial response or stable disease were maintained by stereotactic radiotherapies and metronomic chemotherapies using oral etoposide and temozolomide.
Conclusions: By therapeutic regimen including redused-dose irradiation, 5y-PFS, 5y-OS and survival time after recurrence in group 4 are significant longer than those in group 3. Molecular subgrouping may predict recurrent patterns, response against treatment and prognosis in each group.

P-050

A FUNCTIONAL GENOMICS APPROACH TO IDENTIFY MECHANISMS OF DRUG RESISTANCE IN SHH MEDULLOBLASTOMA MURINE MODELS

K.C. Bertrand[1], C.C. Faria[2], S.C. Mack[3], A.J. Luck[1], X. Wang[3], S. Agnihotri[1], X. Wu[3], L. Garzia[3], C.A. Smith[1], P.B. Dirks[3], M.D. Taylor[3], J.T. Rutka[4]

[1]Cell Biology, The Hospital for Sick Children, Toronto, Canada; [2]Neurosurgery, Hospital de Santa Maria Centro Hospitalar Lisboa Norte, Lisboa, Portugal; [3]Developmental Biology, The Hospital for Sick Children, Toronto, Canada; [4]Department of Surgery, University of Toronto, Toronto, Canada

Objectives: Despite improvements in survival, Medulloblastoma (MB) patients face a multitude of long-term neurocognitive sequelae due to aggressive chemo- and radio- therapy. Many novel MB targeted therapies are emerging, however these are likely to reveal drug resistance pathways that are present or acquired in response to therapy. Previous work from our group has demonstrated that Foretinib, an inhibitor of cMET activity, is an effective treatment of Sonic Hedgehog (SHH) subgroup MB. Currently we seek to identify pathways that may lead to Foretinib resistance in SHH MB, such that informed up-front combinatorial therapies could be uncovered and evaluated.
Methods: A MB Sleeping Beauty transposon mutagenesis murine model (Ptch+/-/SB11/T2Onc) was used which frequently and spontaneously develops primary and metastatic MB. Mice were treated with vehicle or Foretinib, via Alzet osmotic pump slow-infusion into the cerebrospinal fluid for 28 days at a rate of 0.25ul/hour. Transposon common insertion sites were identified by SPLINK PCR of tumour DNA, followed by paired-end Illumina next-generation sequencing (HiSeq 2500). This data identified different insertions in control mice versus Foretinib treated mice, relating to different pathways that had been selected in response to treatment.
Results: We demonstrate that Sleeping Beauty MB mice have a statistically greater survival upon treatment with continuous CSF infusion of the cMET inhibitor Foretinib. Despite an improvement in survival, Foretinib treated mice eventually succumb to tumour formation and metastasis. Using an unbiased functional genomics screen, we have identified novel mechanisms and pathways of resistance to cMET inhibition. The targets identified converge upon regulators of cell cycle, apoptosis, and tumour invasion, and reveal pathways that may be leveraged for combinatorial treatment with Foretinib.
Conclusions: Our study has identified potential pathways that SHH MB cells may co-opt to overcome Foretinib inhibition, and provides a system for which drug resistance pathways to other MB targeted therapies may be identified.

P-052

LONGITUDINAL CHILD AND PARENT REPORTED HEALTH RELATED QUALITY OF LIFE IN CHILDREN ENROLLED ON A PROTON RADIOTHERAPY PHASE II MEDULLOBLASTOMA STUDY

J. Lucas[1], K. Kuhlthau[2], J. Delahaye[2], M. Pulsifer[3], E. Weyman[4], S. McBride[5], S. MacDonald[4], N. Tarbell[4], T. Yock[4]

[1]Radiation Oncology, Wake Forest Baptist Medical Center, Winston- Salem, USA; [2]Pediatrics, Massachusetts General Hospital, Boston, USA; [3]Psychiatry, Massachusetts General Hospital, Boston, USA; [4]Radiation Oncology, Massachusetts General Hospital, Boston, USA; [5]Radiation Oncology, Memorial Sloan Kettering, New York, USA

Objectives: To describe the longitudinal HRQoL in patients treated on a prospective phase II trial for pediatric medulloblastoma with proton radiotherapy (PRT).
Methods: Fifty-nine patients with medulloblastoma (enrolled 2003-2009) were assessed with PedsQL during PRT and annually thereafter. 38 had evaluable PedsQL surveys at follow-up (FU). Patients received PRT (median dose: 23.4 GyE CSI (18-36)), and tumor bed (TB) or posterior fossa (PF) boost (54 GyE, (54-59.4GyE)). We compared HRQoL by risk group (SR/HR), age, SES (address-derived median income, >= vs < $60,000), and boost volume (TBv. PF) using ANOVA and paired t-tests.
Results: Median HRQoL follow up (FU) among those with baseline evaluations was 4.0 years (n = 38). Parent Proxy Report (PPR) were non-significantly less than Child Self-Reported (CSR) at baseline for Total Core Score (TCS) 57.8 vs. 69.2, Physical Score (PS) 51.6 vs.66.5, and Psychosocial Score (SS) scores 62.8 vs. 72.7. The mean TCS, PS, and SS at last FU were similar across PPR & CSR; [n = 29] 73.6 vs. 78.4, [n = 29] 76.4 vs. 81.3, and [n = 35] 71.3 vs. 76.6 (p's = NS). Both PPR & CSR HRQoL measures improved following treatment although this difference was significant for only TCS and PS and among PPR. Across HRQoL domains, SS minimally improved with time. FU HRQoL scores improved differentially across age (<= 7 vs.>= 8) in TCS (+9.6 [95% CL 0.3-18.8] vs. 23.7 [95% CI 13.3-34.1], p = 0.04) and PS (17.1 vs. 34.6, p = 0.05) among PPR but not CSR. There was no difference in change over time in TCS, PS or SS across gender, risk category, SES or boost volume.
Conclusions: PPR/CSR HRQoL domains improved over time across all domains but SS, with the largest improvement in PPR of TCS and PS. SES was not correlated to HRQoL scores at baseline, FU or the change over time.

P-053

SIOP PODC: ADAPTED REGIMENS TO MANAGE CHILDREN WITH STANDARD RISK MEDULLOBLASTOMA IN LOW- AND MIDDLE-INCOME SETTINGS.

J. Parkes[1], A. Davidson[2], S. Bailey[3], M. Hendricks[4], P. Ssenyonga[5], E. Molyneux[6], J. Mugamba[5], A.Y.N. Schouten-van Meeteren[7], I. Qaddoumi[8], E. Bouffet[9], S. Luna-Fineman[10], S. Howard[8]

[1]Radiation Oncology, University of Cape Town, Cape Town, South Africa; [2]Paediatric Oncology, Red Cross children's hospital, Cape Town, South Africa; [3]Paediatric Oncology,

Great North Children's hospital, Newcastle-upon-Tyne, United Kingdom; [4]Paediatric Oncology, University of Cape Town and Red Cross Children's Hospital, Cape Town, South Africa; [5]Neurosurgery, Cure Children's Hospital, Mbale, Uganda; [6]Paediatrics, College of medicine, Blantyre, Malawi; [7]Paediatrics, Emma Children's Hospital, Amsterdam, Netherlands; [8]Paediatric Oncology, St Jude children's research Hospital, Memphis, USA; [9]Paediatric Oncology, Hospital for sick children, Toronto, Canada; [10]Paediatric Oncology, Stanford University, Palo Alto, USA

Objectives: Effective treatment of children with medulloblastoma requires a functioning multi-disciplinary team with adequate neurosurgical, neuroradiological, pathological, radiotherapy and chemotherapy facilities and personnel. The treating center should also have the capacity to effectively screen and manage any treatment associated toxicity. These requirements have made it difficult for many low and middle-income countries (LMIC) centres to offer curative treatment. This presentation describes management recommendations for children with standard risk medulloblastoma according to the level of facilities (settings) available.
Methods: Under the auspices of the SIOP PODC group, a multidisciplinary writing group composed of doctors from the LMIC and developed countries was established to produce guidelines to assist professionals working in LMIC to treat children with standard risk medulloblastoma. To start, a survey was conducted amongst doctors in LMIC to establish what difficulties they encountered in treating children with medulloblastoma. There were 104 respondents from 47 countries. Following a number of web conferences, guidelines based on the best available evidence and appropriate for the different settings (graded 0-4) were drawn up. These were then circulated to professionals in LMIC for comments on its usefulness. Further enhancements were made following these comments.
Results: The guideline used standard settings developed by the overall SIOP PODC group with modifications appropriate to treatment of medulloblastoma. Those in settings 0 and 1 are not recommended to treat children with medulloblastoma. Surgical, radiotherapy and chemotherapy options appropriate to the settings are included in the guideline. In addition, suggestions for investigation and management of potential toxicities are included. The importance of a functioning multidisciplinary team is emphasised.
Conclusions: Guidelines such as these may be useful for those working in LMIC. However, it is important that appropriate consultation with the potential users of such documents is conducted.

P-054

TREATMENT OF MEDULLOBLASTOMA AND PNET CHILDREN ABOVE THREE YEARS OF AGE IN SAUDI ARABIA: A PROSPECTIVE MULTICENTER STUDY

M. Al-Harbi[1], S. Abdullah[2], Q. Alharbi[3], M. Alshahrani[4], O. Mosleh[1], A.L.I. Balbaid[1], A. Alkofide[5], N. Alkhayat[4], O. Ahmed[3], S. El-Badawy[3], E. Bouffet[6]

[1]Pediatric Hematology Oncology, King Fahad Medical City, Riyadh, Saudi Arabia; [2]Pediatric Hematology Oncology, King Abdulaziz Medical City-National Guard, Jeddah, Saudi Arabia; [3]Pediatric Hematology Oncology, King Fahad Specialist Hospital, Dammam, Saudi Arabia; [4]Pediatric Hematology Oncology, Prince Sultan Medical Military Hospital, Riyadh, Saudi Arabia; [5]Pediatric Hematology Oncology, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; [6]Pediatric Hematology Oncology, Hospital for Sick Children-University Of Toronto, Toronto, Canada

Objectives: Treatment for children with medulloblastoma in Saudi has been heterogeneous and essentially institution-based. A cooperative protocol was launched in 2009 between 4 tertiary centers.
Methods: Patient above 3 years with medulloblastoma and PNET received postoperative craniospinal radiation according to their risk group with concurrent oral etoposide 35mg/M2/days. They then received six cycles of chemotherapy alternating cycle A (Cisplatin 90 mg/m2/day, day 1 and Etoposide 35 mg/m2/day P.O. days 1-21 of a 4-week cycle) and Cycle B (Cyclophosphamide 1.5 g/m2/day, days 1-2 with Vincristine 1.5 mg/m2, days 1,8,15 for each 4weeks cycle). Post-chemotherapy, maintenance with Isotretinoin 160mg/M2/day1-14 was given for 6 months.
Results: 62 patients (36males/26 female) were enrolled from 09/2009 to 02/2014. 56 patients had Medulloblastoma, 2 SPNET, and 4 pinealoblastoma. Median age was 7.1 years; 35 patients (56%) underwent gross total resection, 8 near-total, 12 subtotal, 2 partial and 5 patients underwent a biopsy only. 22 patients had M2/3 disease. 26 patients were treated as average-risk (AR,42%) and 36 treated as high-risk (HR,58%). Radiation started at a median interval of 35 days post-surgery (18-105). Etoposide was well tolerated during radiation, but most patients experienced grade3-4 hematological toxicity during post-radiation chemotherapy. Only 50% of the patients received isotretinoin. No toxic death occurred on treatment. Hearing assessment (Brock scale) was available for 51 patients and showed gr0 toxicity in 30 patients (48.4%), gr1-2 in 16, and gr3-4 in 5. At a median follow-up of 23 months, 56 patients are alive and 6 have died (3/26 AR patients, and 3/36 HR patients). The 2 year overall survival (OS) is 91.5+5% and the projected 5 year OS 80.7+8%.
Conclusions: Although it is still too early to draw conclusions on survival with this approach, initial results are encouraging showing mild toxicity, in particular in terms of hearing loss.

P-055

MEDULLOBLASTOMA IN CHILDREN ABOVE 3 YEARS; REPORTING TREATMENT RESULTS FROM KING FAISAL SPECIALIST HOSPITAL & RESEARCH CENTRE, RIYADH, SAUDI ARABIA

A. AlKofide[1], M. Ayas[1], E. AlShail[2], M. Hassounah[2], H. Al-Hindi[3], M. Dababo[3], I. Al-Fawaz[1], M. Anas[1], Y. Siddiqui[1], Y. Khafaga[4]

[1]Pediatric Hematology Oncology, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [2]Neurosurgery, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [3]Pathology, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia; [4]Radiation Oncology, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

Objectives: Medulloblastoma is the most common malignant brain tumor seen in childhood. Long term survival of medulloblastoma has improved over the past few decades. We analyzed data from our institution on children above 3 with medulloblastoma.
Methods: From 2005 until 2012, 89 eligible patients were identified.
Results: 66 were male (64.1%), median age at diagnosis was 6 years (range, 0.81-13.21 years), males: 5.9years, females: 6.2years). Tumor was confined to the posterior fossa in 50 patients (56.2%), 30 (33.7%) spine metastases (mets), and 9 (10%) disseminated disease within the brain. CSF metastases in 11 pts who had spine mets (36.6%). Symptoms at presentation were headache (74.2%), vomiting (70.8%), and ataxia (31.5%). One patient had neurofibromatosis. Surgical intervention was performed on all patients; 59 gross total resection, 20 had subtotal resection, 7 had debulking and 3 had biopsy only. 58 pts (65.2%) were high risk disease (>1.5 cm^2 residual tumor and/or M1- M4) and 31 (34.8%) standard risk. The therapeutic regimen consisted of full dose craniospinal for high risk pts and reduced neuro-axis dose for standard risk pts with concurrent weekly vincristine followed by 8 cycles of cisplatinum, lomustine and vincristine. The 5-year OS for all pts was 79% ± 5%. The 5-year overall survival for standard risk vs high risk pts was 84.1% (± 7.6) vs. 76.3% (± 6.5), (P = 0.380) and for non-metastatic versus metastatic disease was 85.9% (± 5.5) vs. 69.6% (± 8.8), (P = 0.114). The 5-year event free survival for standard risk vs high risk was 73.5% (± 8.8) vs. 61.2% (± 7.5), (P = 0.331) and for non-metastatic vs. metastatic 70.95% (± 7.5) vs. 57.9% (± 9.2), (P = 0.1).
Conclusions: The outcome analysis for high risk patients was very good and comparable to standard risk pts. It may be possible to further refine stratification of patients utilizing molecular markers thereby minimizing use of potentially harmful therapeutic modalities.

P-056

RELAPSE AND OUTCOME PATTERNS OF CENTRAL NERVOUS SYSTEM (CNS) 'SECRETING' GERM CELL TUMORS (GCT) TREATED WITHOUT IRRADIATION: FINDINGS FROM THE THIRD INTERNATIONAL CNS GCT STUDY

R. Pruitt[1], N. Saba DaSilva[2], A. Cappellano[2], B. Diez[3], S. Gardner[4], J. Allen[4], M. Weinblatt[5], N. Gottardo[6], G. Dhall[1], J.L. Finlay[1]

[1]Children's Center for Cancer & Blood Diseases, Children's Hospital Los Angeles, Los Angeles, USA; [2]Neuro-oncology Program, GRAACC Institute of Pediatric Oncology, Sao Paolo, Brazil; [3]Neuro-oncology Program, Fundacion para la Lucha contra Enfermedades Neurologicas de la Infancia, Buenos Aires, Argentina; [4]Hassenfeld Children's Center for Cancer & Blood Diseases, New York University Medical Center, New York, USA; [5]Pediatric Hematology/Oncology, Winthrop-University Hospital, Mineola, USA; [6]Pediatric Oncology, Princess Margaret Hospital, Perth, Australia

Objectives: To evaluate patterns of relapse and outcome in patients newly-diagnosed with CNS 'secreting' (or Mixed Malignant) GCT treated initially with chemotherapy without irradiation on the International CNS GCT Study III.
Methods: A retrospective chart review was conducted using all 25 patients enrolled on the International CNS GCT Study III, with at least 7 years follow-up for all patients. Details of the chemotherapy regimen have been published previously (DaSilva *et al*: Pediatric Blood & Cancer, 54:337-383, 2010).
Results: Thirteen patients at diagnosis had 'secreting' CNS GCT by pathology and tumor markers (n = 11) or tumor markers alone (n = 2). Twelve were treated with chemotherapy alone, one receiving focal irradiation following chemotherapy prior to relapse. Six patients (46%) relapsed (mean of 30.5 months; range 6 to 59 months), two beyond and 4 within the primary site alone. Three patients relapsed 'early' (between 6 and 23 months from diagnosis), 2 with alpha-fetoprotein (AFP) elevations and one without tumor markers assessed; all 3 expired of progressive disease at 2-10 months following initial relapse. Three patients relapsed 'late' (between 37 and 59 months), all without AFP elevations, one with pathologically-pure germinoma, two with mild beta-human chorionic gonadotropin elevations (<20mIU/mL in serum/cerebro-spinal fluid); these patients survive disease-free at 86+, 94+ and 126+ months following additional chemotherapy and irradiation.
Conclusions: Patients with CNS 'secreting' tumors who relapse following chemotherapy-only regimens display two distinct patterns of recurrence and outcome; patients relapsing 'early' appear to possess 'secreting' elements and have a dismal prognosis, while patients relapsing 'late' appear to do so with pure germinomatous elements and have an excellent outcome. Current international cooperative group studies utilizing more localized fields of irradiation should evaluate closely the patterns of relapse and outcome; late recurrences with germinomatous elements might be avoided by initial use of low-dose larger field irradiation (whole ventricular or craniospinal).

P-057

TUMOR VOLUME OF PRIMARY INTRACRANIAL GERMINOMAS IS CHANGING DYNAMICALLY BEFORE CHEMORADIOTHERAPY

N. Kagawa[1], R. Hirayama[1], Y. Fujimoto[2], Y. Chiba[1], M. Kinoshita[3], K.O.J.I. Takano[1], D. Eino[1], S. Fukuya[1], F. Yamamoto[4], K. Nakanishi[1], N. Hashimoto[1], Y. Hashii[5], J. Hara[6], T. Yoshimine[1]

[1]Department of Neurosurgery, Osaka University Graduate School of Medicine, Osaka, Japan; [2]Department of Neurosurgery, Osaka Neurological Institute, Osaka, Japan; [3]Department of Neurosurgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan; [4]Department of Neurosurgery, Suita Manucipal Hospital, Osaka, Japan; [5]Department of Developmental Midicine, Osaka University Graduate School of Medicine, Osaka, Japan; [6]Department of Pediatric Hematology/Oncology, Osaka City General Hospital, Osaka, Japan

Objectives: Spontaneous regressions in intracranial germinomas have been reported in some cases, but the natural history of them has not been well known. To answer a part of that question, we retrospectively measured the tumor volume before and after chemo-radiotherapy and analyzed volumetric changes and the correlation with other clinical parameters.
Methods: Twenty-nine cases with primary intracranial germinomas and HCG-producing germinomas were treated in our hospital from 1994 to 2013. In eight of them, plural MRI scans were done before the first course of chemotherapy regimen. Their age ranged from 16 to 26 years. Endoscopic or open biopsies were performed in all. Two were bifocal type. Tumor volume of ten lesions was analyzed by volumetric assessment based on MRI. Ratio of volumetric change between the first MRI on admission and the scan immediately before chemotherapy was defined as shrinking rate (%). Ratio of volumetric change influenced by the first course of chemotherapy was defined as response rate (%). Period between disease onset and the first chemotherapy was 22 to 47 days.
Results: Initial tumor volume ranged from 0.962 to 24.15 cubic centimeter (mean: 6.39). Diagnostic radiation dose was estimated to be from 52.2 to 910.1 mSv. Shrinking rate ranged from -57.8 to 85.3% (mean: 29.1). Only in 3 cases, shrinking rate was within $\pm$ 30%. There is no significant relationship between diagnostic radiation dose and shrinking rate. Shrinking rate had no correlation with age, sex and response rate. Shrinking rate was negatively influenced by initial volume ($p = 0.049$).
Conclusions: This study shows the possibility that the volume of intracranial germinomas are changing dynamically for a short time before chemoradiotherapy in most cases and spontaneous regression is a part of volumetric changes. More information about large-scale study is needed to give light on the biological nature of them.

P-058

INTEGRATIVE ANALYSES OF PEDIATRIC HIGH GRADE ASTROCYTOMAS REVEAL SIMILARITIES BETWEEN ANAPLASTIC ASTROCYTOMA AND GLIOBLASTOMA

N. Gerges[1], T. Haque[2], M. Kool[3], J. Schwartzentruber[4], D.A. Khuong-Quan[1], T. Gayden[1], A. Fontebasso[2], A. Montpetit[5], M. Shirinian[6], P. Hauser[7], D. Faury[8], S. Albrecht[9], S.M. Pfister[3], N. Jabado[10]

[1]Human Genetics, McGill University, Montreal, Canada; [2]Experimental Medicine, McGill University, Montreal, Canada; [3]Pediatric Neurooncology, German Cancer Research Center, Heidelberg, Germany; [4]Biotechnology, Wellcome Trust Sanger Institute, Hinxton, United Kingdom; [5]Sequencing, McGill University and Genome Innovation Center, Montreal, Canada; [6]Internal Medicine, American University of Beirut, Beirut, Lebanon; [7]Pediatrics, Semmelweis University, Budapest, Hungary; [8]Pediatrics, Montreal Children's Hospital Research Institute, Montreal, Canada; [9]Pathology, Montreal Children's Hospital, Montreal, Canada; [10]Pediatrics, McGill University and the McGill University Health Center Research Institute, Montreal, Canada

Objectives: Brain tumors are the leading cause of cancer-related mortality in children. Pediatric high-grade astrocytomas (HGA), including grade III (anaplastic astrocytomas, pAA) and grade IV (glioblastoma, pGBM), are rare but devastating brain tumors accounting for 15% of brain tumors in children. pAA are rare and consequently have not been investigated as a separate entity. pGBM have been well-characterized and, to date, several subgroups of this tumor have been found including those related to mutations in *H3F3A* or *IDH1*. In the literature, HGA are often studied together and as such, no molecular data is available for pAA.
Methods: To identify genetic differences based on tumor grade in children, we investigated pediatric HGA by integrating data from whole exome sequencing, DNA methylation and gene expression analyses.
Results: Our results demonstrate that there is no significant segregation between these two tumor groups, neither at a genomic nor at an epigenomic level. At the RNA expression level, genes related to cell cycle progression, DNA repair, or apoptosis inhibition are upregulated in pGBM compared to pAA (ex. *KIAA0101, PRR11, BIRC5, GTSE1*). In addition, *GAS7*, a gene responsible for the growth and morphological differentiation of cerebellar neurons is downregulated 2.5 fold in pGBM relative to pAA. pGBM segregate into molecular subgroups based on underlying mutations, and our data indicates that the same molecular subgroups apply to pAA. Kaplan Meier analyses show no significant difference in overall survival ($p = 0.8622$) between the two groups emphasizing a similar clinical course between both tumor types.
Conclusions: Our integrative analysis not only indicates that pAA may not be a distinct entity from pGBM, but also highlights the need for molecular diagnostic criteria in pediatric HGA. We propose that pAA and pGBM be grouped together in the hope that molecular-based treatment of this tumor group can improve the clinical outcome of these patients.

P-059

MULTIDISCIPLINARY TREATMENT AND ROLE OF SYSTEMIC CHEMOTHERAPY IN LOW GRADE GLIOMA

M. Fawzy[1], A. Elhemaly[1], M. Awad[2], M. Elbeltagy[3], M. Zaghlol[4], H.A.L.A. Taha[5], M. Elwakeel[6], N.A.D.A. Elkhatib[7], A.L.A.A. Elhaddad[1]

[1]Pediatric Oncology, National Cancer Institute, Cairo, Egypt; [2]Pediatric Oncology, Children Cancer Hospital of Egypt, Cairo, Egypt; [3]Neurosurgery, Children Cancer Hospital of Egypt, Cairo, Egypt; [4]Radiotherapy, Children Cancer Hospital of Egypt, Cairo, Egypt; [5]Surgical Pathology, Children Cancer Hospital of Egypt, Cairo, Egypt; [6]Radiodiagnosis, Children Cancer Hospital of Egypt, Cairo, Egypt; [7]Clinical Research, Children Cancer Hospital of Egypt, Cairo, Egypt

Objectives: The aim of this study was to evaluate the role of multidisciplinary therapeutic approach including surgery and systemic chemotherapy, and the outcome in pediatric patients with different low grade glioma (LGG) subtypes.
Methods: Study patients wereprospectively included. All patients were diagnosed as LGG betweenJuly 2007 andJune 2012. Upfront surgical resection was attempted in all tumors of other than optic pathway sites. Systemic chemotherapy was given according to CCG- A9952 protocol.
Results: Total of 225 patients were enrolled onto study with male to female ratio of 1.2:1. The median age was at 1 year (range: 1-18 yr) with only 9 patients (4%) above 14 years old. Grade-I pilocytic astrocytoma (PA) was the most frequently encountered histologic subtype (43%) with cerebellar site predominance (43.1%), while optic pathway glioma constituted 5.8% of cases. Gross total/near total resection was feasible in 40.8% of the study patients while 26.7% underwent subtotal resection followed by adjuvant chemotherapy because of big residual size and/or symptomatic disease. The 5 year OS and EFS of the entire group were 87.3% and 65.5% respectively. Compared to chemotherapy patients underwent surgical tumor resection had OS and EFS of at 89.9% and 65.1% versus 86.1% and 59.9% for chemotherapy patients. Tumor site, histological subtype, and extent of residual tumor were significantly associated with OS.
Conclusions: Although GTR remains the standard initial treatment in LGG, yet systemic chemotherapy can be a comparable alternative when surgery can not be safely accomplished or being not technically feasible.

P-060

ACTUAL TREATMENT STRATEGIES IN INFANTS WITH PROGRESSIVE HYPOTHALAMIC CHIASMATIC GLIOMA

A. Azizi[1], A.Y.N. Schouten-van Meeteren[2]

[1]Division of Neonatology Pediatric Intensive Care and Neuropediatrics Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria; [2]Pediatric oncology, Emma Children's Hospital Academic Medical Center, Amsterdam, Netherlands

Objectives: Treatment of infant hypothalamic chiasmatic glioma (iHCG) is challenging, since about 30% of the children progress during chemotherapy and despite subsequent treatments the 5 year overall survival rate is only 70%. This study investigates the treatment strategies as currently applied for iHCG.
Methods: A webbased questionnaire about the dillemma in the treatment of iHCG was sent out to the members of the SIOP Brain tumor group as well as the Low Grade Glioma group.
Results: The questionnaire was answered by 48 respondents (44 paediatric oncologists, 4 other professionals). Progressive disease during first line therapy with carboplatin-vincristine would be treated with (intensified) chemotherapy by 16 (33%) and with surgery plus changed chemotherapy by 24 respondents (50%). Components suggested for this second line chemotherapy were 72% vinblastine, 40% cisplatin, 30% cyclophosphamide and 25% etoposide. As components for third line therapy bevacizumab was considered as suitable by respondents in 62%, irinotecan 47% and vinblastine by 40% respectively. Experience with bevacizumab in iHCG is quite common (median treated 1-5 patients at any age) for 57% mostly in combination with irinotecan with a 12 month duration. Effect was reported for all patients with at least stable disease while severe complications were rarely mentioned (1 proteinuria & hypertension, 1 bleeding). Bevacizumab would be available for future protocols for patients of 86% of respondents. Radiotherapy was considered as treatment option after failure of two or three treatment lines with a wide range 3-18 years for lower age limit (median 8 years).
Conclusions: Multiple different cytostatic drug regimens are applied for progressive iHCG often combined with surgery, while bevacizumab is often used at a satisfactory level in third line in combination with irinotecan.

P-061

UNRAVELING THE BIOLOGICAL ROLE OF SPINT2 IN GLIOMAS

M.S. Pereira[1], F. Pinto[1], F. Pardal[2], J. Amorim[3], M. Pires[4], C. Pinheiro[5], J.M. Lopes[6], J. Pimentel[7], C. Jones[8], M. Viana-Pereira[1], R. Reis[9]

[1]Life and Health Research Institure, Minho University, Braga, Portugal; [2]Department of Pathology, Hospital de Braga, Braga, Portugal; [3]Department of Oncology, Hospital de Braga, Braga, Portugal; [4]Department of Pathology, Hospital S. António, Porto, Portugal; [5]Department of Neurosurgery, Hospital S. António, Porto, Portugal; [6]Department of Pathology, Hospital S. João, Porto, Portugal; [7]Laboratory of Neuropathology, Santa maria Hospital, Lisbon, Portugal; [8]Institute of Cancer Research, Institute of Cancer Research, London, United Kingdom; [9]Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, Brazil

Objectives: *SPINT2* is a tumor suppressor gene that codifies protein SPINT2, a serine protease involved in the HGF/MET signaling pathway. *SPINT2* has been demonstrated to be hypermethylated in a variety of cancers, including medulloblastomas. Herein, we intent to determine the clinical relevance of SPINT2 expression/hypermethylation in pediatric and adult high-grade gliomas (HGG), as well as to elucidate the functional role of the different transcripts of *SPINT2* in pediatric glioma cell lines.
Methods: A cohort of 410 adult and 78 pediatric primary HGG samples was used to characterize protein expression (immunohistochemistry) and methylation status (methylation-specific PCR) of SPINT2. Moreover, 424 glioblastoma patients from TCGA were used to evaluate *SPINT2* mRNA expression and methylation levels. Plasmids containing SPINT2a and SPINT2b transcripts were constructed and the role of each transcript in cell migration and viability were evaluated by wound-healing and MTS assay.
Results: We observed that SPINT2 protein is frequently absent in adult HGG (88%), and in all (100%) pediatric cases. These results together with *in silico* analysis demonstrate that down-regulation of *SPINT2* is a common event of brain tumors. We found that down-regulation of *SPINT2* is associated with methylated status of *SPINT2* promoter, *In vitro* analysis showed that ectopic expression of each *SPINT2* transcripts reduced cell migration capacity and cell metabolic viability. Furthermore, we revealed for the first time that SPINT2b has a more pronounced effect in migration while SPINT2a has a stronger effect on cell viability.
Conclusions: We concluded that low expression of SPINT2 and gene hypermethylation are common events in both pediatric and adult HGG, which are associated with higher tumor aggressiveness.

P-062

CHROMATIN ARCHITECTURE IN PEDIATRIC GLIOMAS

A. Fontebasso[1], J. Fraser[2], J. Lambourne[3], J.P. Farmer[4], J.L. Montes[4], J. Atkinson[4], T. Pastinen[3], S. Albrecht[5], J. Dostie[2], N. Jabado[6]

[1]Experimental Medicine, Montreal Children's Hopsital McGill University Health Centre, Montreal, Canada; [2]Biochemistry, McGill University, Montreal, Canada; [3]Human Genetics, McGill University and Genome Quebec Innovation Centre, Montreal, Canada; [4]Neurosurgery, Montreal Children's Hospital McGill University Health Centre, Montreal, Canada; [5]Pathology, Montreal Children's Hospital McGill University Health Centre, Montreal, Canada; [6]Pediatrics and Human Genetics, Montreal Children's Hopsital McGill University Health Centre, Montreal, Canada

Objectives: The epigenome has emerged as one of the core elements de-regulated in pediatric gliomas. A key facet that has not been investigated in this context and is only beginning to be understood in human cancer, is the spatial organization of chromatin and its influence on the regulation of gene expression in cancer cells. The chromatin landscape can influence gene regulation and even promote oncogenic alterations by virtue of geographic proximity in the nucleus.
Methods: To this effect we decided to explore the spatial organization of chromatin in pediatric gliomas with a focus on the *BRAF* locus in pilocytic astrocytoma (PA) utilizing genome-wide chromosome conformation capture (Hi-C) technology in freshly-resected patient tumors.
Results: *BRAF* is altered in a significant proportion of PA tumors, in the form of tandem duplication at chromosome 7q34 leading to in-frame fusions of *KIAA1549-BRAF*, with a notable predilection to tumors arising in the cerebellum. Interestingly, Hi-C analyses reveal a putative topologically-associated domain (TAD) consistent across tumors within the cerebellum in the study; bordered strikingly by *KIAA1549* and *BRAF* regions. This TAD appears to be consistent across other cell types originating from hematological, fibroblast and other sources from publically available datasets.
Conclusions: To best confirm this TAD we intend to profile heterochromatin H3K9me3 marks, and integrate this data with gene expression. In this way, we may be able to elucidate structural determinants that may favor *BRAF* fusion in PA that may originate from inherent DNA conformation.

P-063

MOLECULAR CHARACTERIZATION OF MAPK PATHWAY AND ONCOGENE-INDUCED SENESCENCE IN A BRAZILIAN COHORT OF PILOCYTIC ASTROCYTOMA PATIENTS

A.P. Becker[1], W. Menezes[1], J. Sheren[2], C. Scapulatempo-Neto[3], D. Aisner[2], L.T. Bidinotto[1], L. Neder[4], M. Varella-Garcia[2], R.M. Reis[1]

[1]Center of Research in Molecular Oncology, Barretos Cancer Hospital, Barretos, Brazil; [2]Cancer Center, University of Colorado, Aurora, USA; [3]Pathology, Barretos Cancer Hospital, Barretos, Brazil; [4]Pathology, University of Sao Paulo, Ribeirao Preto, Brazil

Objective: Pilocytic astrocytoma (PA) is an indolent glioma, with up to 10% of cases progressing poorly. Activation of MAPK, its main molecular pathway, may trigger Oncogene-induced senescence (Ois). Loss of expression of *MTAP* has been described in aggressive neoplasms, including gliomas, but no data concerning PAs has been published. Conversely, its overexpression has been related to senescence in neurodegenerative diseases. Our aim was to assess the relationship between the expression of Mtap by immunohistochemistry (IHC) and molecular markers of MAPK activation (FGFR1 mutation and *KIAA-BRAF* [*K:B*] fusion).
Methods: In this retrospective study, IHC was performed with an antibody against Mtap in the FFPE in tissue microarray platforms (TMAs). In the available samples, *FGFR1* mutation was evaluated by Sanger sequencing and *K:B* fusion by a customized dual-target, dual-color fluorescence in situ hybridization (FISH) probe set in samples in the TMAs validated in Agilent 8 × 60K aCGH and RT-PCR assays in 5 cases.
Results: Overall 75 samples from 69 patients were evaluated (1.2 M/F - median age of 11.6 years). Cerebellum was the main location (53.6%). There was overexpression of Mtap in 66/69 patients, significantly related to: cerebellar location ($p = 0.025$); point mutation of *FGFR1* ($p = 0.022$), which was noted in 2/44 cases; and *K-B* fusion ($p = 0.028$) that was detected in 38/64 samples. In adjacent cortex (9 cases) astrocytes had weak expression of Mtap, while Purkinje neurons had strong reaction.
Conclusions: As far as we are concerned, this is the first study to show overexpression of *MTAP* in PAs. This seems to reinforce a positive relationship between constitutive activation of MAPK pathway and the Ois phenomenon, which is one of the mechanisms responsible for the indolent behavior of PAs. Further studies with larger cohorts are necessary to confirm this relationship.

P-064

RESULTS OF VARIOUS METHODS OF TREATMENT FOR CHILDHOOD ANAPLASTIC EPENDYMOMA

O. Geludkova[1], I. Borodina[2], A. Korshunov[3], L. Shishkina[4], M. Ryzhova[4], A. Kislyakov[5], Y.U. Kushel[6], A. Melikyan[6], O. Shcherbenko[1], E. Abbasova[1], V. Emtsova[7], E. Kumirova[8], S. Gorbatyh[9], L. Olhova[9], V. Popov[9], L. Privalova[10], M. Mushinskaya[11], N. Yudina[12], Y.U. Punanov[13], O. Popova[14], S. Ozerov[15], V. Ozerova[16], A. Nechesnyuk[17]

[1]Pediatric Oncology and Radiology, Russian Research Center Rentgenradiology, Moscow, Russia; [2]Neurooncology, Russian Research Center Hematology Oncology and Immunology, Moscow, Russia; [3]Neuropathologisches, Institute Pathologisches, Heidelberg, Germany; [4]Neuromorphology, Institute Neurosurgery, Moscow, Russia; [5]Neuromorphology, Moscow Children Hospital, Moscow, Russia; [6]Pediatric Neurosurgery, Neurosurgery, Moscow, Russia; [7]Ambulans, Research Center Pediatric Hematology Oncology and Immunology, Moscow, Russia; [8]Neurooncology, Research Center Pediatric Hematology Oncology and Immunology, Moscow, Russia; [9]Oncology, Moscow Children Hospital, Moscow, Russia; [10]Oncology, Children Hospital, N-Novgorod, Russia; [11]Oncology, Children Hospital, Perm, Russia; [12]Oncology, Children Hospital, Voronezh, Russia; [13]Oncology, St Petersburg, Russia; [14]Oncology, Volgograd, Russia; [15]Surgery, Research Center Hematology Oncology And Immunology, Moscow, Russia; [16]MRI, Neurosurgery, Moscow, Russia; [17]Radiology, Research Center Pediatric Hematology Oncology and Immunology, Moscow, Russia

Objectives: Presently there are no standards treatment for anaplastic ependymoma.
Methods: We evaluated the treatment results for 169 children with AE. Median age was 4 y.o. Most patients were over 3 y.o (119; 70.4%). There were 104 males (61.5%) and 65 females (38.5%). Infratentorial tumors were in 81 pts (48%); supratentorial, in 82 (48.5%), and 6 pts (3.5%) had the tumor in the spinal cord. 118 pts (70%) had stage M0; 14 (8%) had metastases or detected tumor cells; for 37 patients (22%), the stage was not known. 78 pts (46%) received chemo- and radiotherapy according to protocol HIT 2000/2008; 57 (34%) received only radiotherapy after the surgical operation; 25 (15%) patients got chemotherapy; and 9 (5%) pts were treated using only surgical intervention. Most patients underwent total ($n = 70$) or subtotal ($n = 91$) tumor resection; for 8 (5%) patients, the extent of the resection was not evaluated.
Results: 3-year PFS 0.47 ± 0.05, 5-year PFS 0.32 ± 0.05, median PFS 32 months (2 to 34 months). 3-year survival was better in children over 3 in comparison with younger than 3 y.o: 0.50 and 0.36, respectively. 3-year survival among females was 0.36; among males, 0.22 ($p = 0.19$). 3-year PFS were better for supratentorial tumors in comparison with intratentorial: 0.54 and 0.39, respectively ($p = 0.19$). Survival results were better among patients with stage M0 in comparison with stage M+: 0.50 and 0.39, respectively. In the case of total tumor resection, the 3-year survival was better than in the case of subtotal resection: 0.42 and 0.22, respectively ($p = 0.44$). PFS were the same among patients who received chemoradiotherapy or only radiotherapy: 0.53 and 0.50, respectively. Among patients who got chemotherapy after tumor resection, the 3-year PFS were 0.19; after surgery only, all patients had recurrence ($p = 0.0002$).
Conclusions: Chemotherapy does not improve the results of treatment for anaplastic ependymoma.

P-065

TWO SUBSEQUENT AIEOP PROTOCOL FOR CHILDHOOD AND ADOLESCENT EPENDYMOMA: LOOKING AT PROGNOSTIC IMPROVEMENT

M. Massimino[1], V. Biassoni[1], F. Di Meco[2], M.L. Garré[3], E. Schiavello[1], I. Sardi[4], L. Genitori[4], D. Bertin[5], E. Viscardi[6], P.G. Modena[7], S. Barra[8], G. Scarzello[9], G. Cinalli[10], P. Peretta[11], A. Mussano[12], R. Migliorati[13], A. Mastronuzzi[14], F. Giangaspero[15], M. Antonelli[15], F. Buttarelli[15], E. Pecori[16], L. Gandola[16]

[1]Pediatrics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [2]Neurosurgery, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy; [3]Neurosurgery, IRCCS Istituto Giannina Gaslini, Genova, Italy; [4]Pediatrics, Ospedale Pediatrico Meyer, Firenze, Italy; [5]Pediatrics, Ospedale Pediatrico Regina Margherita, Torino, Italy; [6]Pediatrics, Clinica Pediatrica dell'Università, Padova, Italy; [7]Genetics, Ospedale S. Anna, Como, Italy; [8]Radiotherapy, Istituto dei Tumori, Genova, Italy; [9]Radiotherapy, Istituto Oncologico del Veneto, Padova, Italy; [10]Neurosurgery, Ospedale Santobono, Napoli, Italy; [11]Neurosurgery, Ospedale Pediatrico Regina Margherita, Torino, Italy; [12]Radiotherapy, Azienda Ospedaliera S.Anna, Torino, Italy; [13]Pediatrics, Ospedale Santobono, Napoli, Italy; [14]Pediatrics, Ospedale Pediatrico Bambino Gesù, Roma, Italy; [15]Neuropathology, Università Sapienza, Roma, Italy; [16]Radiotherapy, Fond. IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Objectives: Ameliorating ependymoma patients prognosis throuh two subsequent Italian protocols.
Methods: In first protocol, patients were given: focal radiotherapy (HFRT) if with no evidence of disease (NED), or 4 VEC chemotherapy HFRT for residual disease (ED). HFRT dose was 70.4 Gy; VEC was VCR 1.5 mg/m2 1/w, VP16 100 mg/m2/day 1-3, CTX 3 g/m surgery was recommended. The 2nd study stratified pts according to the two prognostic factors found: surgical results and histology was upfront centrally reviewed as in previously. Children/adolescents aged over 1 yr/below 21 if with NED/gr2 tumors were focally 1.8Gy/d up to 59.4Gy, while if with NED/gr3 tumors also received 4 VEC after irradiation. ED pts received 4VEC, second-look possible, 59.4Gy irradiation plus a 8Gy boost into 2 fractions on surgical residue.
Results: Between 1994/December 2012, 60+141 patients, respectively in the 1st and 2nd protocol, were treated and actively followed. At of 10 and 5 years, 5 years-PFS/OS were 53%/72% and 69%/84%, for the first and second protocol, respectively, showing improvement for EFS ($P = 0.009$) and OS ($P = 0.02$). We analyzed the two populations: first series (1994-2001) contained significantly whose tumor aroused in posterior fossa, while the second contained more patients with grade 3 tumors and younger ones (cut-off of 6 years of the first series); surgical results and hydrocephalus needing shunts were not different. At multivariate analysis, posterior fossa origin confirmed to be risk factors for both EFS and OS while treatment according to the second protocol was better EFS (P 0.0003) and OS (P 0.0007).
Conclusions: The aim at improveing treatment strategies seems to have been satisfied even if a longer 2nd series follow-up is needed to confirm this benefit.

P-066

CRIBRIFORM NEUROEPITHELIAL TUMOR (CRINET): A SMARCB1-DEFICIENT NON-RHABDOID TUMOR WITH FAVORABLE PROGNOSIS.

M. Hasselblatt[1], V. Ruland[1], K. Bartelheim[2], P. Johann[3], C.R. Pierson[4], C. Hawkins[5], E. Widing[6], S.G. Kim[7], M. Kool[3], M.C. Frühwald[2], W. Paulus[1]

[1]Institute of Neuropathology, University Hospital Münster, Münster, Germany; [2]Swabian Childrens' Cancer Center, Childrens' Hospital Augsburg and EU-RHAB Registry working group, Augsburg, Germany; [3]Division of Pediatric Neurooncology, German Cancer Research Center DKFZ, Heidelberg, Germany; [4]Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital and Ohio State University College of Medicine, Columbus OH, USA; [5]Division of Pathology, The Hospital for Sick Children, Toronto, Canada; [6]Dept. of Pediatric Oncology, Oslo University Hospital Rikshospitalet, Oslo, Norway; [7]Department of Pathology, Keimyung University Dongsan Medical Center, Daegu, Korea

Objectives: The majority of atypical teratoid/rhabdoid tumors (AT/RT) is characterized by inactivation of the SMARCB1/INI1gene and dismal prognosis. Few children harboring unusual non-rhabdoid SMARCB1-deficient tumors, for which the term *cribriform neuroepithelial tumor* (CRINET) has been coined, are on record. Anecdotal evidence suggests a relatively favorable prognosis of CRINET. We therefore aimed to investigate clinical features and prognosis in a first series of these rare tumors.
Methods: Clinical details, neuropathological and molecular genetic data as well as information on outcome were collected for 9 children harboring CRINET. Data on survival and recurrence-free survival were compared to 59 SMARCB1-deficient AT/RT from the European Rhabdoid Tumor Registry EURHAB.
Results: Median age of the 6 males and 3 females was 20 months (range: 10-27 months). The majority of CRINET was located supratentorially, often in the midline. Neuropathologically, all tumors were characterized by cribriform strands and ribbons and well-defined epithelial membrane antigen-immunopositive surfaces. Tumoral staining for SMARCB1/INI1 was lost. After a mean observation time of 54 months, only one child had died due to respiratory failure in the early postoperative phase. On Kaplan-Meyer analysis, children with CRINET experienced significantly longer progression-free survival as compared to AT/RT [103 months (95% confidence interval: 61-146 months) vs. 18 months (12-23 months), $P = 0.009$] and overall survival [124 (95-152) months vs. 25 (18-32) months; $P = 0.005$].
Conclusions: CRINET is a rare non-rhabdoid SMARCB1-negative tumor with favorable prognosis as compared to AT/RT.

P-067

PROGNOSTIC FACTORS IN PATIENTS OF AT/RT OF THE CENTRAL NERVOUS SYSTEM

O. Geludkova[1], E. Kumirova[2], I. Borodina[2], A. Korshunov[3], M. Ryzhova[4], A. Melikyan[5], Y. Kushel[5], L. Olkhova[6], S. Gorbatyh[6], V. Popov[7], M. Mushinskaya[8], N. Popova[9], L. Privalova[10], R. Shammasov[11], O. Scherbenko[12], E. Abbasova[12]

[1]Pediatric Oncology and Radiology, Research Center Rentgenradiology, Moscow, Russia; [2]Neurooncology, Research Center Hematology Oncology And Immunology, Moscow, Russia; [3]Neuropathologie, Pathologishes, Heidelberg, Germany; [4]Neuromorphology, Neurosurgery, Moscow, Russia; [5]Pediatric Neurosurgery, Neurosurgery, Moscow, Russia; [6]Oncology, Moscow Children Hospital, Moscow, Russia; [7]Neurosurgery, Moscow Children Hospital, Moscow, Russia; [8]Oncology, Children Hospital, Perm, Russia; [9]Oncology, Children Hospital, Volgograd, Russia; [10]Oncology, Children Hospital, N-novgorod, Russia; [11]Oncology, Children Hospital, Kazan, Russia; [12]Oncology And Radiology, Research Center Rentgenradiology, Moscow, Russia

Objectives: AT/RT is a malignant tumor with an agressive behavior.
Methods: We have evaluated the prognostic factors in 43 patients with AT/RT. Most patients were younger than 3 years old (28, 65%), and 15 patients (35%) were above 3. The males and females were 20 and 23, respectively. The tumor was infratentorial in 21 patients (48.8%); 2 patients (4.7%) had infratentorial and renal tumors; and 20 patients (46.5%) had supratentorial tumors. Stage M0 was in 24 patients (55.8%); 11 patients (25.6%) had metastases or detected tumor cells at diagnosis; and the stage was not precisely determined for 8 patients (18.6%). Treatment according to protocol ATRT-2006 was administered to 24 patients (55.8%); protocol CWS, to 8 patients (18.6%); HIT-SKK, to 4 patients (9.3%); and 7 patients (16.3%) got off-protocol treatment.
Results: 13 patients (30.2%) are alive, and 30 (69.8%) have died: 26 due to disease progression, 4 due to chemotherapy toxicity. The PFS was $30\% \pm 0.06$, and the OS was $38\% \pm 0.06$. The median survival time was 18 months; and the median observation time was 14 months (range 2 to 89 months). The survival rate was significantly higher among patients over 3 y.o in comparison with younger patients: 53 and 14%, respectively ($p = 0.004$); among patients after total tumor resection in comparison with subtotal or partial resection: 55%, 31%, and 12%, respectively ($p = 0.015$); among patients who got radiotherapy in comparison with those who did not: local radiotherapy, 50%; craniospinal radiation, 35%; no radiotherapy, 0% ($p = 0.033$); among patients with stage M0 in comparison with stage M+: 37% and 0%, respectively ($p = 0.007$). Therapy according to the ATRT-2006 protocol led to better survival rate (43%) in comparison with protocols CWS (12%) and HIT-SKK (18%), $p = 0.01$.
Conclusions: The factors that affected the prognosis were the patient's age, the extent of the surgical resection, the chemotherapy program, the use of radiotherapy, and the presence of metastases.

P-068

PROSPECTIVE STUDY ON PEDIATRIC PATIENTS WITH ATYPICAL TERATOID RHABDOID TUMORS (ATRT) OF THE CENTRAL NERVOUS SYSTEM (CNS)

J. Chang[1], A. Chang[2], M. Confer[2], S. Goldman[3], M. Dunn[4], W. Hartsell[1]

[1]Radiation Oncology, Ann & Robert H. Lurie Childrens Hospital of Chicago, Chicago, USA; [2]Radiation Oncology, Oklahoma City Procure Proton Therapy Center, Oklahoma City, USA; [3]Medical Oncology, Ann & Robert H. Lurie Childrens Hospital of Chicago, Chicago, USA; [4]Radiation Oncology, Proton Collaborative Group, Warrenville, USA

Objectives: ATRT is a rare and aggressive CNS tumor usually presenting in very young children. Aggressive treatments have improved outcomes. Such strategies have included radiation therapy. However, at such a young age, short and long term radiation toxicities are prevalent. We prospectively enrolled pediatric CNS ATRT patients onto the Proton Collaborative Group registry protocol to evaluate the efficacy and toxicities of proton radiation therapy in this population.
Methods: 13 consecutive pediatric ATRT patients were treated with at the Central DuPage Hospital Proton Center and the Oklahoma City Procure Proton Therapy Center between March 2010 – December 2013 utilizing 3D Conformal Proton Therapy.
Results: 13 patients were evaluated. They were all 3 years of age or younger (4.4 – 37.7 months). Eight patients had gross total resections, while 4 had subtotal resections along with another 1 not documented. Nine patients received multiagent intensive chemotherapy per the Dana Farber Cancer Institute regimen while 4 had treatment either on or per ACNS 0333 protocol with intensive multiagent chemotherapy along with stem cell transplants. Radiation was to local fields for 10 patients, while 3 had craniospinal irradiation. The mean follow up was 14.9 months (range of 1-43 months) and median follow up 14.2 months. At last follow up, 11 patients were alive without evidence of disease. Only 4 children had grade 3 toxicities (all acute nausea, vomiting and anorexia during radiation therapy that responded to steroids). Proton therapy was able to reduce the dose to the cochlea, optic chiasm, hippocampus, temporal lobes and integral whole brain.

Conclusions: The initial results on the largest prospective series of CNS ATRT patients treated with proton therapy seem to be favorable. The aggressive treatment regimens utilizing proton beam therapy yield proven efficacy and improved toxicity profiles, which is critically important in this young patient population with such an aggressive disease.

P-069

PROGRESSIVE DECLINE IN HEALTH-RELATED QUALITY OF LIFE AMONG LONG-TERM SURVIVORS OF BRAIN TUMOURS IN CHILDHOOD AND ADOLESCENCE

R. Barr[1], J. Duckworth[2], T. Nayiager[2], A. Whitton[3], J. Horsman[4], W. Furlong[4]

[1]Pediatrics, McMaster University, Hamilton, Canada; [2]Pediatrics, Hamilton Health Sciences, Hamilton, Canada; [3]Juravinski Cancer Centre, Hamilton Health Sciences, Hamilton, Canada; [4]N/A, Health Utilities Inc, Dundas, Canada

Objectives: The trajectory of health-related quality of life (HRQL) was assessed in survivors of brain tumours in childhood and adolescence during a longitudinal study over a decade
Methods: An inception cohort of 40 patients comprised the study sample in 2000/2001. All were at least 2 years from completion of therapy with no evidence of progressive or relapsed disease; aged 5 years or more; and able to communicate in English. Children and parental proxy respondents were interviewed using 40 item questionnaires for Health Utilities Index (HUI) Mark 2 (HUI2) and Mark 3 (HUI3). The HUI utility scores for single attribute (domains/dimensions) morbidity and for multi-attribute HRQL have an upper limit of 1.00. Negative scores for HRQL represent states of health considered worse than being dead. The subjects were re-assessed 5 and 10 years later.
Results: Medians and ranges for HUI2 scores of HRQL at the 3 time points were: 0.93 (0.49 to 1.00); 0.90 (0.36 to 1.00); 0.88 (0.16 to 1.00). Corresponding HUI3 scores were 0.88 (0.13 to 1.00); 0.85 (0.01 to 1.00); and 0.77 (−0.19 to 1.00). The differences over time are statistically significant and clinically important. Main burdens of morbidity were in attributes of HUI2 sensation, emotion, cognition; and HUI3 vision, cognition and pain. For comparison, median HUI2/HUI3 scores were 1.00/1.00 for survivors of Wilms' tumour (n = 52), 1.00/0.97 for acute lymphoblastic leukemia (n = 194) and 0.92/0.90 for neuroblastoma treated by myeloablative chemotherapy with stem cell rescue (n = 99).
Conclusions: Over the 10 year study period, survivors of brain tumours in childhood and adolescence exhibited a progressive decline in overall HRQL with important burdens of morbidity in numerous attributes, especially cognition. These findings identify the need for interventions to minimize these deteriorations in health.

P-070

A CROSS-SECTIONAL COHORT STUDY OF CEREBROVASCULAR DISEASE AFTER RADIATION THERAPY FOR CRANIOPHARYNGIOMA

A. Lo[1], F. Howard[2], A. Nichol[1], H. Hasan[1], M. Martin[3], H. Manraj[4], K. Goddard[3]

[1]Radiation Oncology, BC Cancer Agency, Vancouver, Canada; [2]School of Population and Public Health, University of British Columbia, Vancouver, Canada; [3]Radiology, BC Cancer Agency, Vancouver, Canada; [4]Radiology, Vancouver General Hospital, Vancouver, Canada

Objectives: To determine the prevalence and characteristics of cerebrovascular disease in craniopharyngioma patients treated with radiotherapy (RT).
Methods: Craniopharyngioma survivors, who were diagnosed at age ≤21 and treated with RT in British Columbia between 1971-2007, were eligible for the study. Of the 35 eligible patients, 20 patients were recruited to participate. Patients underwent a clinical assessment, blood work, and a magnetic resonance angiogram (MRA) if possible. Two patients had computed tomography angiograms (CTAs) because of metal implants that precluded them from MRAs. One patient exceeded equipment weight limitations and could not have imaging. Fasting lipid profiles were obtained on 18 patients, and fasting glucose or hemoglobin A1c tests on 20 patients.

Table 1: Description of CVAs and MRA or CTA abnormalities

Patient Number	Type of previous CVA	Timing of CVA	Age at CVA (years)	Type of Imaging	MRA or CTA findings
1	Ischemic	Post-operative setting, before RT	10	MRA	Small supraclinoid right internal carotid artery (ICA) and M1 segment
2	Ischemic	7 years after RT	12	MRA	Irregularity and narrowing of the right middle cerebral artery
3	Ischemic	25 years after RT	38	MRA	Possible short segment stenosis of the right P1 segment
4	Hemorrhagic	2 years after RT	22	CTA	Stable clipped aneurysm, mature right anterior frontal lobe infarct, and mature small lacunar infarct
5	Ischemic	3 years after RT	15	None – could not be imaged due to weight	Not applicable (N/A)
6	None	N/A	N/A	MRA	Left ICA stenosis and a small left posterior cerebral artery
7	None	N/A	N/A	MRA	Cavernous malformation or a remote focus of hemorrhage in the periventricular white matter

Results: Median age was 10 years at diagnosis (range: 2-21) and 29 years at the time of the study (range: 17-62). Vascular abnormalities were detected in 6 of the 19 (32%) patients' angiograms. Five of 20 patients (25%) had a history of CVA, of whom 4 had abnormalities on angiogram, and the remaining patient was the one who could not be imaged. Two patients with no history of CVA had abnormalities on MRA. The remaining 13 patients had normal angiography and no history of CVA. At the time of the study, 12 of 18 (67%) patients had hyperlipidemia, 1 of 20 (5%) had diabetes, and 1 of 20 (5%) had pre-diabetes. Five patients (25%) had a body mass index (BMI) >30 and 8 patients (27%) had a BMI of 25-30.
Conclusions: Young patients treated with RT for craniopharyngioma have a high prevalence of hyperlipidemia, CVA, and cerebrovascular abnormalities on imaging. These patients should undergo careful monitoring and aggressive modification of stroke risk factors.

BRAIN TUMOURS

P-071

IMPACT OF AGE AT DIAGNOSIS ON OBESITY IN PEDIATRIC BRAIN TUMOR SURVIVORS

K. Strobel[1], P. Simpson[2], P. Donohoue[3], S. Firat[4], S. Jogal[5]

[1]Medical Student, Medical College of Wisconsin, Wauwatosa, USA; [2]Quantitative Health Sciences, Medical College of Wisconsin, Wauwatosa, USA; [3]Pediatric Endocrinology, Children's Hospital of Wisconsin, Wauwatosa, USA; [4]Radiation Oncology, Children's Hospital of Wisconsin, Wauwatosa, USA; [5]Pediatric Hematology/Oncology, Children's Hospital of Wisconsin, Wauwatosa, USA

Objectives: Obesity is a long-term morbidity for children diagnosed with CNS tumors. Body Mass Index (BMI) normally declines until the age of adiposity rebound (AR), after which it increases. Tumor location, radiation therapy, or surgery near the hypothalamus increases the risk of obesity. We hypothesized hypothalamic involvement would result in a greater BMI, and diagnosis/treatment before AR would lead to the greatest BMI.
Methods: Retrospective cohort of brain tumor survivors diagnosed from 2001-2011 at Children's Hospital of Wisconsin: chart review extracted BMI (recorded as BMI z-score) at diagnosis and two-year follow-up. Children were categorized into six groups, based on age at diagnosis and hypothalamic involvement (HI). Consistent with CDC growth curves, ages were classified as 'before AR' (0-41.99 months), 'during AR' (42-83.99 months) and 'after AR' (84.00 – 120 months old). BMI z-scores were compared using Wilcoxon signed ranks tests.
Results: 116 children had two-year follow-up. BMI z score at diagnosis was similar across groups. Children pre-AR and post-AR with HI had higher two-year follow up BMI z scores than at diagnosis (before AR 0.466 to 1.589 $p = 0.004$ $N = 12$, after AR 0.519 to 1.268 $p = 0.001$ $N = 18$). No group without HI had increased BMI z score at two year follow up (before AR 0.663 to 0.518 $N = 24$, during AR 0.279 to 0.278 $N = 18$, after AR 0.658 to 0.793 $N = 24$). The before AR and during AR cohort with HI had a higher BMI z score at two-year follow up then those without HI ($p = 0.004$ and 0.015). The after AR cohort did not significantly differ from those without HI at two-year follow up.
Conclusions: Children with CNS tumors with hypothalamic involvement have increased BMI compared to those without hypothalamic involvement. Diagnosis before adiposity rebound is associated with a greater BMI than diagnosis at later age. Future studies can help elucidate the endocrine causes of these changes.

P-072

ASSESSING THE ACCURACY OF DEATH RECORDS AND PRE-MORTEM CLINICAL DIAGNOSES: A RETROSPECTIVE CHART REVIEW OF DECEASED CHILDREN DIAGNOSED WITH BRAIN TUMOURS IN BRITISH COLUMBIA, CANADA

H. Hasan[1], G. Hendson[2], F. Howard[3], R. Rassekh[4], J. Hukin[5], C. Dunham[2], T. Ahmed[3], A. Lo[1], N. Bradley[6], K. Goddard[1]

[1]Radiation Oncology, BC Cancer Agency, Vancouver, Canada; [2]Pathology and Laboratory Medicine, BC Children's Hospital, Vancouver, Canada; [3]School of Population and Public Health, University of British Columbia, Vancouver, Canada; [4]Division of Oncology/Hematology/BMT, BC Children's Hospital, Vancouver, Canada; [5]Division of Neurology and Oncology, BC Children's Hospital, Vancouver, Canada; [6]Pediatric Oncology Group of Ontario Networked Information System & Analytic Support, Pediatric Oncology Group of Ontario, Vancouver, Canada

Objectives: Despite advances in diagnostic and imaging techniques, disparities exist between pre-mortem and post-mortem diagnoses. To the best of our knowledge, there are currently no studies investigating the relationship of pre-mortem diagnoses with post-mortem autopsy findings in children diagnosed with a pediatric brain tumour (PBT). The purpose of this study was to determine whether discrepancies exist in pre-mortem diagnoses and provincial cancer registry death records when compared to post-mortem autopsy findings in deceased children diagnosed with a PBT.
Methods: A retrospective review of medical records and autopsy reports of all deceased children (0-14 years) diagnosed with PBT in British Columbia, Canada who had an autopsy

from 1980 to 2012 was performed. Pre-mortem diagnoses were compared to post-mortem diagnoses and classified based on major or minor discrepancies according to the Goldman criteria and concordance.
Results: In total 238 deaths occurred during the study period, of which 33 (13.9%) had autopsies. Of the 33 patients that had autopsies, 24 patients had an autopsy available for review. Analysis of pre-mortem and post-mortem clinical diagnoses in these 24 cases, revealed 5 (20.8%) had minor discrepancies, 9 (37.5%) had major discrepancies, and 10 (41.7%) had no discrepancies. Analysis of cause of death from the British Columbia Cancer Registry and post-mortem autopsy findings determined 13 (54.2%) cases were discordant, 9 (37.5%) were concordant, and 2 (8.3%) could not be determined due to missing cause of death information.
Conclusions: In deceased children diagnosed with a PBT who had an autopsy, there were discrepancies between pre-mortem and post-mortem findings in a significant proportion of cases. Autopsies provide valuable information that serves to educate clinicians and are an invaluable tool for providing feedback regarding the accuracy of diagnostics and appropriateness of patient management. A very small proportion of deceased PBT patients have autopsies and efforts should be made to increase this number.

P-073

AVOIDING DELAYS IN THE DIAGNOSIS OF UK PAEDIATRIC CNS TUMOUR PATIENTS: A RETROSPECTIVE MULTICENTRE AUDIT OF THE SOUTH WEST REGION

N. Cork[1], M. Carter[2], M. Chandra[3], N. Cohen[3]

[1]School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom; [2]Department of Neurosurgery, Frenchay Hospital, Bristol, United Kingdom; [3]Department of Neuropathology, Frenchay Hospital, Bristol, United Kingdom

Objectives: Prompt recognition of paediatric central nervous system (CNS) tumours is uncommon in the United Kingdom (UK). The median symptom interval (SI) - from first symptom onset to diagnosis - has been measured at 3.3 months, comparing poorly with similar nations. This retrospective multicentre audit aimed to establish the common clinical presentation with the SI achieved most recently in the South West region, outlining strategies to limit systematic delays.
Methods: From 15 hospitals, 131 paediatric patients newly diagnosed with a primary CNS tumour between 01 January 2006 and 01 November 2012 were identified. On approval from the local review board, the following data were retrieved from clinical notes: date of birth, gender, ethnicity, social deprivation, age at symptom onset and diagnosis, clinical features at onset and diagnosis, date and location of first presentation, date and modality of first imaging, tumour pathology, tumour grade, tumour location and available referral pathway data until treatment.
Results: Regardless of tumour pathology, grade or location, the most common features at onset were: headache, motor system abnormalities, nausea and/or vomiting and seizures. At diagnosis, these were: visual system abnormalities, motor system abnormalities, headache, nausea and/or vomiting and behavioural change. Signs and symptoms increased from a median of 1 at onset to a median of 4 at diagnosis. Median SI was 3.3 months. High-grade tumours were significantly associated with a reduced SI ($p = 0.005$). There was no significant association between SI and patient gender, social deprivation or first presentation in the community or in hospital.
Conclusions: Visual and motor system abnormalities and behavioural change commonly emerged during the SI; typically bilateral papilloedema, diplopia, reduced visual acuity, reduced coordination and new onset lethargy. These features, within an otherwise non-specific symptom profile, should prompt urgent clinical reassessment. SI was consistent with reports from other regions. Measures to restrict SI in the UK are recommended.

P-074

COMBAT (COMBINED ORAL METRONOMIC BIODIFFERENTIATING ANTIANGIOGENIC TREATMENT) THERAPY IN POOR PROGNOSIS PEDIATRIC MALIGNANT BRAIN TUMORS-IS THERE A ROLE?

G. Chinnaswamy[1], M. Prasad[1], V. Dhamankar[1], T. Vora[1], T. Gupta[2], A. Moiyadi[3], E. Sridhar[4], S. Banavali[1], R. Jalali[2], P. Kurkure[1]

[1]Department of Pediatric and Medical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, India; [3]Department of Neurosurgery, Tata Memorial Hospital, Mumbai, India; [4]Department of Pathology, Tata Memorial Hospital, Mumbai, India

Objectives: The outcome of children with recurrent/high risk malignant brain tumors continues to be poor with conventional modalities of therapy. Metronomic therapy (COMBAT) has been found to be beneficial in many disseminated and aggressive pediatric solid tumors. We evaluated the impact (efficacy and toxicity) of this strategy in children with poor prognosis malignant brain tumors.
Methods: Children deemed to have a poor risk malignant brain tumor (by histology, site, metastatic status) were started on COMBAT regimen after completion of conventional therapy. Relapsed high grade tumors were also included. The treatment strategy consisted of the COMBAT regimen which includes low dose temozolomide, etoposide, sodium valproate and 13-cisretinoic acid administered in 12-weekly cycles. All children were followed up at 3 monthly intervals with clinical evaluation and MR imaging.
Results: Thirty four children were started on COMBAT therapy between the year 2010-2013 and 32 were available for evaluation. The median age of the study population is 10 years with a male:female ratio being 2:1. Among the 32 patients, 13 (40.6%) had relapsed/progressive medulloblastoma, 7 (21.9%) had metastatic/recurrent PNET (supratentorial), 7 (21.9%) had recurrent anaplastic ependymoma and 5 (15.6%) were diagnosed with diffuse pontine glioma. 23/32 (71%) of patients showed a response (SD/PR/CR) to therapy while 9 (28%) of patients continued to progress with no response documented. Toxicity included grade III/IV cytopenia in 2 patients and 1 patient developed myelodysplastic syndrome. Isotretinoin skin toxicity was noted in majority and was manageable with topical interventions. In the final analysis 62.5% (20) of patients had progressed with median time to progression being 9 months (2-44 months) while 37.5% (12) patients had shown a positive sustained response.
Conclusions: COMBAT regimen is a feasible, well tolerated and effective treatment option for children with high risk or metastatic brain tumours. The data is a retrospective analysis and hence a prospective study to evaluate this strategy systematically is warranted.

P-075

TUMOR CELLS IN THE CEREBROSPINAL FLUID IN LOW GRADE CHOROID PLEXUS TUMOR: DO NOT OVERTREAT!

U.R. Kordes[1], M. Benesch[2], S. Hartung[1], K. Petrasch[1], S. Rutkowski[1], V. Ruland[3], T. Pietsch[4], M. Hasselblatt[3], J.E.A. Wolff[5]

[1]Pediatric Hematology and Oncology, University Medical Center Hamburg Eppendorf, Hamburg, Germany; [2]Division of Pediatric Hematgy and Oncology, Department of Pediatrics and Adolescent Medicine Medical University of Graz, Graz, Austria; [3]Institute of Neuropathology, University Hospital Münster, Münster, Germany; [4]Institute of Neuropathology Brain Tumor Reference Center, Bonn University, Bonn, Germany; [5]Department of Pediatric Hematology Oncology, Cleveland Clinic Children's Hospital, Ohio, USA

Objectives: Cytomorphology of cerebrospinal fluid (CSF) remains essential for treatment stratification in many embryonal brain tumors. However, incidence and significance of positive CSF in choroid plexus tumors (CPT) is not well understood. Therefore CSF was evaluated in the CPT-SIOP-2000 study (01/2001-03/2010) and the CPT-SIOP registry (03/2010-04/2014).
Methods: Chart review and central review of cytology from lumbar and or ventricular CSF.
Results: Cytospin preparations of 18 patients (7 males, 11 females; median age at diagnosis 0.55 years) with low grade CPT (choroid plexus papilloma [CPP], $n = 9$; atypical choroid plexus papilloma [APP], $n = 9$) were positive ($n = 13$) or highly suspicious ($n = 5$) for tumor cells. Positive CSF was detected for a median of 17 days after tumor resection (range from pre-operative day -1 to post-operative day 288). Complete resection of the primary tumor was achieved in all patients. MRI showed leptomeningeal dissemination in 3/12 patients. No patient was irradiated. Nine patients were observed, nine patients diagnosed before 2011 received a mean of six chemotherapy cycles: Two patients with APP and postoperative residual tumor, one patient with primarily unresectable CPP, three patients with positive CSF, three patients prior to down-grading from CPC to APP or CPP by reference histology; one patient with APP was treated by systemic and intrathecal chemotherapy because of M1 stage. All patients are alive without relapse or progression at a median of 5.4 years.
Conclusions: Cytomorphological examination of CSF is required for complete staging of CPT. Differentiation between plexus papilloma cells and normal choroid plexus or ependymal cells can be challenging. Persistence of tumor cells longer than 14 day after tumor resection can be an innocuous finding in low grade CPT and may reflect the unique properties of cells derived from the choroid plexus. Deferral of chemotherapy is justified for CPP and completely resected APP with positive CSF cytology.
Acknowledgment: Funded by the German Childhood Cancer Foundation (DKKS)

P-076

DECREASED MORBIDITY AND MORTALITY OF POST-INDUCTION MARROW-ABLATIVE CHEMOTHERAPY WITH AUTOLOGOUS HEMATOPOETIC RESCUE FOR CHILDREN WITH NEWLY-DIAGNOSED MALIGNANT BRAIN TUMORS: THE "HEAD START " CONSORTIUM TRIALS, 1991-2009

C. Altshuler[1], J.L. Finlay[1], K. Haley[1], G. Dhall[1], L. Vasquez[1], R. Sposto[1], L. Ji[1], S. Gardner[2], for the "Head Start" Consortium

[1]Hematology/Oncology, Children's Hospital Los Angeles, Los Angeles, USA; [2]Pediatrics (Oncology Division), NYU Langone Medical Center, New York, USA

Objectives: Since 1991, three sequential prospective multi-national clinical trials (including 39 participating institutions) have been conducted by the 'Head Start' Consortium for young children newly-diagnosed with malignant brain tumors, to improve their cure rate and quality of survival through avoidance (
Methods: Overall treatment design has remained unchanged throughout the 3 prospective trials, and has been previously reported; five 21-28 day cycles of induction chemotherapy [cisplatin, vincristine, cyclophosphamide, etoposide (HSI) with/without high-dose

methotrexate (HSII-III), oral etoposide and oral temozolomide (HSIII)] were followed – for patients with minimal residual, non-progressive tumor - by a single marrow-ablative cycle with thiotepa and etoposide days -5 to -3, preceded by carboplatin days -8 to -6. Bone Marrow (HSI) or leukapheresed peripheral hematopoietic cells under Neupogen stimulation (HSII-III) were obtained following recovery from the first and/or second induction cycles. Radiotherapy was reserved for patients with residual tumor following completion of induction or >6yo.
Results: A total of 226 children were enrolled on 3 consecutive HS trials with primary malignant brain or spinal cord tumors *and* underwent marrow-ablative chemotherapy, the 100 day toxic mortality for whom steadily declined from HSI (3/47 = 6.4%) through HSII (1/48 = 2.1%) to HSIII (1/131 = 0.8%). Grade IV transplant-related oropharyngeal mucositis/stomatitis/pain declined from 14.9% (HSI) to 5.3% (HSIII) and grade IV infection declined from 8.5% (HSI) to 0.8% (HSIII).
Conclusions: Increasing experience with the marrow-ablative chemotherapy regimen, combined with improved leukapheresis and post-reinfusion supportive care techniques, have likely contributed to the steady decline in transplant-related morbidity and mortality in this patient population, contributing towards improved overall survival.

P-077

MANAGEMENT OF PEDIATRIC BRAIN TUMORS: REPORT FROM THE MOROCCAN SOCIETY OF PEDIATRIC HEMATOLOGY AND ONCOLOGY

L. Hessissen[1], F. El Midaoui[1], S. Cherkaoui[2], S. Benmiloud[3], M. El Kababri[1], A. Kili[1], J. Houdzi[4], I. Qaddoumi[5], E. Bouffet[6], M. Karkouri[7]

[1]Mohamed V University Souissi, Hemato-Oncology Pediatric Center, Rabat, Morocco; [2]Medical School of Casablanca, Hemato-Oncology Pediatric Center, Casablanca, Morocco; [3]Medical School of Fez, Hemato-Oncology Pediatric Center, Fez, Morocco; [4]Medical School of Marrakech, Hemato-Oncology Pediatric Center, Marrakech, Morocco; [5]ST Jude Children Research Hospital, Hemato-Oncology Pediatric Center, Memphis, USA; [6]Sick Children Hospital, Hemato-Oncology Pediatric Center, Toronto, Canada; [7]Medical School of Casablanca, Pathology Center, Casablanca, Morocco

Objectives: Brain tumors (BT) are the most frequent solid tumor in children, but information about its management in low income countries is lacking.
Methods: A national multidisciplinary group for children with BT was implemented on February 2011 in Morocco to improve communication among healthcare providers, develop adapted protocols, decrease referral time and treatment delays, and improving data collection. The group included the four pediatric oncology centers of Morocco (Rabat, Marrakech, Fez and Casablanca) and international experts from ST Jude Children Research Hospital and Sick Children Hospital in Toronto. E-mail communications and online meetings via www.cure4kids.org web site were used to discuss patient care, develop protocols, administrative issues, and plan two brain tumors workshops in Morocco.
Results: From January 2012 till December 2013, data on 84 pediatric BT cases from 3 centers estimated to treat 75% of all pediatric cancers in Morocco were available. These 84 cases represent approximately 5% (range, 2% - 7.5%) of all pediatric cancers treated at these three centers for the study period. The male/female ratio was 1.1 and median age 7 years (range, 4 months - 16 years). 53/63 patients had fossa posterior lesions. The histological types according to WHO 2007 classification were reported for 75 patients (30 astrocytoma, 29 medulloblastoma/PNET, 12 ependymoma, 2 plexus choroid carcinoma, one pineoblastoma and one oligodendroglial tumor). Follow up data were available for 66 patients: 7 were alive in complete remission, 31 alive with residual disease 2 had progressive disease, 12 died. Status was unknown for 14 (7 Lost of follow up, 5 abandonment, 2 referral abroad).
Conclusions: Low accrual rate, poor survival, and abandonment are still major obstacles facing BT management in Morocco. We hope that the national BT group, the multidisciplinary approach and collaboration with international experts will overcome such obstacles.

P-078

CAN-COL-BRAIN-KIDS: WORK IN PROGRESS…WHAT HAVE WE LEARNED?

A. Fonseca[1], A. Linares[2], I. Sarmiento[3], K. Scheinemann[4]

[1]Pediatric Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Pediatric Hematology/Oncology, Universidad Nacional de Colombia/Fundacion Hospital la Misericordia, Bogota, Colombia; [3]Pediatric Hematology/Oncology, Fundacion Hospital la Misericordia, Bogota, Colombia; [4]Pediatric Hematology/Oncology, Universitätsklinikum Münster, Münster, Germany

Objectives: A collaboration between Canada and Colombia to improve the management of Central Nervous System (CNS) tumors was started at the beginning of 2013. Colombia, a middle-income country, has an estimated 400 brain tumors diagnosed per year. Health insurance is the individual's responsibility in most cases, which brings intrinsic challenges to the timely diagnosis and treatment of brain tumors.
Methods: A monthly teleconference tumor board using the cure4kids platform has been held since March 2013. The only requirement is a computer with internet access in each participating center.
Results: Over the last 12 months 9 tumor boards have been held and 25 cases have been reviewed with an average of 2.7 cases per session. The average number of attendees was 11. Up to 5 centers have been present for the tumor boards with 2 centers present at all 9 sessions held. Centers in multiple cities in Colombia (Bogota, Cartagena and Neiva) have participated. Diagnoses reviewed included Low-grade astrocytomas (8), medulloblastoma (4), ependymomas (3), PNETs (3), CNS Sarcomas (2) and others (5).
Some areas of improvement have been identified. It is not uncommon to identify delays in referral to a tertiary center for adjuvant treatment after initial surgical intervention. Unfortunately, administrative healthcare issues negatively impact the timely management of patients with brain tumors; delays in the acquisition of appropriate imaging for intervention or follow-up are frequent. No national guidelines for management have been developed.
Conclusions: A collaboration project has been established and needs widespread participation of multiple centers for appropriate impact. Development of national and institutional treatment guidelines are crucial to improving timely work-up, treatment and follow-up. Guideline development will be a priority moving forward in the management of CNS tumors in Colombia.

P-079

METASTATIC RHABDOID PAPILLARY MENINGIOMA WITH BRAF V600E MUTATION AND GOOD RESPONSE TO PERSONALIZED THERAPY

O.Z. Mordechai[1], S. Postovsky[1], E. Vlodavsky[2], A. Eran[3], S. Constantini[4], E. Cagnano[5], M. Ben Arush[1]

[1]Pediatric Hematology Oncology, Rambam Health Care Campus, Haifa, Israel; [2]Pathology department, Rambam Health Care Campus, Haifa, Israel; [3]Radiology Department, Rambam Health Care Campus, Haifa, Israel; [4]Pediatric Neurosurgery Unit, Tel Aviv-Elias Sourasky Medical Center, Tel Aviv, Israel; [5]Pathology Department, Tel Aviv-Elias Sourasky Medical Center, Tel Aviv, Israel

Objectives: Papillary rhabdoid meningioma is an agressive histological variant of meningioma which accounts for 1-2.5% of all meningiomas. The clinical course is very agressive and in most of the time the disease disseminates through the CSF after frequent local recurrences.
Methods: We describe the case of a 6 years old female with a history of headache, phonophobia and photophobia. Brain MRI demonstrated a right temporal extra-axial tumor. Frontotemporal craniotomy was performed with tumor macroscopic excision. Histopathological examination demonstrated the diagnosis of papillary rhabdoid meningioma. Spine MRI and CSF cytology excluded metastasis; external involved-field radiation therapy was delivered (5400 cGy). Three months later, she developed recurrent headache with photophobia, CNS imaging revealed massive right hemisphere recurrence with leptomeningeal spread. The child's neurological status deteriorated rapidly with left hemiplegia, anisocoria and grade II coma despite urgent craniospinal irradiation.
Results: A specimen from the tumor was sent for comprehensive genomic profiling. The assay revealed activating BRAF mutation (V600E). Therapy with a BRAF inhibitor (Dabrafenib) was initiated at a dose of 30 mg bid for one month and then 35 mg bid. The clinical condition of the child improved progressively and 6 months later, she started to walk without any help. We added a MEK inhibitor (Trametinib) at a dose of 0.45 mg daily and then 0.9 mg according to PK values.
Our patient, one year from the start of targeted therapy is now going school with complete recuperation of the right hemiplegy and normal neurological functions.
Conclusions: An effective strategy to build upon the successes seen with Dabrafenib and Trabetinib monotherapies in melanoma has been to combine these agents with the goal of further improving response rates and delaying resistance. The role of BRAF rearrangements and tailoring therapies for pediatric malignancies needs further researches in a larger pediatric population.

P-080

NEUROCYTOMA: THE CLEVELAND CLINIC EXPERIENCE

T. Tekautz[1], E. Murphy[2], S. chao[3], V. Recinos[4], G. Barnett[1], J. Wolff[5]

[1]Burkhardt Brain Tumor Neuro-Oncology Center, Cleveland Clinic, Cleveland, USA; [2]Radiation Oncology, Cleveland Clinic, Cleveland, USA; [3]Neurooncology Center, Cleveland Clinic, Cleveland, USA; [4]Pediatric Neurosurgery, Cleveland Clinic, Cleveland, USA; [5]Pediatric Hematology/Oncology, Cleveland Clinic, Cleveland, USA

Objectives: Neurocytoma is an uncommon tumor and the need for postoperative therapy is controversial. We reviewed the Cleveland Clinic experience.
Methods: Patients with histologic diagnosis of neurocytoma between 1994 and 2011 were identified through an IRB-approved database. Clinical, tumor, and treatment factors were evaluated. Survival times were calculated using the Kaplan-Meier method.
Results: Seventeen patients with neurocytoma were treated, age at diagnosis 16.8 - 66.8 years; (median 35.3 years). Thirteen patients were male, all were Caucasian. Most common presenting symptoms: headaches (n = 12) and gait disturbance (n = 3). Sixteen patients had intraventricular lesions. All patients underwent surgery (gross total resection, GTR: 5, subtotal resection, STR: 10). Three patients (2 with STR and 1 with a biopsy) underwent adjuvant radiation; 2 with fractionated RT and one with stereotactic radiosurgery. Median event free survival (EFS) was 6.3 years and the projected 10 year EFS was 23%. Overall survival (OS) was 92%. The degree of resection did not correlate with EFS. After median

follow-up of 8.4 years, 5 patients are without evidence of disease, 4 of which had developed recurrent disease and subsequently underwent GTR. Patients treated with adjuvant radiation did not experience disease recurrence (n = 3). Twelve patients had Ki-67 results available from diagnosis (median 1.3%,), 4 had Ki-67 results at recurrence which was invariably higher than at presentation (median 10.5%) Ki-67 was not predictive for EFS or OS.
Conclusions: In this cohort of patients, median EFS was only 6.3 years, and suggested a possible benefit to adjuvant radiotherapy in select cases. The excellent OS of 94% suggests that these patients benefit from salvage therapy with a combination of surgery and radiation. Prospective and molecular analyses of these tumors may identify risk factors for disease recurrence and help determine who would benefit from more aggressive upfront therapy.

P-081

NO RADIATION FOR CHOROID PLEXUS CARCINOMA PATIENTS WITH LI-FRAUMENI SYNDROME?

M. Bahar[1], J. Wolff[2]

[1]Pediatrics, Cleveland Clinic, Cleveland, USA; [2]Pediatric Hematology/Oncology, Cleveland Clinic, Cleveland, USA

Objectives: Choroid plexus carcinomas (CPC's) are rare pediatric tumors often associated with Li-Fraumeni Syndrome (LFS), a germ line mutation in the TP53 tumor suppressor gene, predisposing to cancer. The standard of care is controversial. Some studies recommend radiation therapy as a treatment modality. We used a literature analysis to evaluate the hypothesis that radiation therapy should be avoided in patients with CPC and LFS.
Methods: Expanding a preexisting CPC literature database, we added all cases of CPC with LFS identified in PubMed through the end of 2013 and compared survival using Kaplan Meier curves and log rank tests. We restricted the analysis to CPC patients identified by the presence of TP53 dysfunction or phenotypic characteristics of LFS. We compared overall survival between patients who received radiation therapy and patients treated without radiation therapy.
Results: 25 patients were documented with CPC and LFS. Ten of those had received radiation and fifteen did not receive radiation therapy. The median overall survival of all LFS CPC patients was 0.83 years + 0.58 standard error. The survival of patients receiving radiation was inferior to those without radiation (mOS 3.25 years versus 0.16). Kaplan Meier curves did not cross and the log rank tests suggested the difference to be statistically significant ($p = 0.04$).
Conclusions: Different from previous analyses we find a survival disadvantage for patients with LFS and CPC, who received radiation versus those that did not. This does not simply suggest that radiation shortened the lives of these patients, since the chemotherapy was very different in the two patient groups. However, the finding does provide evidence to pursue treatment approaches that do not include radiation in these patients and to continue developing them.

P-082

A NATIONAL BRAIN TUMOUR CONSORTIUM- THE CANADIAN PAEDIATRIC EXPERIENCE 2002-2014

T. Brown[1], R. Sinha[2], D. Strother[3], E. Bouffet[4]

[1]Saskatchewan Cancer Agency, University of Saskatchewan, Regina, Canada; [2]Royal University Hospital, University of Saskatchewan, Saskatoon, Canada; [3]Alberta Children's Hospital, University of Calgary, Calgary, Canada; [4]The Hospital for Sick Children, University of Toronto, Toronto, Canada

Objectives: In 2003 Canadian paediatric oncologists recognized the benefit to establish protocols for central nervous system (CNS) tumours where no open international studies were available. This spearheaded the formation of the Canadian Paediatric Brain Tumour Consortium (CPBTC). CPBTC included all 17 Paediatric oncology centers in Canada in the development and collaborative conduct of clinical and pre-clinical studies aimed at improving knowledge of brain tumours, developing more effective therapies and maximizing quality of life. It was also established to foster research, support and encourage young investigators. We reviewed the development, challenges and successes of the group over the past 12 years.
Methods: The CPBTC meetings, minutes and publications were reviewed.
Results: The first CPBTC teleconference was held in November 2002 with 5 centers in attendance. The number of centers participating in the teleconferences peaked at 15 in February 2004. The collaborative studies faced challenges with multiple ethics review board submissions and development of contracts between institutions. Funding was limited and allocated preferentially to pathology reviews and data collection. The Principal Investigators of active studies were representative of the 17 participating centers. There have been 20 publications, 6 abstracts at international meetings, 3 completed clinical trials and 4 prospective research papers with consortium collaboration. A neuro-oncology handbook is in press. Participation in the consortium is comprehensive, reflecting the multidisciplinary approach in managing paediatric brain tumour patients. Preclinical and clinical studies complement Children's Oncology Group (COG), International Society of Paediatric Oncology (SIOP) and other cooperative group trials.
Conclusions: The CPBTC has facilitated the completion of several nationally based projects and is recognized as a vehicle for collaborative research. Future goals include the development of a national virtual tumour bank, advocacy for a Canadian national ethics review board, academic recognition of participation and contribution, and a website. Success in grant applications will be key to funding future collaboration.

P-083

THE USE OF POSITRON EMISSION TOMOGRAPHY IN PAEDIATRIC BRAIN TUMOURS

A. Gilbert[1], A. Shankar[1], F. Fraioli[2], M. Gaze[3], S. Stoneham[1], J. Bomanji[2]

[1]Department of Paediatric and Adolescent Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [2]Department of Nuclear Medicine, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [3]Department of Clinical Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom

Objective: Magnetic resonance imaging is conventionally used to image central nervous system (CNS) tumours. There are significant limitations in evaluating response to treatment with MR imaging, and positron emission tomography (PET) is now widely utilised in imaging cancers. However, ^{18}F-fluoro-deoxy-glucose (FDG) - the main tracer in clinical use - is unsuitable for brain imaging as glucose is the primary substrate for brain metabolism. We investigated whether simultaneous ^{18}F-fluoroethylcholine (FECH) PET/MRI with functional semi-quantitative parameters; **M**aximal **S**tandardized **U**ptake **V**alue (SUVmax/mean) and **A**pparent **D**iffusion **C**oefficient (ADC) max and mean is a viable option for diagnosis, and treatment response assessment, in children with histologically confirmed astrocytic tumours.
Methods: Eleven patients with biopsy proven astrocytomas were injected with 250 MBq 18 F-Choline. Imaging was performed 40 minutes later using a hybrid PET/MRI scanner. PET data were acquired simultaneously with MR sequences. SUVmax and SUVmean and ADC max and mean of the whole tumoural Region of Interest were recorded.
Results: At baseline the areas of ^{18}F-choline up-take matched areas of contrast enhancement and restricted diffusion. There was a negative correlation trend between SUV_{max} and ADC_{mean}, and a positive correlation trend between SUV_{max} and tumour size. There was concordance between reduction in tumour size and reductions in SUV_{max} and SUV_{mean} in four children, in three of whom, ADC_{mean} values were increased. In two patients, although anatomical tumour size remained stable, SUV_{max} and SUVmean values were increased and there was a reduction in the ADC_{mean} values. Additionally, in two children cross-sectional MRI showed an increase both in tumour size as well as increased SUV_{max} but a reduction in ADC values.
Conclusion: The results suggest that fluoroethylcholine PET combined with functional MRI has a high degree of sensitivity and specificity, and may be a better tool for response assessment when compared to conventional cross sectional MRI alone.

CNS/BRAIN

P-084

MULTI-SEGMENTS INTRAMEDULLARY SPINAL CORD TUMORS IN ADOLESCENT PATIENTS

J. Sun[1], Z. Wang[1]

[1]Neurosurgical Department, Peking University Third Hospital, Beijing, China

Objectives: To prospectively analyze the clinical features and characteristics of multi-segments intramedullary spinal cord tumors in adolescent patients.
Methods: In our study, 30 consecutive adolescent patients with multi-segments intramedullary spinal cord tumors were recruited, who underwent microsurgery for the tumor using a posterior approach and were hospitalized in Peking University Third Hospital within a period of 10 years. The tumor was exposed through dorsal myelotomy. Preoperative and postoperative neurological functions were scored using the Improved JOA (IJOA) grading system. The functional outcome was defined as postoperative IJOA score minus preoperative IJOA score. All the patients were followed-up until Jan. 30, 2014.
Results: There were 20 male and 15 female adolescent patients younger than 25 years. Their mean age was (15.3 ± 6.83) years. The most common initial symptom was sensory disturbance (including pain and/or numbness, 51.4%, 18/35), followed by motor disturbance (including limbs weakness and gait deterioration, 25.7%, 9/35), pain and motor disturbance (22.9%, 8/35), as well as fever, limbs deformities, and sphincter dysfunction, respectively. The preoperative IJOA scores of the patients were (14.4 ± 3.38). The postoperative IJOA scores of the patients were (15.5 ± 3.31). The most commonly involved location was the cervicothoracic segments (37.1%, 13/35), followed by the conus terminalis (25.7%, 9/35), the cervical region (17.1%, 6/35), the thoracic region (14.3%, 5/35), and the lumbus region (5.7%, 2/35). The average involved segments were (4.4 ± 1.38). The most frequent tumors were neurodevelopmental tumors (including lipoma, epidermoid cyst and teratoma) (34.3%, 12/35), followed by astrocytomas (28.6%, 10/35), ependymomas (20%, 7/35), hemangioblastomas (11.4%, 4/35), and glioblastomas and schwannomas, respectively.
Conclusions: In adolescent patients with multi-segments intramedullary spinal cord tumors, the most commonly involved locations are the cervicothoracic segments and the conus terminalis, while the most frequent tumors are neurodevelopmental tumors and astrocytomas. Good prognosis in adolescent patients is observed in a long-term follow-up.

P-085

CHILDHOOD MALIGNANT DISEASES ASSOCIATED WITH NEUROFIBROMATOSIS TYPE 1: HACETTEPE EXPERIENCE

A. Varan[1], H. Sen[1], B. Aydin[1], B. Yalcin[1], T. Kutluk[1], C. Akyuz[1]

[1]Dept. of Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: To evaluate clinical characteristics and prognosis of patients with NF 1 and malignancy excluding optic glioma.
Methods: Between 1975 and 2013, 92 of 473 patients (19%) with NF 1 who were followed up at our center were found to have malignant disease. 67 (14%) of them had optic glioma and in 25 (5%) of them there were other malignant disorders. Files of these 25 patients were analyzed retrospectively in terms of clinical features and treatment results.
Results: The male to female ratio of these 25 patients was 16/9. The age of diagnosis of NF 1 was between 3 months-16 years (median 5.5 years) and diagnosis of malignancy at age between was 1.5 - 33 years (median 8), respectively. Sixteen patients were diagnosed with NF1 and malignancy simultaneously. Histological subtypes were 12 soft tissue tumors (6 malignant peripheral nerve sheath tumor (MPNST), five rhabdomyosarcoma and one malignant fibrous histiocytoma), 10 brain tumors (three grade 3-4 astrocytoma or glioblastoma, four astrocytoma, two medulloblastoma and one cervical pilocytic astrocytoma), two neuroblastoma and one non-Hodgkin's lymphoma. Disease was located in the posterior fossa in three patients with brain tumors. Three patients with high grade glioma, one with non-Hodgkin's lymphoma, one with medulloblastoma, two with rhabdomyosarcoma, and one with astrocytoma have died with disease progression despite treatment. Five of 6 patients with a diagnosis of MPNST died with disease, one patient diagnosed at age 1.5 years is being followed up in remission during 32 months. Twelve out of 25 patients are still alive.
Conclusions: Five percent of the patients with NF1 have developed malignant diseases. The prognosis is poor despite the treatment. Close and regular follow-up is crucial for early detection of malignancy for NF 1.

EPIDEMIOLOGY

P-086

ESTIMATING THE INCIDENCE OF ACUTE LEUKEMIA IN CHILDREN IN WESTERN KENYA BY REVIEW OF MALARIA BLOOD SMEARS: A PILOT AND FEASIBILITY STUDY

F. Njuguna[1], J. Skiles[2], A. Moormann[3], R. Mukhwana[1], T. Vik[2]

[1]Child Health and Paediatrics, Moi University College of Health Sciences School of Medicine, Eldoret, Kenya; [2]Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [3]Pediatrics, University of Massachusetts School of Medicine, Worcester, USA

Objectives: A retrospective review of malaria slides was undertaken as an epidemiology study to estimate the incidence of acute leukemia in Kenya, and to determine the feasibility of utilizing malaria slides to improve detection of acute leukemia.
Methods: Over one year, 22,000 malaria slides were collected at Kitale District Hospital in Kenya for secondary review. A trained technologist performed the review of all slides. On first screening, potential positive slides were identified using the following criteria: (1) estimated white blood cell (WBC) count over 50,000/mm3 or (2) Less than 10% neutrophils seen on the blood smear. Once identified, two authors reviewed and photographed each of the positive slides. 100 cell count differentials were done on each of the positive slides, and clinical data about the slides were obtained from hospital records.
Results: 299 slides were identified as showing signs of possible leukemia, including leukocytosis or severe neutropenia. On further review of slides and clinical data, 9 slides showed a combination of findings making them highly probable as indicating leukemia. Of the slides not showing definitive signs of leukemia, many (∼25%) had neutrophilia suggesting acute infection. Other slides with neutropenia were from infants, under one year of age with malaria. A third group of slides were screened as showing neutropenia, but on review, the neutrophils were distorted such that neutropenia was not present.
Conclusions: This study demonstrates the feasibility of using a slide made to screen for malaria, to also screen for leukemia. Based on the numbers of likely positive slides we identified, our estimate of the incidence of acute leukemia, 4.2 cases/100,000 children/year, is similar to that in high-income countries. We are planning a prospective trial to screen slides and identify patients for earlier referral for diagnosis and treatment.
Acknowledgements: Supported by Alex's Lemonade Stand Foundation.

P-087

THE LANDSCAPE OF PEDIATRIC, ADOLESCENT AND YOUNG ADULT THYROID CANCER IN ONTARIO: 1992-2010

J. Pole[1], A. Zuk[2], J.D. Wasserman[3]

[1]Research Unit, Pediatric Oncology Group of Ontario, Toronto, Canada; [2]Dalla Lana School of Public Health, University of Toronto, Toronto, Canada; [3]Division of Endocrinology, The Hospital for Sick Children, Toronto, Canada

Objectives: To describe the current landscape of Thyroid Carcinoma (TC) diagnoses and demographics in Ontario among children, adolescents and young adults over an eighteen year period.
Methods: A retrospective cohort was assembled from data extracted from the provincial cancer registry and administrative health-care databases. Direct age-adjusted incidence rates were calculated.
Results: A total of 2,552 children and youth less than 30 years of age were diagnosed with thyroid cancer between 1992 and 2010 in the province of Ontario, Canada. The overall age-adjusted thyroid cancer incidence rate per 100,000 increased from 2.00 [95% CI 1.80-2.22] in 1992-1995 to 4.10 [95% CI 3.84-4.36] in 2006-2010. The sex specific age-adjusted incidence rate of TC between 1992-1995 and 2006-2010 has nearly doubled for both females and males: 3.23 [95% CI 2.85-3.60] to 6.77 [95% CI 6.29-7.25] and 0.81 [95% CI 0.63-0.99] to 1.42 [95% CI 1.21-3.65], respectively. The most common histologic types are papillary-93.4% (including the follicular variant-28.9%), follicular-4.6%, and medullary-1.9%. There were no documented cases of anaplastic thyroid carcinoma in this cohort. TC was a second primary malignancy for 47 individuals, and of those patients that had a primary thyroid cancer, 22 developed a subsequent malignant neoplasm. The majority of all TC cases (92%) resided in urban area, and there were 12 deaths among all diagnosed TC cases during this period.
Conclusions: As reported in other populations, there is a rising incidence in TC diagnoses over time, though the extent of this increase appears more limited than elsewhere. Explanation for this rising incidence, as well as the observed association with multiple primary malignancies and well as long-term outcomes merit further investigation.

P-088

CHILDHOOD LEUKEMIA INCIDENCE AND SURVIVAL IN SOUTHERN THAILAND FROM 1989-2011

K. Demanelis[1], H. Sriplung[2], R. Meza[3], L.S. Rozek[1], P.J. Lupo[4], M.E. Scheurer[4]

[1]Environmental Health Sciences, University of Michigan, Ann Arbor, USA; [2]Epidemiology Unit, Prince of Songkla University, Songkhla, Thailand; [3]Epidemiology, University of Michigan, Ann Arbor, USA; [4]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: Disparities exist in childhood leukemia detection, diagnosis and treatment between developing and developed countries. We analyzed childhood acute myeloid (AML) and acute lymphoblastic (ALL) leukemia incidence and survival trends from 1989-2011 in Songkhla, Thailand. For a point of reference, we compared these results to childhood leukemia incidence in the United States (US) using Surveillance, Epidemiology, and End Results (SEER) data.
Methods: Using population-based registry data from Songkhla, 324 cases of leukemia were diagnosed in children age 0-19 from 1989-2011. Among those, 87% had vital status and follow-up time. Leukemia subgroups were classified using International Classification of Childhood Cancer definitions. SEER data was obtained from SEER*Stat. Age-adjusted two-year incidences were computed and standardized using WHO 2000 standard population. Incidence trends were analyzed using joinpoint regression. Percent survival was computed for 1,3, and 5 years for each year of diagnosis from 1989-2006 and analyzed using univariate linear regression.
Results: AML and ALL composed 22% and 56% of leukemia cases from Songkhla, respectively. The overall age-adjusted incidence of ALL and AML was 1.85 and 0.70 cases per 100,000, respectively. ALL incidence increased 1.3% per year in Songkhla ($p = .057$), but was lower compared to the US ($p = .002$) from 1989-2010. AML incidence increased 4.0% per year ($p = .096$) in Songhkla while it decreased 1.7% ($p = .005$) in the US from 1989-2010. AML incidence was higher in Songkhla compared to US ($p = .034$). In Songkhla, the median survival was 1.00 year for AML and 7.53 years for ALL. Five-year percent survival for ALL improved 2.2% annually ($p = .022$) from 40.0% in 1989 to 71.4% in 2006.
Conclusions: The incidence of leukemia is increasing in Songkhla. The proportion of AML cases is higher compared to the US. While survival is improving for ALL, it is lower than the US. These temporal changes in leukemia incidence and survival warrant investigating novel risk factors throughout Thailand.

P-089

TRENDS IN HEPATOBLASTOMA INCIDENCE AMONG CHILDREN AND ADOLESCENTS IN THE UNITED STATES, 1999-2010: RACIAL AND ETHNIC DISPARITIES

R. Amorim[1], R. Naves[1], K. Ribeiro[1], C. Rodriguez-Galindo[2]

[1]Department of Social Medicine, Faculdade de Ciências Médicas da Santa Casa de São Paulo, Sao Paulo, Brazil; [2]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA

Objectives: Low birth weight (LBW) is associated with a high risk of developing hepatoblastoma. Prevalence of very low (VLBW) and LBW have significantly increased in the United States in the last decades, particularly among Hispanics, due to increased specialization in delivering pre-, peri- and neonatal health care. The aim of our study was to evaluate trends in hepatoblastoma incidence according to sex, race, and ethnicity.

Methods: We retrieved data from the National Program Cancer Registries (NPCR) database (49 states and the District of Columbia, 1999-2010). All children ages 0-19 years diagnosed with hepatoblastoma (ICCC group VIIa) were included in the study. Age-standardized incidence rates (ASIR) were calculated according to sex, race, and ethnicity using Segi population. Trends over time and average annual percent changes (AAPC) were assessed using Joinpoint Regression Model.
Results: 1409 new hepatoblastoma cases were registered in the period Incidence was significantly higher among males (Rate Ratio = 1.47, 95%CI 1.32-1.64). Highest and lowest incidence rates were observed among Asians (ASIR = 2.42/million) and blacks (ASIR = 1.18/million), respectively. Hispanics showed a higher incidence (ASIR = 2.03/million) compared to non-Hispanics (ASIR = 1.80/million), but difference was not statistically significant (RR = 1.13, 95%CI 0.99-1.28). Overall, a significant increase in the incidence of hepatoblastoma was observed in the period 1999-2010 (AAPC = 2.80, 95%CI 1.05-4.59). However, trend was statistically significant only for males (AAPC = 4.11, 95%CI 1.72-6.55). Stratified analysis by ethnicity has shown a 2% per year increase for non-Hispanics (AAPC = 1.96, 95%CI 0.49-3.46), while a larger increase has been observed for Hispanics, although not statistically significant (AAPC = 4.39, 95%CI -0.42-9.43). The largest increasing trend in hepatoblastoma incidence was observed among Blacks (AAPC = 6.04, 95%CI 0.11-12.32).
Conclusions: We have documented substantial differences in the incidence of hepatoblastoma among different ethnic and racial groups. Given the known correlation between hepatoblastoma and LBW, whether these differences represent ethnic and racial variations or barriers in prenatal and neonatal care needs to be determined.

P-090

USE OF TREND ANALYSIS TO ILLUSTRATE RESIDUAL CANCER DISPARITIES IN SURVIVAL FROM CHILDHOOD NON-CNS EMBRYONAL TUMORS

P. Friedrich[1], E. Itriago[1], C. Rodriguez-Galindo[1], K. Ribeiro[2]

[1]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Department of Social Medicine, Faculdade de Ciências Médicas da Santa Casa, Sao Paulo, Brazil

Objectives: Trends in survival from childhood non-CNS embryonal tumors have not been fully explored from the perspective of cancer disparities. In this study we aimed to assess these trends and identify residual disparities.
Methods: Cases of neuroblastoma, retinoblastoma, nephroblastoma, hepatoblastoma, rhabdomyosarcoma, and non-CNS germ cell tumors (GCT) among children 0-19 years old diagnosed 1/1/1993-12/31/2010 were retrieved from SEER-13 for data from 1993-1999 and SEER-18 for data from 2000-2010. Race/ethnicity categories included: White-non-Hispanic, Black-non-Hispanic, Hispanics, American Pacific Islander (API), and American Indian/Alaska Native. Three-year overall survival was obtained using the Kaplan Meier Methods. Annual percentage change (APC) was obtained using Jointpoint.
Results: Inclusion criteria retrieved 8,188 cases. Pairwise comparison between race/ethnicity categories for the most recent analyzable period (2005-2007) showed significant difference in 3-year survival only for neuroblastoma (Blacks vs. Whites 73% vs. 84%, p = 0.035) and rhabdomyosarcoma (API vs. Whites 52% vs. 78%, p = 0.025). Trend analysis for the cohort showed significant increase in APC for Whites (+0.43) and although positive, not significant for the other minorities (Hispanics +0.55, Blacks +0.22, API +0.06). Positive trends achieving significance were found in neuroblastoma for Whites (+1.26), Hispanics (+1.44) and API (+12.4 since 2003), but not for Blacks (−2.49). Hispanics with hepatoblastoma or nephroblastoma showed negative survival trends achieving significance (−2.66 and -0.82, respectively), while Whites showed significant improvement in survival for hepatoblastoma (+3.41), but not for nephroblastoma (+0.02). Relatively flat or converging trends were noted for retinoblastoma, rhabdomyosarcoma, and germ cell tumors. Possibly diverging trends were noted in neuroblastoma, nephroblastoma and hepatoblastoma.
Conclusions: Standard survival analysis using pairwise comparison of magnitude at a specific recent time interval would have missed the disparities identified. Although the number of cases is relatively low in pediatric oncology non-CNS solid tumors, trend analysis using Jointpoint allowed better illustration of possible residual pediatric cancer survival disparities.

P-091

SPATIAL CLUSTERING OF CANCER IN CHILDREN AND YOUNG PEOPLE FROM NORTHERN ENGLAND

R. McNally[1], P.W. James[1], A.W. Craft[2]

[1]Institute of Health & Society, Newcastle University, Newcastle upon Tyne, United Kingdom; [2]Northern Institute of Cancer Research, Newcastle University, Newcastle upon Tyne, United Kingdom

Objectives: The aetiology of childhood cancer is not well understood. Both genetic and environmental factors are likely to be involved. 'Spatial clustering' occurs if the cases display an irregular geographical distribution, with a small numbers of localised areas with large excesses or a large number of areas with modest excesses. To assess whether localised environmental factors may play a role in aetiology we tested for spatial clustering of both address at birth and diagnosis using population-based data from northern England.
Methods: We extracted all 5612 cases of cancer diagnosed in children and young people aged 0-24 years during the period 1968-2003 from the Northern Region Young Persons' Malignant Disease Registry. This is a population-based registry and includes all cases of cancer in children and young adults who were resident at time of diagnosis in northern England (population aged 0-24 years = 898,000; area = 15727 km^2). Overall clustering analysis was performed using point process methods, testing the null hypothesis that disease risk does not vary spatially and cases occur independently. Kulldorff's scan statistic, based on a Bernoulli model was used to test for individual clusters.
Results: Based on both address at birth and diagnosis there was evidence of overall clustering for leukaemia, lymphomas, central nervous system (CNS) tumours, sympathetic nervous system tumours, retinoblastoma, germ cell tumours and carcinomas (all $P < 0.05$). Based on address at birth there was evidence of overall spatial clustering for soft tissue sarcomas ($P = 0.03$). Based on address at birth, Kulldorff's scan statistic detected individual spatial clusters for CNS, renal and bone tumours ($P < 0.05$). Based on address at diagnosis, there was an individual spatial cluster for all carcinomas ($P = 0.01$).
Conclusions: This study suggests that spatially varying environmental factors may be implicated in the aetiology of a number of different cancers.

P-092

RACIAL AND ETHNIC DISPARITIES IN PEDIATRIC NON-CNS EMBRYONAL TUMORS INCIDENCE IN THE UNITED STATES: TRUE EFFECT OR CONFOUNDING BY SOCIOECONOMIC STATUS?

P. Friedrich[1], E. Itriago[1], C. Rodriguez-Galindo[1], K. Ribeiro[2]

[1]Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Department of Social Medicine, Faculdade de Ciências Médicas da Santa Casa, Sao Paulo, Brazil

Objectives: Racial and ethnic disparities in the incidence of non-CNS embryonal tumors have not been fully explored. Existing studies often address racial disparities, but fail to incorporate ethnicity or control for socioeconomic status (SES).
Methods: Cases of neuroblastoma, retinoblastoma, nephroblastoma, hepatoblastoma, rhabdomyosarcoma, and non-CNS germ cell tumors (GCT) among children 0-19 years old diagnosed 1/1/2000-12/31/2010 were retrieved from SEER-18 database. Race/ethnicity categories included: White-non-Hispanic, Black-non-Hispanic, Hispanics, American Pacific Islander (API), and American Indian/Alaska Native. Age-adjusted incidence rates and rate ratios (RR) were obtained. County data on poverty level was used to stratify analysis by SES.
Results: Hispanics presented a lower incidence of neuroblastoma compared to Whites (RR = 0.53; p < 0.001) and effect remained significant after adjusting for SES. Higher incidence of retinoblastoma was observed among Hispanics (RR = 1.26; p = 0.005) and for bilateral disease in particular (RR = 1.4, p = 0.02), but effect dissipated when controlling for SES. Compared to Whites, Hispanics (RR = 0.80; p < 0.001) and API (RR = 0.43; p = 0.001) had a lower risk of nephroblastoma, although for Hispanics association lost significance in the low SES group. Risk of hepatoblastoma was lower among Blacks (RR = 0.44; p < 0.001) and effect remained significant after adjusting for SES. Rhabdomyosarcoma incidence was lower among Hispanics (RR = 0.85; p = 0.02), but no effect was observed when controlling for SES. Incidence of GCT was higher among Hispanics (RR = 1.30; p < 0.001) and lower among Blacks (RR = 0.52, p < 0.001) and API (RR = 0.79, p = 0.003), but effects for Hispanics and API were modified by SES.
Conclusions: Ethnic disparities in the incidence of these tumors were documented using population-based data, particularly for neuroblastoma and hepatoblastoma. Effect modification or confounding by SES was observed in most subgroup analyses. Adequately controlling for SES is key when analyzing and interpreting racial and ethnic disparities in childhood embryonal tumors incidence.

P-093

INFERIOR SURVIVAL AMONG ABORIGINAL CHILDREN WITH CANCER IN ONTARIO

S. Marjerrison[1], J.D. Pole[2], L. Sung[3]

[1]Division of Hematology/Oncology, McMaster Children's Hospital, Hamilton, Canada; [2]Research Division, Pediatric Oncology Group of Ontario, Toronto, Canada; [3]Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: Pediatric cancer distribution and outcomes have not been examined in Canadian Aboriginal children. Our objective was to describe the distribution, event-free survival and overall survival of Aboriginal children with malignancies that reside in Ontario compared with non-Aboriginal children.
Methods: This population-based study included 10,520 Ontario children (<18 years) with cancer diagnosed between 1985 and 2011. Cases were identified from the Pediatric Oncology Group of Ontario Networked Information System database. Aboriginal children were identified by self-reported ethnicity or postal code on Native reserve at diagnosis. Cases were presented with descriptive statistics and compared using the Fisher's exact test. Event-free and overall survival probabilities were calculated for Aboriginal and non-Aboriginal children, described with Kaplan-Meier curves and compared with log-rank tests.

Results: We identified 65 Aboriginal and 10,364 non-Aboriginal children with malignancy. Distribution of malignancy type was similar. There were no significant differences in baseline characteristics, presence of metastatic disease, or treatment approach (clinical trial, standard of care or individualized protocol) between the groups. Five-year event-free survival (± standard error) was 56.3 ± 6.2% among Aboriginal children *vs*. 72.8 ± 0.4% among non-Aboriginal children (P = 0.0042), and 5-year overall survival was 64.0 ± 6.0% *vs*. 79.3 ± 0.4% (P = 0.0017) respectively. Cause of death did not vary by Aboriginal ethnicity.
Conclusions: Survival was significantly inferior among Aboriginal children with cancer as compared to non-Aboriginal children with cancer Ontario. Future studies are required to define the etiology of this disparity, evaluate the issue nationally, and create interventions to improve outcomes for Aboriginal children.

P-094

GENETIC SUSCEPTIBILITY TO LANGERHANS CELL HISTIOCYTOSIS: A PILOT GENOME-WIDE ASSOCIATION STUDY USING CASE-PARENT TRIADS

P. Lupo[1], M. Scheurer[1], J. Belmont[2], S. Tsavachidis[1], A. Shih[1], S. Simko[1], H. Abhyankar[1], R. Chakraborty[1], K. Lim[1], K. McClain[1], C. Allen[1]

[1]Pediatrics Hematology-Oncology, Baylor College of Medicine, Houston, USA; [2]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: Langerhans cell histiocytosis (LCH) is an inflammatory myeloid neoplasia characterized by the accumulation of clonal CD207+ myeloid dendritic cells. LCH presents most commonly in infants and children. The incidence of LCH has been estimated to be two to ten cases per million in children 15 years of age or younger. In spite of the clinical complications associated with LCH, very little is known about genetic susceptibility to this condition. To further characterize germline genetic susceptibility to childhood LCH, we performed a preliminary genome-wide association study (GWAS) using case-parent triads.
Methods: A case-parent triad study design was utilized, which is robust to population stratification bias. The Baylor College of Medicine Institutional Review Board approved the study protocol, and informed consent was obtained from all participants. LCH cases and parents were recruited from Texas Children's Cancer Center. DNA samples on 69 case-parent triads were genotyped in the Laboratory for Translational Genomics at Baylor College of Medicine using the Illumina HumanOmni5-Quad BeadChip. Single nucleotide polymorphisms (SNPs) were excluded based on the following criteria: genotyping success rate $<10^{-6}$, and minor allele frequency http://www.biostat.harvard.edu/fbat/fbat.htm).
Results: After all exclusions, 1,702,122 SNPs were included in the association analysis. Eleven SNPs were identified with a p-value $^{-5}$. Three SNPs were identified with a p-value $^{-6}$. Specifically, intronic or intergenic SNPs on chromosome 12 ($p = 3.5 \times 10^{-8}$); chromosome 10 ($p = 4.7 \times 10^{-8}$); and chromosome 6 ($p = 4.8 \times 10^{-7}$) were associated with LCH risk.
Conclusions: While our findings must be replicated in an independent population, they do suggest that inherited genetic variation may be relevant in susceptibility to LCH. We are currently expanding this study and have plans to validate our findings through expanded analyses and methodologies.

P-095

A PRELIMINARY TRIO-BASED GENOME-WIDE ASSESSMENT OF MATERNAL GENETIC EFFECTS ON CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

P. Lupo[1], S. Plon[1], D. Ritter[2], D. Wheeler[2], S. Tsavachidis[1], R. Zabriskie[1], D. Marquez-Do[1], M. Scheurer[1]

[1]Pediatrics Hematology-Oncology, Baylor College of Medicine, Houston, USA; [2]Human Genome Sequencing Center, Baylor College of Medicine, Houston, USA

Objectives: Recent evidence from genome-wide association studies (GWAS) suggests susceptibility to childhood acute lymphoblastic leukemia (ALL) is influenced by several genetic loci. While these studies have focused on the role of single nucleotide polymorphisms (SNPs) carried by affected individuals, other biological mechanisms may also be involved. As ALL may arise *in utero*, one such mechanism involves "maternal genetic effects." Specifically, variation in the maternal genome could affect the intrauterine environment essential to normal hematopoeisis. We therefore conducted a preliminary genome-wide assessment of maternal genetic effects and the risk of childhood ALL.
Methods: ALL cases and parents were recruited from the Texas Children's Cancer Center for the period 2009-2013. The Baylor College of Medicine Institutional Review Board approved the study protocol, and informed consent was obtained from all participants. DNA samples on 94 complete trios were genotyped using the Illumina HumanCore BeadChip. We applied log-linear models to investigate whether polymorphisms of maternal genes influence risk of ALL in cases.
Results: Three maternal SNPs were identified where the association was $p < 5.0 \times 10^{-5}$. Specifically, maternal genotypes for *PPP1R12B* ($p = 1.6 \times 10^{-9}$); *SYNE2* ($p = 4.2 \times 10^{-5}$); and *TSC22D1* ($p = 4.4 \times 10^{-5}$) were significantly associated with childhood ALL risk. These maternal genetic effects were independent of the respective genotypes of the child with ALL.
Conclusions: We completed a genome-wide evaluation of maternal genetic effects on leukemia risk. We were able to identify SNPs with significant effects in three genes that have been implicated in diverse physiology including previous GWAS of obesity-related and cardiovascular traits (*PPP1R12B* and *SYNE2*), transmission of alleles from fathers (*PPP1R12B*), and tumor suppression (*TSC22D1*). While our findings must be validated, they do suggest that maternal genetic effects may be relevant in ALL risk.
Acknowledgements: Cancer Prevention and Research Institute of Texas Grant Number: RP10189.

P-096

IMPROVEMENT OF ABANDONMENT AND REFUSAL OF THERAPY IN PEDIATRIC PATIENTS WITH CANCER IN GUATEMALA AT UNIDAD NACIONAL DE ONCOLOGÍA PEDIÁTRICA (UNOP)

E. Alvarez[1], M. Seppa[1], K. Messacar[2], J. Kurap[3], E. Sweet-Cordero[1], S. Rivas[4], M. Bustamante[4], S. Howard[5], B. Efron[6], S. Luna-Fineman[1]

[1]Pediatric Hematology/Oncology/SCT/Cancer Biology Division, Stanford University, Palo Alto, USA; [2]Department of Pediatrics Infectious Diseases, University of Colorado, Denver, USA; [3]Family Medicine, Hilo Bay Clinic, Hilo, USA; [4]Oncología Pediatrica, Unidad Nacional de Oncología Pediatrica, Guatemala City, Guatemala; [5]Pediatric Oncology, Saint Jude Children's Research Hospital, Memphis, USA; [6]Department of Statistics and Biostatistics, Stanford University, Palo Alto, USA

Objectives: Abandonment of cancer therapy is a major cause of therapeutic failure. Historically, Guatemala had a very high rate of abandonment, up to 42% in 1999. This study examines the rate of abandonment over time in Guatemalan children and identifies the factors associated with increased risk of abandonment.
Methods: A retrospective study of children with cancer, ages 0-18 seen at UNOP, of Guatemala from 2001-2008 was performed. Patient data collected from the Pediatric Oncology Networked Database was analyzed for 3 years after starting therapy. Abandonment was defined as a lapse of 4 weeks in planned treatment. Refusal was defined as failure to begin treatment. Cox proportional hazards analysis identified the effect of age, sex, year of diagnosis, distance, ethnicity, and principal diagnosis on abandonment of therapy. Outcome measures were abandonment and refusal.
Results: 1789 charts were analyzed. 234 abandoned and 133 refused therapy. Over time, the rate of abandonment/refusal decreased from 21% in 2001 to 3.5% in 2008. Greater distance to the center ($p = 0.000$), younger age ($p = 0.017$) and earlier year of diagnosis ($p = 0.000$) were associated with increased risk of abandonment or refusal. Indigenous ethnicity ($p = 0.002$) was additionally associated with increased risk of abandonment. Sex and cancer diagnosis were not significant. Abandonment of therapy correlates with decreased survival in those patients with known outcomes; the cumulative survival at 5 years was 0.20 ± 0.03 (survival ± SE) for those that abandoned vs 0.59 ± 0.01 for those that completed therapy.
Conclusions: Abandonment of therapy has decreased over time in Guatemala; and corresponds with the establishment of UNOP, a centralized pediatric cancer treatment center in 2000; and the creation of a psychosocial team in 2005 to target families at risk of abandonment. Research is needed to further investigate the effect of socioeconomic factors and targeted interventions on abandonment.

P-097

SURVIVAL GAP FOR CHILDREN WITH CANCER IN A MIDDLE- INCOME COUNTRY: LESSONS FROM KING HUSSEIN CANCER CENTER IN JORDAN

I. Sultan[1], R. Rihani[1], F. Madanat[1], S.C. Howard[2]

[1]Pediatric, King Hussein Cancer Center, Amman, Jordan; [2]Pediatric, St. Jude Children's Research Hospital, Memphis, USA

Objectives: With heterogeneity in the outcome of children with cancer around the world. A standardized method to compare outcome of children with cancer is needed. We used an open access database and compared survival of children at our center.
Methods: Our department used the Pediatric Oncology Network Database (POND) to register patients since Jun2006. Data collected included demographics, pathology, staging, risk stratification, major toxicities and outcome. We compared the distribution of cases and outcome registered from Jun2006 till Dec2013 to data obtained from the SEER database from Jan2006 till Dec2010.
Results: We compared 1721 patients registered in POND to 17505 patients registered in SEER. The mean age for the 2 groups were 7.4 and 8.2 years, respectively ($P < .001$). Diagnosis distribution was similar but with higher percentages of patients with bone tumors and retinoblastoma at our center. There was a significantly better survival in SEER patients when compared to our population (SEER 3-yr OS = 85 ± 0.33% vs. POND 3-yr OS = 75 ± 1.3%, $P < .001$). When analysis was restricted to specific diseases, survival of patients with ALL and lymphoma was similar to that recorded in the SEER (P,0.59 and 0.86; respectively). On the other hand, patients with AML, solid tumors, CNS tumors and retinoblastoma had worse outcome in our population. Among our patients, outcome of Jordanian was superior to that of Non-Jordanians, particularly in patients with solid tumors. When compared to previous reports from our center, we noticed previous publication bias in medulloblastoma and rhabdomyosarcoma but not in ALL and retinoblastoma.
Conclusions: We used a combination of prospective databases to calculate survival gap in our population. Further analysis is needed to study the reasons for this difference, particularly in patients with solid tumors and brain tumors. This could reflect different referral patterns and

variations in management. The proposed method can be easily used in other centers to calculate survival gap accurately.

P-098

ESTABLISHING THE INCIDENCE AND CHARACTERISTICS OF SYMPTOMATIC VENOUS THROMBOTIC EVENTS IN PEDIATRIC ONCOLOGY PATIENTS IN THE MARITIMES, CANADA: A POPULATION BASED STUDY

K. Kulkarni[1], T. Mac Donald[1], V. Price[1], C. Fernandez[1], P. Cox[1], J. Berman[1], M. Bernstein[1], B. Crooks[1], S. Afzal[1], M. Yhap[1]

[1]Pediatric Hematology Oncology, IWK Health Centre and Dalhousie University, Halifax, Canada

Objectives: Venous thrombotic events (VTE) are recognized as an important complication in pediatric cancer patients. The reported incidence (0.7-73%) and characteristics of VTE in literature are highly variable due to varying study methodology and lack of population based data. The present study was done to establish the incidence and characteristics of symptomatic VTE in pediatric cancer patients in the 3 Maritime provinces of Nova Scotia, New Brunswick and Prince Edward Island who receive centralized oncology care at a single tertiary care centre.
Methods: All pediatric cancer patients in the Maritimes are managed at IWK Health Center in Halifax in a shared care model with regional provincial hospitals. After ethics approval, case records of all cancer patients (<20 years of age) diagnosed and managed at the IWK health center from January 2000 to March 2014 were retrieved.
Data from multiple databases was integrated including (i) pediatric oncology hospital database, (ii) Provincial Children in Young People (CIYP-C) database, (iii) Electronic medical records, (iv) Pharmacy database and (v) Hospital Health records. Using these databases, patients with symptomatic VTE (patients with $\geq$1 signs/symptoms directly related to VTE) who were treated with anticoagulants were identified. Data was analyzed using the SPSS version-22.
Results: 854 cancer patients were diagnosed during the study period. Of these 2.7% (n = 23) had symptomatic VTE. The mean age at VTE diagnosis was 12.1 ± 6.4 months (65% >10 years). The male:female ratio was 1.5:1. Median time to VTE from cancer diagnosis was 46 days (46% within 1 month). Approximately 22% had a second VTE. Approximately 44% of the patients with VTE required >1 central venous catheters.
Conclusions: The present study is one of the first to establish a population based incidence of symptomatic VTE in pediatric oncology population. Additional analysis incorporating a larger geographic area and duration will be needed to further validate these observations.

P-099

ROUTES TO DIAGNOSIS FOR CHILDHOOD AND YOUNG ADULT CANCER WITHIN INPATIENT HOSPITAL CARE SERVICES IN YORKSHIRE, UK

C. Lethaby[1], R. Feltbower[1], S. Kinsey[2], S. Picton[2], M. van Laar[1]

[1]Centre of Biostatistics and Epidemiology, Leeds Institute of Genetics Health and Therapeutics, Leeds, United Kingdom; [2]Yorkshire Regional Centre for Paediatric Oncology and Haematology, Leeds Teaching Hospitals Trust, Leeds, United Kingdom

Objectives: The pathways to diagnosis for children and young adults (CYA) with cancer are often complex. Developing an understanding of these pathways is vital to the development of effective strategies for improving the time to diagnosis. This population-based study investigates pre-diagnosis admission routes to inpatient care for CYA's diagnosed with cancer in order to improve our understanding of how this unique cohort access healthcare.
Methods: All cases of cancer diagnosed aged 0-24 years between 2004 and 2009 in Yorkshire were identified from the Yorkshire Specialist Registry of Cancer in Children and Young People (N = 1098). Case data were linked to inpatient hospital records containing coded clinical data and admission route for each inpatient event. Cancer specific alert codes were identified from inpatient events preceding or coinciding with the date of definitive diagnosis and reviewed against accepted UK CYA cancer awareness campaigns. Initial admission routes for pre-diagnosis inpatient events containing alert codes were identified, and assessed for children (0-14 years) and young adults (15-24 years).
Results: We identified 641 (58%) cases with cancer specific alert codes within their pre-diagnosis inpatient admissions. Of these, 418 cases (65%) were initially admitted via an emergency route. Emergency routes included 204 (32%) admissions via accident and emergency (A&E), 123 (19%) via primary care, 21 (3%) via outpatient care and 70 (11%) categorised as 'other emergency' routes. Overall, the proportion of initial emergency admission routes was similar for children (66%) and young adults (64%); the distribution of emergency subgroups was also similar between age groups.
Conclusions: Emergency admissions play an important role within the pathways to diagnosis for both children and young adults with cancer. The predominance of A&E admissions within the initial pre-diagnosis inpatient events potentially identifies the need for targeted interventions within this area of the healthcare structure.

P-100

CLINICAL FINDINGS OF ONCOLOGIC EMERGENCY AT DIAGNOSIS

T. Iehara[1], K. Tsuchiya[1], K. Ouchi[1], M. Miyachi[1], Y. Kuwahara[1], S. Fumino[2], T. Tajiri[2], H. Hosoi[1]

[1]Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan; [2]Pediatric Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan

Objectives: Oncologic emergency is a life-threatening condition that requires immediate intervention. All children with cancer require an emergency response at the time of diagnosis; however, those requiring intensive care management are especially in need of rapid diagnosis and control. To aim of this study was to clarify how to care for oncologic emergency cases by examining the clinical features at the first visit as well as the prognosis.
Methods: We retrospectively reviewed the data for 200 patients with cancer treated at our institution during a period of seven years between 2007 and 2013.
Results: Seventeen children exhibited oncologic emergency at their first visit (17/200; 8.5%). The median age at diagnosis was 6.2 years among the oncologic emergency patients and 6.6 years among the non-emergency patients. The average length of stay in the PICU (Pediatric Intensive Care Unit) among the emergency patients was 9.2 days. The most frequent symptoms at the first visit to our hospital were dyspnea due to acute airway obstruction, followed by coughing and abdominal pain (41%, 29% and 29%, respectively). The most frequent oncologic emergency disease was lymphoma (41%). As to emergency treatments, intubation, surgery and drainage were performed (59%, 41% and 24%, respectively). Only one patient experienced death during the acute phase within 30 days from the first visit. There were no differences in overall survival between the oncologic emergency and non-emergency cases (3-year overall survival rate: 83.3% and 89.0%, respectively, $P = 0.46$).
Conclusions: The prognosis of children with oncologic emergency is not necessarily poor, if the physician understands the clinical signs and provides appropriate management.

P-101

PERCEPTION AND ATTITUDES TOWARDS GENETIC TESTING FOR CANCER IN PARENTS OF CHILDREN WITH CNS TUMORS

K. Khaleifeh[1], A. Al-omari[2], D. Al-rimawi[2], U. Tabbori[3], E. Bouffet[3], N. Amaviri[4]

[1]Nursing departement, King Hussein Cancer Center, Amman, Jordan; [2]Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan; [3]Pediatric Hematology Oncology, Hospital for Sick Children, Toronto, Canada; [4]pediatrics, King Hussein Cancer Center, Amman, Jordan

Objectives: Genetic predisposition is an increasingly accepted cause of childhood cancers. We aim to explore perception and attitudes of parents of children with CNS tumors towards genetics and cancer. This is especially important in countries with high consanguinity where cultural factors may have negative impact.
Methods: Paper validated 42-item questionnaire was administered to parents during their regular outpatient visit to the pediatric neuro-oncology clinic at King Hussein Cancer Center, Jordan. We analyzed parents' demographics, knowledge and perception about genetic predisposition, and attitudes toward genetic testing.
Results: Fifty-two questionnaires were distributed; with 100% response rate. Twenty-seven parents (33%) reported family history of cancer with 44% relatives' deaths from cancer. Consanguinity was found in 11.5% of families. Genetic predisposition is thought to cause cancer by 33 parents (63%), while half of parents agreed that consanguineous marriage increases that risk. Forty-eight parents (92%) believe that early detection and cancer screening improves cure rates and knowledge of a genetic predisposition may contribute to survival. More than half of parents think that a positive genetic test would affect negatively the future lives of their children. However, the majority (92%) believe that pediatric oncologists should inform them if genetic predisposition is suspected. Forty-eight parents (92%) would do a genetic test, if available, and 98% want to know a positive result. Forty-nine parents (94%) will inform other family members about a positive result to start screening and improve their survival. When a genetic test is positive, most parents (81%) will comply with cancer screening investigations, even if frequent.
Conclusions: Majority of parents want to do genetic testing for cancer and they strongly believe that cancer screening improves survival. This should encourage oncologists to challenge the social and cultural barriers to discuss this sensitive topic with families and offer genetic testing, especially in communities with high consanguinity.

P-102

CLINICAL CHARACTERISTICS OF PATIENTS WITH GERMLINE SUFU MUTATIONS

L. Guerrini-Rousseau[1], M. Guillaudbataille[2], F. Bourdeaut[3], S. Puget[4], C. Dufour[5], J. Grill[5], B. Bressac[2], E. Sariban[6], C. Vilain[6], B. Isidor[7], L. Mansuy[8], I. Winship[9], O. Delattre[10], D. Valteau Couanet[5], L. Brugieres[5]

[1]Pédiatrie, Gustave Roussy, Villejuif, France; [2]Genetic, Gustave Roussy, Villejuif, France; [3]Pediatry, Institut Curie, Paris, France; [4]Pediatry, Necker University Hospital, Paris, France; [5]Pediatry, Gustave Roussy, Villejuif, France; [6]Pediatry, Hopital Universitaire des Enfants de la Reine Fabiola, Bruxelles, Belgium; [7]Pediatry, CHU Nantes, Nantes, France; [8]Pediatry, CHU Nancy, Nancy, France; [9]Genetic, University of Melbourne, Melbourne, Australia; [10]Genetic, Institut Curie, Paris, France

Objectives: Germline mutations of the *SUFU* gene have recently been described in association to medulloblastoma. Only a few cases have been described in literature so far.
Methods: We performed a retrospective review of the clinical files and molecular data of all patients in whom a germline *SUFU* mutation had been diagnosed in Institut Gustave Roussy and Institut Curie genetics laboratories.
Results: Twenty-one patients from 17 families were diagnosed with a germline *SUFU* mutation: 6 frameshift, 6 splice, 2 nonsense, 2 large rearrangement, one missense. All patients but 2 had been diagnosed with a medulloblastoma at a median age of 18 months [range 1-35] (desmoplastic in 9, extensive nodularity in 6, classical in 4). The indication for testing the other two patients was the presence of familial history of medulloblastoma and criteria for a Gorlin syndrom with basocellular carcinomas (CBC) without germline *PTCH* mutation in the second. A macrocrania was described in 13 patients. An history of medulloblastoma in siblings was described in 4 families. Mutations were inherited in 12/13 patients whose parents underwent genetic testing and de novo in 2 cases. Overall, 36 healthy carriers have been identified in 12 families. Second malignancies were described in 3 medulloblastoma patients including multiple CBC (1pt), ovarian tumor and meningioma (1pt) and thyroid carcinoma (1pt). In addition several mutation carriers in family members were diagnosed with cancer: breast cancer at 37, meningioma at 38, CBC at and sarcoma at 63 years of age.
Conclusions: *SUFU* germline mutations predispose to medulloblastomas mostly of desmoplastic/nodular or extensive nodularity subtypes during the first 3 years of life, often associated with macrocrania. Some patients also develop basocellular carcinomas. Due to incomplete penetrance, genetic counselling is difficult. International collaboration is necessary in order to better define the risk associated with these mutations and guidelines for surveillance.

GERM CELL TUMOURS

P-103

RETROPERITONEAL TERATOMAS: LESSONS LEARNED FROM 16 CASES

Y. Heloury[1], Y. Nyo[1], S. King[1], M. Nightingale[1], P. Ferguson[2], M.d. Leclair[3], P.k. Krishnan[4]

[1]Urology, Royal Childrens'hospital, Melbourne, Australia; [2]Pediatric Surgery, Monash Children, Clayton, Australia; [3]Pediatric Surgery, Nantes University Hospital, Nantes, France; [4]Pediatric Surgery, Singapore, Singapore

Objectives: Retroperitoneal teratoma (RPT) is an uncommon tumor in children. The purpose of this paper was to review the presentation, management and outcome of children with RPT between 2001 to 2014.
Methods: A retrospective multi centric (Melbourne Children Hospitals, National University Hospital Singapore and Nantes University hospital) review of 16 children with RPT encountered in over a 14 year period was carried out. Age at presentation, sex, tumor marker levels, operative findings, surgical complications, histology and outcomes were evaluated.
Results: Thirteen patients were female. 2 had Down's Syndrome. 11 patients had surgery before 1 year of age. 2 of the patients had raised AFP for age. Median size of the tumor was 145mm (range 115 to 180mm). Surgical resection was performed for all patients. Difficulty in resection due to distortion of vascular anatomy was reported in 11 with injury to vessels in 3 (IVC, splenic artery, polar renal artery) and organs removal in 2 (nephrectomies). Complete resection was achieve in 13 patients. The histology was mature teratoma for 11 patients and immature teratoma for 5. Median duration of follow up was 19 months (range from 1 month to 12 years) with 1 recurrence of immature teratoma (lung, iliac bone). Post operative complications included 2 intussusceptions requiring operative reduction, one splenic artery thrombosis and one persistent hypertension.
Conclusions: RPT is an uncommon tumor in childhood, primarily presenting in infant. Majority of the tumors are benign. Preoperative evaluation by CT scan and/or MRI of anatomical distortions is mandatory to manage the complexity of surgical resection. Complete excision is the cornerstone of treatment.

P-104

IMPROVING SURVIVAL IN EXTRACRANIAL GERM CELL TUMOR IN A DEVELOPING COUNTRY: CHILDREN'S HOSPITAL LAHORE EXPERIENCE

A. Ahmad[1], N. Asghar[1], A.W. Rathore[1], M. Faizan[1], A.S. Ali[1]

[1]Paediatric Oncology, Children's Hospital & ICH, Lahore, Pakistan

Objectives: Children's Hospital Lahore is a tertiary government centre providing the free cancer treatment to over 500 new cancer patients per year. The purpose of this study was to analyze the outcome of children with Extracranial GCT and to discuss the role of multidisciplinary team management and social support to improve the survival in a developing country.
Methods: Retrospective review of 80 patients enrolled between January 2011 – January 2014 was done. Data regarding their age, site, stage, histopathology, risk stratification, AFP levels, treatment, outcome and impact of MDT approach was analyzed. Patients were treated according to UKCCSG GC 2005 04 protocol.
Results: A total of 80 patients with age ranging from< 1-12 years (60% <5 yrs) were included. M: F Ratio was 1:2.2. The HPE showed predominance of yolk sac tumor 30/80 (38%) followed by mature teratoma 18/80 (23%), dysgerminoma 7 (9%) MMGCT 5 (6%), JGCTO 4 (5%), Immature 4 (5%) unspecified 12 (15%). 39/80 (49%) presented with stage IV,30 (38%) with stage III and 11 (13%) at stage II. Gonads 32/80 (40%) were the most common site followed by SCCT 23/80 (29%) abdominal 20/80 (25%) Head & Neck 3/80 and thorax 2/80 (2%). AFP level >10,000 found in 36/80 (45%) p-value-0.002. Total 53/80 (66%) have completed treatment, 4/80 (5%) are on treatment, 6/80 (8%) LAMA and 15/80 (19%) expired due to metastatic and progressive disease. 9/15 (60%) expiries were in SCCT group 9/23 (40%). Two patients (2.5%) relapsed after completed therapy.77 events were noted with 39/77 (50%) in stage IV Patients and 28/77 (37%) in stage III patients, p-value = 0.012. Efficient MDT utilized in 50/80 (63%) cases reducing the LAMA rate from 19% to 8% (comparing with 2011 SIOP DATA).
Conclusions: Survival is fair 53/80 (66%) for the whole group and 51/53 (96%) for the treated group. Mortality of 19% can be reduced by early management and infection control strategies. The prognosis can significantly be improved by public awareness to seek early treatment and establishing multidisciplinary team approach and effective social support especially for the SCCT group.

ICCCPO (PARENT/SURVIVORS)

P-105

NATIONWIDE AWARENESS-RAISING ACTIVITIES FOR INTERNATIONAL CHILDHOOD CANCER DAY BY CHILDREN'S CANCER ASSOCIATION OF JAPAN (CCAJ) IN 2014

T. Kawaguchi[1], A. Katayama[1], K. Nonomura[1], K. Okabe[1]

[1]Secretariat, Childrens Cancer Association of Japan, Tokyo, Japan

Objectives: Children's Cancer Association of Japan (CCAJ) is a non-profit organization founded in 1968 through desperate efforts of two parents who have lost their children due to cancer. On or around the International Childhood Cancer Day (ICCD) this year, CCAJ and its nationwide 18 branches implemented an enlightening campaign together to let the ordinary public know that even children have chances to suffer from cancer through handing out our campaign cards, which include such statement as "early detection is very important to save children with cancer" with showing Early Warning Signs.
Methods: CCAJ defined the period between February 1 and March 14 as the dates for the campaign. As for the tools for the campaign, we prepared 40,000 campaign cards and 900 original blue T-shirts with a yellowish logo of "International Childhood Cancer Day 2014". Those T-shirts were distributed in exchange for donations. Also, we prepared 20,000 pieces of original pocket tissue with the description of CCAJ's contact lists. CCAJ announced the campaign for ICCD 2014 and its specific schedules to our members, government offices, hospitals, public health centers, business corporations and so on by means of our bulletin, website, and weblog. Our activities for the campaign were also released to the national and local media.
Results: As for the tools for the campaign on ICCD 2014, we handed out about 30,000 campaign cards and 20,000 pieces of original pocket tissue, and distributed 850 T-shirts.
Conclusions: We could strengthen our teamwork between CCAJ headquarters and its branches through our activities for the campaign on around ICCD. Also, we could share the importance of "awareness of childhood cancer" not only with our branch members but also with the third parties involved for the campaign, i.e. government offices, hospitals, public health centers, business corporations, and volunteers.

P-106

HISTORICAL FOCUS ON CHILDHOOD CANCER SURVIVORS, 1960-2014: LONGEVITY, AWARENESS AND NEW APPROACHES

R. Rohrer[1]

[1]Humanities, Seton Hill University, Greensburg, USA

Objectives: To construct an overview of the historical development of childhood cancer survivorship from the 1960s and the first numbers of long term survivors to the present time. The study explores how survival issues changed as survival rates increased.
Methods: The author has consulted the archives of the National Cancer Institute, the National Library of Medicine. the National Institutes of Health Library and the archives of the Memorial Sloan Kettering Cancer Center. Personal accounts from childhood cancer survivors and their families as well as letters and articles authored by them are the primary source for the study. In the period since 1990 patient and family interviews were also a key source.
Results: From the 1960s to present a more focused, organized and proactive approach has been taken by medical and psycho social teams to provide 'cure of the whole child.' With the advance of supportive therapy and rehabilitation therapies diverse late effects in their are more often being identified in developed countries. In the United States, the focus of this study, more emphasis is being placed upon the role of the internist or family physician's role in providing follow up care to former pediatric cancer patients. Self awareness of long term effects are also a mission of the Children's Oncology Group, and the American Medical Association.
Conclusions: The identification of long term effects from childhood cancer and its treatment is a problem that only came about from the success of of therapy first in childhood leukemias

in the 1960s and the evolution of effective multi modal therapies for most cancers in children by the 1990s. There is still a great need for the support of childhood cancer survivors as they age through adulthood. These efforts continue to be needed not only for medical assessment and disease prevention but psycho socially as well.

P-107

THE TOGETHER SERIES: THERAPEUTIC STORIES FOR CHILDREN AND FAMILIES

M. Mccarthy[1], P. Dearn[2], S. Morse[3], K. Peters[4], M. McGowan[4]

[1]Clinical Sciences, Murdoch Childrens Research Institute, Melbourne, Australia; [2]Children's Cancer Centre, Royal Children's Hospital, Melbourne, Australia; [3]Speech Pathology, Royal Children's Hospital, Melbourne, Australia; [4]Children's Cancer centre, Royal Children's Hospital, Melbourne, Australia

Objectives: This project involved the development of a series of children's books designed to assist children to manage the physical and emotional impact of childhood cancer treatment, hospitalisation and the transition period following treatment.
Methods: A series of five story books were written by a parent of a young child undergoing leukaemia treatment to assist her child's adaptation to the cancer experience and in particular the end-of-treatment period. Topics include coping with hair loss, addressing fears of returning to school, attempting new activities, adapting to fewer hospital visits and understanding parental reactions to end of treatment. Both the individual stories and concept of the series were collaborated on by a family therapist, speech pathologist, play therapist and the author and an additional book was added for children to write their own story. A brief was sent to the illustrator outlining the therapeutic intention of each story. A formal evaluation of the books was undertaken with 26 participants: 6 children, 4 parents, 1 grandparent, 6 health professionals (5 psychologists, 1 social worker) and 9 teachers. The books were evaluated for their relevance, usefulness and creative appeal, using a specifically developed survey.
Results: Overall approval rating for the books from health professionals, parents and children was high, with the books assessed as most relevant to children aged 2-9. Specific comments were examined for editing purposes and two additional books directly addressing children's broader experiences of hospitalization were developed as a result. Philanthropic funding enabled publication of the books.
Conclusions: Cancer treatment and transitioning to end of treatment are well recognised as highly stressful times for children and families. Despite this, resources particularly for young children are limited. These books offer a creative and relevant resource for parents, enabling them to help their child adjust and potentially find their own stories to tell.

P-108

PERCEPTION OF CHILDHOOD CANCER: PARENTAL ASSESSMENT

A. Srivastava[1], T. Thomas[1], B. Singh[1], A. Singh[1], S. Sapra[1], R. Seth[1]

[1]Pediatrics, ALL India Institute of Medical Sciences, Delhi, India

Objectives: The aim of the study to assess the parents' psychological adjustment, hospitalization problems, behavioral changes in children, financial problems and concern about child health and hygiene.
Methods: The sample of the study consisted of 50 parents whose children (age 2-10years) were undergoing treatment for acute leukemia. The questionnaires were made by investigator in local language (Hindi) for the assessment of parental adjustment about cancer.
Results: Most parents were unaware of cancer prior to diagnosis. Majority of children present with fever. 88% of parents suffer from depression and anxiety. 44% of parents found it difficult to get investigations done in the hospital.50% of patients faced financial problems and mental stress was seen in most. 64% have knowledge about government funding schemes but 52% have problem in documents preparation. 98% of parents were concerned about their child's hygiene. During treatment 58% noticed that their child's behavior had changed. In 33% the life of parents also changed due to child's illness. Siblings of patients also faced problem as 38% of parents are not able to give proper attention. 72% of family did not get any emotional and financial support from relatives.
Conclusions: In this study we found that parents experience high level of anxiety and depression at the time of diagnosis. The investigation and hospitalization affect their daily routine and also affects the siblings.

P-109

A DONOR FOR BELOVED BROTHER

A.A.A. Manullang[1], A. Manullang[1]

[1]The Indonesian Anyo Foundation, Yayasan Anyo Indonesia, Jakarta Barat, Indonesia

Objectives: to share, inspire and encourage other siblings willing to be a donor for their brother/sister with cancer in the family.
Methods: My name is Andri Astarisanna. I am the second child in the family. My brother suffered leukemia since he was 11 years old and I volunteered to be his donor before he finally passed away in 2008. I was only 14 years old when they found out my blood was the one matched to his blood, therefore I was chosen to be the donor. My younger sister also included to be the other candidate for the donor, in the end i was the best option to give my stem cell to my brother. The procedure was quite hard and new for me as of the first time i thought that they were going to take my bone marrow and then they explained me that they had achieved a new method, however I was brave and strong enough until the end of the procedure.
Results: Parents are usually looking for the other candidates outside the core family to be the donor, sometimes because if they choose another siblings to be the donor, it seems that they 'sacrifice' another child to do it. But for some other reasons it was easier, because then the procedure can be part of 'supporting' other sibling with cancer, reduce the risks and errors, also creates a tighter bond in the family.
Conclusions: Although then my brother still had to go, it was indeed a valuable and memorable experience.

P-110

HELP DESK FOR HEMATO-ONCOLOGICAL DEPARTMENT IN CROATIAN CHILDREN HOSPITAL

L. Vuletic[1], S. Pasa[1]

[1]Oncology, Children's Hospital Zagreb, Zagreb, Croatia

Objectives: On average this disease occurs in 118 children in Croatia per year, which means that there is a child diagnosed with cancer every other day. Around 120 children are treated for cancer every year in the Children's Hospital in Zagreb. Inadequate access to information about the rights of the parents and the children regarding various fields. Dispersion and unavailability of information. Difficult psychological and emotional state of parents, who do not know who or how to ask for help and support
Need to organize a single, one-stop information point
Support to the parents and the children through assistance about their rights as well as active involvement in helping the parents exercise their rights.
Information about child treatment with cooperation and support from the Hospital's professional staff.

Methods: To set up a one-stop point providing full and up-to-date information regarding various issues. Setting up parents' meetings with the medical staff and meetings with the persons from various government institutions and services essential for exercising many of their rights. Organization of group support to the parents and the children, conducted by experts. Creative and educational workshops. Organizing and carrying out various activities and events to help the children and their families through the difficult times

Results: We raised public awareness through many medias about malignant disease; We are facilitated the work of medical staff; We raised the active life quality of children and families; We provideed better integration of children and teenagers with reduced abilities in the public and social life. There were 210 help desk users in 2013.
Conclusions: This unit is very helpfull to integrate problems on one place for better solutions of solving them.

LATE EFFECTS

P-111

CHILDHOOD CANCER SURVIVORS OF BONE TUMORS AND SARCOMAS ARE AT AN INCREASED RISK OF HOSPITALIZATION

C. Gonzalez[1], L. Randall[2], J. Ying[3], A. Kirchhoff[1]

[1]Cancer Control and Population Sciences Research Program, University of Utah Huntsman Cancer Institute, Salt Lake City, USA; [2]Department of Orthopedics and Sacroma Services, University of Utah Huntsman Cancer Institute, Salt Lake City, USA; [3]Family and Preventive Medicine, University of Utah, Salt Lake City, USA

Objectives: Identify if childhood cancer survivors of malignant bone tumors and sarcomas are at an increased risk of hospitalization.
Methods: Using data from population-based research resources in Utah, we identified all childhood and adolescent survivors of malignant bone tumors (N = 97) and sarcomas (N = 63) who were diagnosed from 1973-2005 and were ≥five years from diagnosis. We selected a birth year and sex matched comparison cohort (N = 946). Hospitalizations from 1996-2010, excluding pregnancy and delivery, were determined from discharge records. Multivariable Cox, Poisson and Gamma regressions were used to evaluate risk of hospitalization, admission counts, and length of stay for survivors versus the comparison cohort. Estimates for bone tumors and sarcomas were aggregated since regression estimates were similar except where reported.
Results: Average follow-up since 1996 for survivors was 13.5 years (SD = 8.7) and for the comparison 14.0 years (SD = 9.1) (p = 0.1). The hazard ratio (HR) of any hospitalization was higher for survivors than the comparison cohort (HR = 1.58, 95% confidence interval (CI) 1.18-2.12). Survivors experienced a higher hospital admission rate (rate ratio (RR) = 2.33, 95% CI 2.04-2.67, $p < 0.001$) than the comparison cohort. Length of stay was longer for hospitalized survivors (RR = 1.32, 95% CI 1.17-1.50, $p < 0.001$) compared to the cohort. When sarcomas and bone tumors were examined separately, sarcoma survivors had a higher rate of hospital admissions (RR = 2.01, 95% CI 1.67-2.43, $p < 0.001$). Bone tumor survivors experienced an even higher hospitalization rate (RR = 2.92, 95% CI 2.40-3.55, $p < 0.001$) in reference to the comparison cohort.
Conclusions: The number ofhospitalizations, rate of admissions, and lengths of stay are elevated among childhood cancer survivors of bone tumors and sarcomas. Childhood cancer survivors tend to receive less survivorship-focused health care the further they are from their diagnosis. Efforts to prevent and manage sarcoma and bone tumor survivors' health problems in outpatient settings could help reduce their hospitalization risk.

P-112

BONE FRACTURE IN PEDIATRIC AND ADOLESCENT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM PROJECT REACH AT DANA-FARBER CANCER INSTITUTE (DFCI)

L.M. Vrooman[1], J.E. Blackmon[1], L.B. Kenney[1], L.B. Silverman[1], C.J. Recklitis[1], L. Diller[1]

[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: Skeletal toxicities are recognized as serious complications of therapy for childhood cancer, but the occurrence of bone fracture in these survivors is infrequently described. This study assessed the prevalence of and risk factors for the development of fracture in a cohort of pediatric and adolescent survivors of childhood cancer.
Methods: Parents of 190/200 (95%) participants in Project REACH, a prospective cohort study of childhood cancer survivors, completed questionnaires reporting the occurrence of fracture. Medical records were reviewed for treatment and health outcome data. Cancer diagnoses included: acute lymphoblastic leukemia (32.1%), neuroblastoma (22.6%), Wilms tumor (11.6%), sarcoma (11.6%), lymphoma (9.5%), acute myelogenous leukemia/ myelodysplastic syndrome (5.3%), hepatoblastoma (2.6%), other (4.7%). Median age at enrollment was 12.4 years (range = 6.0-18.0) and median time since diagnosis was 8.4 years (range = 2.1-17.8).
Results: Sixty-nine post-cancer treatment fractures were reported in 46 survivors (24%). 16/ 46 survivors (35%) experienced ≥1 fracture (10 survivors with 2 fractures, 5 with 3, and 1 with 4). Median time from completion of therapy to first fracture was 3.8 years (range 0.02-13.6 years). Therapy-directed corticosteroid exposure was associated with increased frequency of post-treatment fracture; 32% (27/84) of survivors who received corticosteroid experienced fracture compared with 18% (19/106) of those who did not receive corticosteroid (OR 2.2, 95%; CI 1.1-4.3, p = 0.026). Survivors treated with dexamethasone had a higher frequency of fracture (37%) compared with survivors without corticosteroid exposure (p = 0.017). Fractures occurred in 28% of survivors exposed to other steroids not including dexamethasone, but this proportion was not significantly different from the no steroid group (p = 0.15).
Conclusions: Almost a quarter ofchildhood cancer survivors experienced fracture after cancer therapy. Exposure to corticosteroid was associated with an increased frequency of post-treatment fracture. These data suggest that a treatment-associated fracture risk may extend beyond cancer therapy completion.

P-113

ELECTROCARDIOGRAPHIC ABNORMALITIES IN AGING SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST. JUDE LIFETIME (SJLIFE) COHORT STUDY

D. Mulrooney[1], E. Soliman[2], G. Armstrong[3], V. Joshi[4], D. Green[3], K. Srivastava[5], M. Krasin[6], R. Luepker[7], L. Robison[3], M. Hudson[1], K. Ness[3]

[1]Oncology and Epidemiology/Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [2]Epidemiological Cardiology Research Center, Wake Forest University School of Medicine, Winston-Salem, USA; [3]Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [4]Pediatrics, University of Tennessee Health Science Center, Memphis, USA; [5]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA; [6]Radiological Sciences, St. Jude Children's Research Hospital, Memphis, USA; [7]Epidemiology and Community Health, University of Minnesota School of Public Health, Minneapolis, USA

Purpose/Objective: Electrocardiographic (ECG) abnormalities, whether major or minor, are predictive of poor prognosis and provide a simple tool for cardiovascular risk assessment. We evaluated prevalence and determinants of ECG abnormalities among adult childhood cancer survivors (CCS).
Materials and Methods: This analysis included 2,706 participants of the SJLIFE cohort (51% male, 15.6% non-white, mean age 8.3 ± 5.6 yrs. at diagnosis and 32.4 ± 8.3 yrs. at evaluation). ECGs were recorded using standardized methods and centrally reviewed at an ECG core laboratory blinded to medical history. Abnormalities were classified into major and minor per the Minnesota ECG Classification. Frequencies were assessed and log-binomial regression models; adjusted for age, sex, race, BMI, and smoking; were used to estimate relative risk (RR) and 95% confidence intervals (CI) for patient and treatment characteristics.
Results: At least one ECG abnormality was identified in 63.7% of participants, 10.8% major, 52.9% minor. The most common major abnormalities were major isolated ST-T abnormalities (7.2%), evidence of myocardial infarction (3.6%), and left ventricular hypertrophy with strain pattern (2.8%). Highest frequencies were among Hodgkin lymphoma (20.2%), Wilms tumor (16.3%), and osteosarcoma (14.8%) survivors. Frequency of major and minor abnormalities by treatment was: chest radiation (RT) 21.7% and 53.7%; anthracyclines 7.6% and 52.6%; and chest RT+anthracylines 17.6% and 55.6%. In adjusted models, risk of major and minor abnormalities was associated with chest RT [RR = 1.57 (CI, 1.33-1.85) and RR = 1.07 (CI, 1.02-1.12)], male sex [RR = 1.16 (CI,1.01-1.38) and RR = 1.07 (CI,1.02-1.12)], and BMI < 18.5 mg/m^2 [RR = 1.49 (CI,1.01-2.25) and RR = 1.07 (CI,1.01-1.23)] but not anthracycline exposure ≥ 300 mg/m^2 [RR = 1.12 (CI, 0.89-1.42) and RR = 1.01 (CI, 0.94-1.09)]. Increasing age (5-year increments) was associated with major abnormalities (RR = 1.05 CI, 1.01-1.11).
Conclusions: ECG abnormalities are common in CCS; nearly two-thirds had at least one abnormality, suggesting a high risk for cardiovascular disease. The risk is highest among those exposed to chest directed RT.

P-114

THE IMPACT OF RADIATION, CARDIOVASCULAR RISK FACTORS AND PHYSICAL ACTIVITY ON ENDOTHELIAL PROGENITOR CELLS AMONG CHILDHOOD CANCER SURVIVORS

K. Pradhan[1], L. Overmyer[1], S. Aranjo[1], J. Mund[2], J. Case[2], S. Gupta[3], Z. Liu[4], J. Renbarger[1], V. Champion[5]

[1]Pediatric Hematology-Oncology, Indiana University School of Medicine, Indianapolis, USA; [2]Neonatology, Indiana University School of Medicine, Indianapolis, USA; [3]Medicine, Indiana University School of Medicine, Indianapolis, USA; [4]Biostatistics, Indiana University School of Medicine, Indianapolis, USA; [5]Nursing Research, Indiana University School of Nursing, Indianapolis, USA

Objectives: The relative-risk of atherosclerotic cardiovascular disease (ACVD) is elevated in childhood cancer survivors (CCS) secondary to cancer-therapies causing vascular endothelial impairment. Novel biomarkers of endothelial inflammation analyzed from the peripheral blood (PB) may aid in identifying CCS at risk for future ACVD. These biomarkers include the bona fide endothelial progenitor cells, termed endothelial colony-forming cells (ECFCs), that are essential for vascular homeostasis and repair, as well as, apoptotic mature circulating endothelial cells (CECs). The purpose of this study was to analyze ECFCs and CECs from the PB of CCS using a novel multi-parametric flow-cytometry protocol.
Methods: In this cross-sectional study we compared Cardiovascular Risk Factors (CRFs), quality of life measures, diet, physical-activity (PA), brachial-artery flow-mediated dilatation (FMD), a measure of endothelial function, and ECFCs and CECs between CCS and age and body-mass index matched healthy controls (HC). In addition, we investigated the effect of

cancer therapies on FMD, ECFCs, and CECs and the associations between these measures and CRFs, PA and diet.
Results: We enrolled 24 CCS, 17 with a prior diagnosis of leukemia. The CCS had significantly lower physical functioning and PA, worse diet, higher fatigue and lower high-density cholesterol (HDL-C) compared to HC (all $p < 0.05$). There was no difference in FMD, ECFCs and CECs between CCS and HC. Within the CCS cohort, those with any radiotherapy (RT) had significantly lower ECFCs and CECs (both $p = 0.02$). In addition, significant positive correlations included, HDL-C with FMD and PA with ECFCs while significant negative correlations included systolic blood-pressure with ECFCs (all $p < 0.05$).
Conclusions: This study involved CCS showing that ECFCs are affected by cancer-therapies, such as RT, further worsened by CRFs such as hypertension and life-styles with inadequate PA. Altering these modifiable risk-factors can potentially improve vascular health to prevent future ACVD.

P-115

ELECTRORETINOGRAPHY AND VISUAL EVOKED POTENTIALS IN CHILDHOOD BRAIN TUMOR SURVIVORS

S. Pietilä[1], A. Mäkipernaa[2], H.L. Lenko[3], A.M. Koivisto[4], S. Oja[3], T. Pietilä[5], R. Korpela[3]

[1]Department of Pediatrics, Rinnekoti Foundation, Espoo, Finland; [2]Department of Hematology, Cancer Center Helsinki University Central Hospital, Helsinki, Finland; [3]Department of Pediatrics, Tampere University Hospital, Tampere, Finland; [4]Tampere School of Public Health, University of Tampere, Tampere, Finland; [5]Department of Neurology, Hatanpää Hospital, Tampere, Finland

Objectives: To evaluate clinical value of electroretinography (ERG) and visual evoked potentials (VEP's) in childhood brain tumor survivors.
Methods: A total of 104 primary brain tumor patients diagnosed below 17 years of age between 1983 -1997 were treated in Tampere University Hospital. Of the 80 survivors 75 potentially eligible patients were invited to participate in this population-based cross-sectional study. Fifty-two (69%) participated and were examined at a mean age of 14.2 years (range 3.8-28.7 years) after a mean follow-up time of 7.5 years (1.5-15.1 years). A flash ERG and a checkerboard reversal pattern VEP or a flash VEP were done.
Results: Abnormal ERG in one and bilaterally delayed abnormal VEP's were obtained in 22/51 (43%) cases. VEP's were abnormal in all patients with chiasmatic, hypophyseal or pineal tumor location and in most patients with hypothalamic tumor location, but the tumor location in the visual pathway was not associated with abnormal responses ($p = 0.567$). Nine out of 25 (36%) patients with infratentorial tumor location had abnormal VEP's. Age at diagnosis ($p = 0.358$), follow-up time ($p = 0.400$), chemotherapy ($p = 0.765$), radiotherapy ($p = 0.565$), combined therapies ($p = 0.743$), hydrocephalus ($p = 0.568$), shunt revisions ($p = 1.000$) and antiepileptic medication ($p = 1.000$) were not associated with abnormal VEP's.
Conclusions: Abnormal ERG's are rarely observed, but abnormal VEP's are common and indicate damage in the visual pathway. The fact that the VEP's are bilaterally delayed suggests a general toxic/adverse effect on the visual pathway, which is possibly multifactorial. ERG and VEP tests may have both clinical and scientific value while evaluating long-term effects of childhood brain tumors and tumor treatment.
Acknowledgements: The authors thank the participants and their families, the personnel of the Department of Clinical Neurophysiology, and Juha Välimäki, MD, PhD, of the Department of Ophthalmology of Tampere University Hospital. The study was supported by The Väre Foundation for Pediatric Cancer Research.

P-116

EXPERIMENTAL FERTILITY PRESERVATION (FP) INTERVENTIONS IN PRE-PUBERTAL (PP) BOYS WITH CANCER: A REPORT ON PREFERENCES OF TEENAGE CANCER SURVIVORS, PARENTS, AND PROVIDERS

A. Lorenzo[1], R. Donen[1], L. Sung[2], K. Boydell[3], D. Stephens[4], C. Portwine[5], S. Pritchard[6], S. Hadipour-Lakmehsari[2], K. Lo[1], A. Gupta[2]

[1]Urology, University of Toronto, Toronto, Canada; [2]Pediatrics, University of Toronto, Toronto, Canada; [3]Psychiatry, University of Toronto, Toronto, Canada; [4]Public Health Sciences, University of Toronto, Toronto, Canada; [5]Pediatrics, McMaster University, Hamilton, Canada; [6]Pediatrics, University of British Columbia, Vancouver, Canada

Objectives: Risk of infertility from cancer therapy is a source of great distress for young cancer survivors. FP can be a challenge in PP males who are unable to produce bankable sperm through ejaculation. We sought to determine factors influencing patient, parental and provider preferences for testicular biopsy (TBx) even though the utility of PP tissue for FP remains experimental.
Methods: Oncology providers, parents, and teenage cancer survivors were recruited from 3 pediatric centers in Canada. During participant interviews and surveys, a hypothetical decision was made between TBx and no TBx. Willingness to accept complications, costs, risk of infertility, chance of technology developing and desire to help others were used to measure strength of preference for TBx. Multiple regression was used to associate predictors with TBx desirability scores (under risk of infertility condition).
Results: The proportion of respondents who preferred TBx (vs no TBx) were: 110/153 (72%) parents, 22/30 (73%) providers, and 52/77 (67%) cancer survivors. The top ranked factor influencing decisions for all groups was risk of infertility. Survivors ranked rate of complications and cost lower and desire to 'help others' higher compared to parents ($p < 0.005$). All 3 groups had similar strengths of preference for TBx compared to no TBx when risks of infertility and chance of technology developing were varied. Child age, type of cancer, ethnicity, or hospital were not significant factors associated with preference for TBx, but parents who reported a higher income were more likely to prefer TBx ($p = 0.05$).
Conclusions: Parents, survivors, and providers strongly favor TBx and ranked risk of infertility as most important in decision-making. Parental income was the only predictor of preferences under the risk of infertility condition. Addressing the costs associated with FP should remain an important focus of advocates for FP.

P-117

OVARIAN TISSUE CRYOPRESERVATION IN PEDIATRIC ONCOLOGY: A GAMBLE ON THE FUTURE

F. Chambon[1], A. David[1], F. Brugnon[1], J.L. Pouly[1], L. Janny[1], A.S. Gremeau[1], E. Merlin[1], F. Deméocq[1], J. Kanold[1]

[1]CRCTCP, CHU Estaing, Clermont-Ferrand, France

Objectives: Because of a significant improvement in the survival of children and adolescents with cancer, fertility preservation has to be a major concern for paediatric oncologists. The aim of our study was to report all our ovarian tissue cryopreservation's (OTC) cases in order to specify the interest and indications of this method and to study the clinical and hormonal outcome in females.
Methods: From September 2000 to September 2013, 36 females had an OTC in our center. Eight patients had no malignant disease and 28, a malignant disease. After informed consent, the surgical ovarian collection consisted in the biopsy of a third of each ovary by laparoscopy which was frozen by a slow cooling protocol. A histological analysis and a follicular account were performed.
Results: Among our 36 patients, OTC's indications were 13 auto-SCT, 19 allo-SCT and 4 sterilizing chemotherapy. Ovarian tissue harvest was performed by intraumbilical laparoscopy using a 3 to 7-mm laparoscop. Two 3 to 10-mm trocars were used. No major postoperative complications occurred excepted for one patient with sickle cell disease and protein S deficiency who had a severe haemorrhage of one ovary. The following chemotherapy regimens were not delayed and started at a median range of 10 days [1-81] after OTC. The anatomopathologic analysis showed 10 primordial follicles/mm^2 [0-83] and no malignant cells in any ovarian tissues. The median follow-up after harvest was 29 months [0-111], 21 females were alive in complete remission, 1 was still on treatment and 10 died. Hormonal results were evaluable for 26 patients with a median age at 17 yrs [5-26] and 14 were in premature ovarian failure.
Conclusions: Feasibility of OTC with sample of a third of each ovary seems to be an appropriate method before transplantation with no consequences on therapeutic program for children to preserve potentially fertility.

P-118

DISEASES OF RENAL FUNCTION AND BONE METABOLISM IN LONG-TERM FOLLOW-UP FOLLOWING TREATMENT OF EARLY-ONSET CANCER. A REGISTRY-BASED STUDY.

M. Grönroos[1], N. Liuhto[2], N. Malila[3], L. Madanat-Harjuoja[3], J. Matomäki[4], P. Lähteenmäki[1]

[1]Pediatrics, Turku University Hospital, Turku, Finland; [2]Faculty of Medicine, University of Turku, Turku, Finland; [3]Epidemiology, Finnish Cancer Registry, Helsinki, Finland; [4]Biostatistics, University of Turku, Turku, Finland

Objectives: Constant progress in cancer therapy has led to a growing number of early-onset cancer survivors who are prone to increased morbidity owing to the late-effects of their anticancer therapy. The aim of this study was to investigate pediatric and young adult cancer survivors' morbidity on renal diseases and on diseases of bone metabolism in a registry setting in a population-based level.
Methods: The patient cohort was identified from the Finnish Cancer Registry, and consisted of 13,860 5-year-survivors of cancer diagnosed below the age of 35. Their siblings without early-onset cancer were identified from the central population register and were used as the control cohort. Information on their morbidity on renal diseases and on diseases of bone metabolism was collected from the national hospital discharge registry and was used to assess hazard ratios for various outcomes. The patient cohort was separated into two age groups, pediatric (age at cancer diagnosis 0-19 years) and young adults (age at cancer diagnosis 20-34 years).
Results: Significantly elevated hazard ratios compared to the controls were observed in the following outcomes: scoliosis HR 1,6 (95% CI 1,3-2,0), osteoporosis HR 5,2 (95% CI 2,4-11,4), osteonecrosis HR 12,7 (95% CI 5,4-29,7), nephritis HR 1,9 (95% CI 1,5-2,2) and kidney failure HR 3,6 (95% CI 2,4-5,3), $p < 0,0001$ for all. All of the mentioned hazard ratios were significantly elevated in both diagnostic age groups. The hazard ratio for obesity was elevated

in the pediatric age group for females HR 3,4 (95% CI 1,6-7,2) and for all survivors of CNS tumors HR 2,8 (95% CI 1,4-5,7).
Conclusions: Survivors of pediatric and young-adult cancers are at increased risk for several long term adverse outcomes, and this must be taken into account in their follow-up. Our study provides new population-based information on the early-onset cancer survivors' morbidity on renal diseases and on diseases of bone metabolism.

P-119

RENAL LATE EFFECTS AFTER TREATMENT OF UNILATERAL NON-SYNDROMIC WILMS TUMOR

S. Kostel Bal[1], B. Yalcin[1], H. Susam Sen[1], B. Aydin[1], A. Varan[1], T. Kutluk[1], C. Akyuz[1]

[1]Pediatric Oncology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Objectives: Due to the improvement in prognosis and increase in survival rates the long term renal consequences in Wilms tumor patients are of greater concern. We aimed to investigate the long term effects of treatment on survivors of non-syndromic unilateral Wilms tumor.
Methods: A total of 45 unilaterally nephrectomized survivors of Wilms tumor treated and followed at our center were enrolled in the study. After the second year following the cessation of treatment; glomerular filtration rate (GFR), urinary protein excretion, urinary ß2 microglobulin levels and blood pressure were assessed as well as general health status and quality of life. Results were analyzed for correlation with clinical variables, chemotherapy and radiotherapy as possible risk factors.
Results: At a median follow-up time of 8.7 years (mean:10.9, range: 2.3-35.4 years), none of the patients included in the study developed end-stage renal disease (ESRD). During the follow-up, 6/45 (13.3%) patients had any of the renal problems; hypertension, proteinuria or tubulopathy. None of the patients had increased urinary ß2 microglobulin levels. Compensatory hypertrophy was observed under ultrasound in 31 patients (72%). Median maximum bipolar length was significantly higher in patients diagnosed after the age of 36 months. 10/45 (23%) and 3/45 (7%) of the patients were hypertensive at the time of diagnosis and study, respectively. Median GFR values were significantly lower at the time of diagnosis. Although at the time of the study all patients had normal GFR values; with longer follow-up intervals, especially after 10 years, a significant declining trend in GFR was observed ($p = 0.004$).
Conclusions: Although the risk of developing ESRD is remarkably low in non-syndromic unilateral Wilms tumor, a group of less serious but progressive renal dysfunction is of concern. Detailed analysis of renal functions should be performed during the long term regular follow-up.

P-120

LONG TERM AUDIOLOGIC OUTCOMES IN CHILDREN TREATED WITH PLATINUM CHEMOTHERAPY

K. Knight[1], J. Middaugh[1], R. Fu[2], E. Neuwelt[3], C. Winter[4]

[1]Pediatric Audiology, Oregon Health and Science University, Portland, USA; [2]Public Health and Prevetative Medicine Emergency Medicine, Oregon Health and Science University, Portland, USA; [3]Neurology Neurosurgery Veterans Affairs Medical Center, Oregon Health and Science University, Portland, USA; [4]Oregon Clinical and Translational Research Institute, Oregon Health and Science University, Portland, USA

Objectives: Childhood cancer survivors treated with platinum chemotherapy appear to be at risk for progressive hearing loss after treatment. The purpose of this study was to evaluate the prevalence and severity of delayed-onset and progressive hearing loss, to evaluate the time course of hearing changes after treatment, and identify possible risk factors.
Methods: A retrospective cohort study of children and adolescents treated with platinum chemotherapy at Oregon Health and Science University was conducted. Inclusion criteria included treatment with cisplatin and/or carboplatin, an end-of-therapy audiologic evaluation within 6 months after the final platinum treatment, and at least one long term follow-up hearing evaluation (LTFU) 12 months or more after completion of platinum therapy. Progressive hearing loss was defined as a $\geq$20 dB decrease in pure tone threshold (s) at LTFU relative to the end-of-treatment evaluation. Severity of hearing loss was graded according to the SIOP Boston hearing loss grades.
Results: 128 patients with various cancer diagnoses met inclusion criteria. 92 were treated with cisplatin, 18 with carboplatin, and 17 with both agents. 52 also received cranial radiation prior to cisplatin. 85 (66%) of patients had ototoxic hearing loss at completion of chemotherapy. Mean length of time from the end-of-treatment hearing evaluation to the most recent post-treatment evaluation was 3.6 years (range 0.6-15.8). Of patients with ototoxicity at the end of therapy, 23/85 (27%) exhibited progressive hearing loss at LTFU. Three medulloblastoma patients had normal hearing at the end of treatment, but had delayed-onset hearing loss at LTFU. Variables including diagnosis, age at treatment, length of LTFU, cranial radiation and platinum dose were examined to explore potential risk factors.
Conclusions: Results document the need for long-term audiologic monitoring and management in childhood cancer survivors treated with platinum agents. Strategies to reduce or prevent hearing loss are needed.

P-121

FATIGUE IN CHILDHOOD CANCER SURVIVORS: A REPORT FROM PROJECT REACH

N. Frederick[1], C. Recklitis[2]

[1]Pediatric Oncology, Dana Farber Cancer Institute, Boston, USA; [2]Perini Family Survivors' Center, Dana Farber Cancer Institute, Boston, USA

Objectives: To better understand the prevalence and etiology of fatigue in adolescent and young adult survivors of childhood cancer and how fatigue-associated factors may differ from older childhood cancer survivors.
Methods: Participants were 270 childhood cancer survivors (Mean age 23 yrs; Mean age at dx 8 yrs; 52% female), enrolled in Project REACH, a longitudinal research study. Fatigue was measured using the PedsQL Multidimensional Fatigue Scale, validated in age groups 25 years. Participants 1 standard deviation below the mean of standardized populations were classified as significantly fatigued. Measures also included the PedsQL, SF-12, BDI-Y, and BSI-18.
Results: Thirty-seven participants (14%) reported fatigue, which is not significantly different from population norms. Stratification by age group (25 years) demonstrated similar results, with age not a significant predictor of fatigue, however a trend of increased fatigue with age was noted ($p = 0.076$). Fatigue cases were associated with poor QoL (PedsQL and SF-12; $p < 0.001$) and poor mental health functioning (BDI-Y and BSI-18; p25 population ($p = 0.002$), but not in the
Conclusions: The prevalence of fatigue was lower than expected in this survivor population. Fatigue was highly correlated with psychosocial well-being across all age-groups, underscoring the importance of fatigue assessment to promote optimal adjustment and QoL. While fatigue was closely related to the number of chronic conditions in older adults, this was not seen in adolescents and young adults closer to treatment. These findings may reflect advancements in cancer care aimed at reducing late-effects or delayed onset of late-effects in younger survivors. Ongoing cohort evaluation will help better elucidate the evolution of fatigue in childhood cancer survivors.

P-122

EXERCISE TOLERANCE AND ENERGY EXPENDITURE AMONG ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY.

K.K. Ness[1], M.M. Hudson[2], R.E. Karlage[1], C.H. Pui[2], W. Chemaitilly[3], J.Q. Lanctot[1], K.C. Hale[2], C.L. Wilson[1], L.L. Robison[1], J.P. DeLany[4]

[1]Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [2]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [3]Pediatrics Division of Endocrinology, St. Jude Children's Research Hospital, Memphis, USA; [4]Medicine Endocrinology and Metabolism, University of Pittsburgh, Pittsburgh, USA

Objectives: Adult survivors of childhood ALL are less active than peers. Lean muscle mass deficits and problems with energy expenditure and fitness may explain low activity levels. The aim of this analysis was to evaluate energy expenditure and fitness among ALL survivors and compare them to controls with no cancer history.
Methods: We evaluated total daily (TDEE) and activity (AEE) energy expenditure in 247 ALL survivors and 247 race-, sex-, and age-matched controls, using the doubly labeled water method. Resting energy expenditure (REE) was estimated with indirect calimetry and exercise capacity (VO_2peak) with cardiopulmonary exercise testing. Energy expenditure was compared between groups in general linear models adjusted for total body mass (TBM). Associations between fitness and energy expenditure were also evaluated in linear models adjusted for TBM.
Results: Survivors were 47.3% male, 90.5% white, a median age of 29 (18-44) years, a median of 5 (0-18) years of age at diagnosis, and had survived a median of 23 (11-30) years. Survivors had similar TBM (mean $\pm$ SD: 80.4 ± 21.8 vs. 81.2 ± 22.3 kilograms (kg), $p = 0.72$), but were shorter (167.8 ± 10.2 vs. 171.1 ± 9.2 centimeters (cm)), and had lower lean mass (54.6 ± 13.3 vs. 57.0 ± 13.3 kg, $p = 0.05$) and VO_2peak (23.7 ± 0.4 vs. 26.6 ± 0.4 milliliters/kilogram/minute (ml/kg/min), $p < 0.001$) than controls. After adjusting for fat mass, there were no differences between groups for TDEE (3013.2 ± 35.1 vs. 2973.9 ± 35.0 (kilocalories) kcal), AEE (1295.2 ± 34.4 vs. 1217.4 ± 34.3 kcal), or REE (1416.6 ± 21.8 vs. 1459.2 ± 21.7 kcal). Among survivors a 3.5 ml/kg/min higher VO_2peak was associated with 94.3 ± 23.0 kcal higher AEE ($p < 0.001$) and a 175.8 ± 21.3 kcal higher TDEE ($P < 0.001$). This association was not evident among controls.
Conclusions: Adult survivors of childhood ALL do not appear to have deficits in energy expenditure when TBM is taken into account. Lower than expected exercise tolerance may explain low activity among survivors whose energy expenditure is associated with VO_2peak.

P-123

OBESITY INDEPENDENTLY INFLUENCES GONADAL FUNCTION IN VERY LONG-TERM ADULT MALE SURVIVORS OF CHILDHOOD CANCER

W. van Dorp[1], K. Blijdorp[2], J.S.E. Laven[3], R. Pieters[4], F.H. de Jong[5], S.M.F. Pluijm[4], A.J. van der Lely[5], M.M. van den Heuvel-Eibrink[4], S. Neggers[6]

[1]Paediatric Oncology/Haematology and Obstetrics and Gynaecology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Paediatric Oncology/Haematology and Medicine, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [3]Obstetrics and Gynaecology, Erasmus University Medical Center, Rotterdam, Netherlands; [4]Paediatric Oncology and Haematology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [5]Medicine, Erasmus University Medical Center, Rotterdam, Netherlands; [6]Paediatric Oncology and Haematology and Medicine, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands

Objectives: Although obesity is associated with gonadal dysfunction in the general population, gonadotoxic treatment might diminish the impact of obesity in childhood cancer survivors (CCS). We aimed to evaluate whether altered body composition is associated with gonadal dysfunction in male CCS, independent of gonadotoxic cancer treatment.
Methods: 351 male CCS were included. Median age at diagnosis was 5.9 years (0-17.8); median age at follow-up 25.6 years (18.0-45.8). We studied total/free testosterone, sex hormone-binding globulin, inhibin B and FSH. Potential determinants were BMI, waist circumference, waist-hip ratio and body composition measures (dual energy X-ray absorptiometry).
Results: Free testosterone was significantly decreased in survivors with high BMI (BMI $\geq$30 kg/m^2) (adjusted mean 9.1 nmol/L versus 10.2 nmol/L, P = 0.015), high fat percentage (10.0 versus 11.2, P = 0.004), and high waist circumference (>102 cm) (9.0 versus 11.0, P = 0.020). Survivors with high fat percentage ($\geq$25%) had significantly lower inhibin B/FSH ratios (inhibin B / FSH ratio: ß -34%, P = 0.041).
Conclusions: Obesity is associated with gonadal dysfunction in male CCS, independent of the irreversible effect of previous cancer treatment. Longitudinal studies and randomized controlled trials will be required to evaluate whether weight normalization through diet modification and physical activity or bariatric surgery could improve gonadal function, especially in obese survivors with potential other mechanisms then lifestyle causing their obesity.

P-124

LONG-TERM BRAIN STATUS AND COGNITIVE FUNCTIONING IN CHILDREN TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA WITH HIGH-DOSE CHEMOTHERAPY ALONE OR COMBINED WITH REDUCED CNS RADIOTHERAPY

O. Zajac-Spychala[1], M. Pawlak[2], K. Karmelita-Katulska[3], J. Pilarczyk[1], K. Derwich[1], J. Wachowiak[1]

[1]Department of Pediatric Oncology Hematology and Transplantology, Poznan University of Medical Sciences, Poznan, Poland; [2]Department of Neurology and Cerebrovascular Disorders, Poznan University of Medical Sciences, Poznan, Poland; [3]Department of Neuroradiology, Poznan University of Medical Sciences, Poznan, Poland

Objectives: The aim of study was to assess the long term consequences of CNS prophylaxis in children treated due to ALL according to ALL IC-BFM 2002 (high-dose chemotherapy alone vs high-dose chemotherapy combined with prophylactic CNS radiotherapy reduced to 12 Gy).
Methods: Seventy-eight children aged 6.3-21.4 years with ALL treated between 2002-2010 were studied, including 34-treated with chemotherapy, 23-treated with chemo- and radiotherapy, and 21-before treatment (control group). To assess volumetric measurements of subcortical structures responsible for cognitive functioning, volumetric MRI sequences were used. Neuropsychological assessment based on battery neuropsychological tests.
Results: In both groups treated due to ALL, with or without CNS radiotherapy, significantly smaller volumes of hippocampus (p = 0.027), amygdala (p = 0.007), putamen (p = 0.002) and globus pallidus (p = 0.001) in comparison to control group were found. In addition, patients treated with CNS irradiation had significantly lower total brain volume as compared to the control group (p = 0.025).
All patients treated for ALL had lower IQ level in both verbal (p = 0.005) and performance scale (p = 0.018) measured by Wechsler Intelligence Scale, worse visual-spatial memory (p = 0.025) via Benton's Visual Retention Test, auditory-verbal memory (p = 0.001) via Verbal Fluency Test and the level of executive functioning (p = 0.001) via Stroop Test and Wisconsin Card Sorting Test, when compared to the control group.
Moreover, patients who received CNS irradiation had lower learning curve (p = 0.002) via Rey Test and worse processing speed (p = 0.026) compared to patients treated with chemotherapy alone and to control group.
Conclusions: In all children treated for ALL according to the ALL IC-BFM 2002 reduction of subcortical structures volumes is observed. In children treated with or without CNS radiotherapy, cognitive deficits in domain of memory and executive functions are found. Children who were irradiated present decrease in learning process probably caused by lower processing speed in this group.
The work supported National Science Centre grant (DEC-2012/05/N/NZ5/00879).

P-125

RADIOTHERAPY RELATED PREMATURE ARTERIAL AGING IN YOUNG ADULT AND ADOLESCENT SURVIVORS OF HIGH RISK NEUROBLASTOMA

A. Vatanen[1], T. Sarkola[2], T.H. Ojala[2], T. Jahnukainen[3], M. Turanlahti[2], U.M. Saarinen-Pihkala[1], K. Jahnukainen[1]

[1]Division of Hematology-Oncology and Stem Cell Transplantation, Children's Hospital University of Helsinki Helsinki University Central Hospital Finland, Helsinki, Finland; [2]Division of Cardiology, Children's Hospital University of Helsinki Helsinki University Central Hospital Finland, Helsinki, Finland; [3]Division of Transplantation, Children's Hospital University of Helsinki Helsinki University Central Hospital Finland, Helsinki, Finland

Objectives: The aim of the study was to evaluate arterial morphology and function in the Finnish national cohort of very long term survivors (>10 years) of high risk neuroblastoma (NBL) treated with high-dose chemotherapy and autologous hematopoietic stem cell transplantation with or without total body irradiation (TBI).
Methods: Common carotid, femoral, brachial and radial artery morphology was assessed with very-high resolution ultrasound (25-55 MHz), and carotid artery stiffness and brachial artery endothelial function were evaluated with conventional vascular ultrasound in 19 adult or pubertal (age 22.7 $\pm$ 4.9 years, range 16-30) NBL survivors transplanted during 1984-1999 at the mean age of 2.5 $\pm$ 1.0 years, and compared with 20 age- and sex- matched healthy controls. Cardiovascular risk assessment included history, body-mass index, fasting plasma lipids and glucose, and 24h ambulatory blood pressure (BP).
Results: The NBL survivors had consistently smaller arterial lumens, increased carotid intima-media thickness (IMT), plaque formation (N = 3) and carotid stiffness compared with the controls. Survivors displayed higher plasma triglyceride and cholesterol levels, increased heart rate, and increased systolic and diastolic BP's. Multiple regression analysis identified TBI (N = 10) and a low body surface area as independent predictors for decreased arterial lumen size and increased IMT. Plaques occurred only among survivors who had received TBI.
Conclusions: Adolescent and young adult high risk NBL survivors treated with TBI display signs of premature arterial aging.

P-126

SUPPORTING THE ACADEMIC NEEDS OF PEDIATRIC CANCER SURVIVORS: A MODEL OF CARE

L. Northman[1], M. Morris[1], S. Ross[1], N. Ullrich[2], P. Manley[3]

[1]Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, USA; [2]Neurology, Boston Children's Hospital, Boston, USA; [3]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: The study objective was to evaluate the effectiveness of a model of psychoeducation, consultation, and advocacy provided by a School Liaison Program (SLP) for families and schools of children whose cancer-related diagnosis or treatment involved the central nervous system compared to a control group of parents of children at risk for neurocognitive deficits based on a diagnosis of Neurofibromatosis type 1 (NF1) who did not receive school-based services.
Methods: After IRB approval, a survey was completed by parents of school-aged children demonstrating academic difficulties associated with their medical diagnosis. Surveys were sent to 125 families of pediatric cancer survivors who received psychoeducation and consultation through the SLP and to the control group of 125 families of children with NF1. The responses of intervention (SLP) and control (NF1) groups were compared using a Wilcoxon rank-sum test.
Results: Ninety-three surveys were returned from the SLP group (74%) and 81 from the NF1 group (65%). Results demonstrated between-group differences in parents' belief that children are meeting academic potential, with parents who received SLP services reporting greater satisfaction with their child's progress, better understanding of learning needs, and an increased ability to access school supports (p = 0.02. 0.003, and 0.096, respectively). In addition, parents of children with longer SLP involvement (> 3 years) had better parental understanding (P = 0.02) and ability to advocate (P = 0.04) than parents of children who had less than 1 year of SLP services. Finally, when the SLP clinician came to patients' schools, there was better parental understanding, better ability to advocate, less difficulty accessing services and greater belief in the child's ability to meet academic potential (p = 0.04,0.03,0.04, and 0.004, respectively).
Conclusions: The consultation, psychoeducation, and parental advocacy training provided by the School Liaison Program improves parent-reported knowledge of special education supports, satisfaction with children's school services, and increased belief that children are meeting their academic potential.

P-127

RISK AND PATTERNS OF UTILIZATION OF COMMUNITY CARE AND MENTAL HEALTH SERVICES AMONG CHILDHOOD, ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS IN BRITISH COLUMBIA, CANADA

M. McBride[1], D. Li[1], K. Goddard[2], S. Pritchard[3], S.R. Rassekh[3], S. Sheps[4]

[1]Cancer Control Research, British Columbia Cancer Agency, Vancouver, Canada; [2]Division of Radiation Oncology, British Columbia Cancer Agency, Vancouver, Canada; [3]Division of Oncology Hematology and Bone Marrow Transplant, British Columbia Children's Hospital, Vancouver, Canada; [4]School of Population and Public Health, University of British Columbia, Vancouver, Canada

Objectives: The CAYACS (Childhood, Adolescent and Young Adult Cancer Survivorship) program examines multidimensional survivorship issues though linkage of clinical data to population-based administrative databases that contain outcome information. This study describes utilization of home and community care (HCC) and mental health (MH) services among a population-based cohort of 5-year survivors of cancer diagnosed before age 25, in British Columbia, Canada.
Methods: Demographic and clinical records of 5-year survivors diagnosed under age 25 years between 1970 and 1999, identified from the provincial cancer registry, were linked to provincial HCC and MH service records from 1990 to 2004. A comparison group was randomly selected from the provincial health insurance plan registry, frequency-matched by birth year and gender. Frequencies and proportions of services for survivors and comparators were calculated and compared.
Results: There were 500 of the 3,425 survivors (14.6%) who had a HCC client record on file, compared to 2.5% of their comparators, a 5.8-fold difference. Survivors showed higher registration rate for each type of HCC service (direct care and long term care (LTC)). Among those who had a client record on file, HCC service utilization by type varies between survivors and the population comparators. 483 of the 500 HCC registered survivors (96.6%) had received direct care services, compared to 743 of the 753 (87.1%) HCC registered comparators. 11.6% of the HCC registered survivors had received LTC care advice; compared to 16.4% of HCC registered comparators. Utilization of MH services showed a different pattern than for HCC. The use of MH services among cancer survivors is only slightly higher than their peers (12.4% vs.%9.2).
Conclusions: CAYAC survivors showed much higher HCC utilization overall than their non-cancer peers, but were only slightly more likely to use MH services. Adult survivors of childhood and AYA cancer require continual surveillance for long-term morbidities.

P-128

MILITARY SERVICE IN MALE SURVIVORS OF CHILDHOOD BRAIN AND SOLID TUMORS

P. Lähteenmäki[1], R. Ahomäki[1], A. Harila-Saari[2], J. Matomäki[3], T. Remes[4], K. Parkkola[5]

[1]Pediatric Hematology and Oncology, Turku University Hospital, Turku, Finland; [2]Pediatric Hematology and Oncology, Karolinska Hospitalet, Stockholm, Sweden; [3]Pediatrics, Turku University Hospital, Turku, Finland; [4]Pediatric Neurology, Oulu University Hospital, Oulu, Finland; [5]Huolto-osasto, Finnish Defence Forces/Merivoimien Esikunta, Turku, Finland

Objectives: The aim of this study was to examine the acceptance of childhood solid and brain tumor (BT) survivors to the still mandatory military service in Finland, how the conscripts perform in the physical and cognitive tests during the service, and what is the level of military education in childhood cancer survivors compared to healthy controls.
Methods: Male survivors of childhood BT and solid tumors, born from 1960 to 1992, and alive at the age of 18 years (call-up age) (N = 1143) were identified from Finnish Cancer Registry. From the Population Registry, five age, sex and place of residence matched controls were identified (N = 5714). Information on call-up decisions and military service of the study subjects was collected from the databases of Finnish Defence Forces.
Results: Enlistment frequency was 55% in Hodgkin lymphoma, 35% in BT, 55% in neuroblastoma, 13% in malignant bone tumors, 56% in soft tissue sarcomas, and 68% in kidney tumors. Treatment with irradiation ($p < 0.001$) and older age at cancer diagnosis ($p = 0.04$) affected the military fitness category. Interruption of service occurred to same extent in survivors and controls. The level of military education did not differ between groups. On average, enlisted solid tumor survivors managed physical tests and training similarly as controls. Only performance in standing long jump was worse ($p = 0.005$). Enlisted BT survivors had slightly poorer physical performance than controls ($p = 0.05$), both in Cooper running test ($p = 0.011$) and in general muscle strenght ($p = 0.023$). Solid tumor survivors managed well in cognitive tests, but BT survivors had a decline in all tested cognitive skills. Irradiation treatment did not explain the findings.
Conclusions: Frequency of enlistment was still quite low for cancer survivors. Proportion of those completing service and the level of military education, however, resembled those of controls. Our data give valid information for discussions with cancer survivors preparing for military call-ups.

P-129

TRANSITIONING CHILDHOOD CANCER SURVIVORS TO ADULT CARE: A SURVEY OF PEDIATRIC ONCOLOGISTS

L.B. Kenney[1], P. Melvin[2], L. Fishman[3], J. O'Sullivan-Oliveira[4], G.S. Sawicki[3], S. Ziniel[2], L. Diller[1], S.M. Fernandes[5]

[1]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA; [2]Program for Patient Safety and Quality, Boston Childrens Hospital, Boston, USA; [3]Department of Medicine, Boston Childrens Hospital, Boston, USA; [4]Department of Surgery, Boston Childrens Hospital, Boston, USA; [5]Department of Pediatrics, Lucile Packard Childrens Hospital at Stanford, Palo Alto, USA

Objectives: Pediatric oncologists are challenged with transitioning adult childhood cancer survivors to adult-focused care. This study describes transition practices, perceived barriers to transfer, and identifies potential areas for intervention.
Methods: An electronic survey of U.S. members of the Children's Oncology Group; 492/1449 responded (34%) and 347/492 (71%) met eligibility (pediatric oncologist caring for outpatients age > 11 years).
Results: Of the 347 respondents, 50% are male, median years practicing 10 (range 5-22), and 37% practice at a free-standing children's hospital. Almost all care for patients up to age 21 years (96%), 42% report care of patients over age 25 years, and only 16% over age 30 years. While 89% of oncologists report having other staff provide transition education to their patients, 66% report also providing this education to their patients themselves. Compared to the 147 (42%) caring for adult patients >25 years, those who do not were more likely to endorse specific criteria for transfer including survivors' age ($p = 0.006$), pregnancy ($p = 0.014$), marriage ($p = 0.010$), college graduation ($p = 0.006$), and substance use ($p = 0.036$). Most oncologists identified barriers to transfer including patients'/parents' attachment to provider (91%), lack of knowledgeable adult providers (86%), cognitive delay (81%), and unstable social situation (80%). Oncologists who care for patients age >25 years are more likely to perceive parents' attachment to provider ($p = 0.037$) and unstable social situation as barriers to transfer ($p = 0.044$). Four themes emerged from 75 responses to an open ended question inviting further input on transition/transfer practices: importance of standardized transition practices, need for flexible transfer criteria, lack of adult providers with survivorship expertise, and lack of resources.
Conclusions: Most pediatric oncologists report transferring adult childhood cancer survivors to adult care and providing transition education to their patients. Transition practices that include education for adult providers, and address survivors' psychosocial challenges might further facilitate successful transfer.

P-130

SECONDARY CANCERS AFTER CANCER DIAGNOSIS IN CHILDHOOD: A HOSPITAL-BASED RETROSPECTIVE COHORT STUDY IN JAPAN

Y. Ishida[1], D. Qiu[2], M. Maeda[3], J. Fujimoto[4], H. Kigasawa[5], R. Kobayashi[6], M. Sato[7], J. Okamura[8], S. Yoshinaga[9], T. Rikiishi[10], H. Shichino[11], C. Kiyotani[12], K. Kudo[13], K. Asami[14], H. Hori[15], H. Kawaguchi[16], H. Inada[17], S. Adachi[18], A. Manabe[19], T. Kuroda[20]

[1]Pediatric Medical Center, Ehime Prefectural Central Hospital, Matsuyama, Japan; [2]Drug Dependence Research, National Center of Neurology and Psychiatry, Tokyo, Japan; [3]Pediatrics, Nippon Medical School, Tokyo, Japan; [4]Epidemiology and Clinical Research Center for Children's Cancer, National Center for Child Health and Development, Tokyo, Japan; [5]Hematology, Kanagawa Children's Medical Center, Yokohama, Japan; [6]Pediatrics, Sapporo Hokuyu Hospital, Sapporo, Japan; [7]Hematology/Oncology, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka, Japan; [8]Pediatrics, National Kyushu Cancer Center, Fukuoka, Japan; [9]Research Center for Radiation Protection, National Institute of Radiological Science, Chiba, Japan; [10]Pediatrics, Tohoku University School of Medicine, Sendai, Japan; [11]Pediatrics and Child Health, Nihon University School of Medicine, Tokyo, Japan; [12]Oncology, National Center for Child Health and Development, Tokyo, Japan; [13]Hematology and Oncology, Shizuoka Children's Hospital, Shizuoka, Japan; [14]Pediatrics, Niigata Cancer Center, Niigata, Japan; [15]Pediatrics, Mie University Graduate School of Medicine, Mie, Japan; [16]Pediatrics, Hiroshima University Hospital, Hiroshima, Japan; [17]Pediatrics, Kurume University School of Medicine, Kurume, Japan; [18]Human Health Sciences, Kyoto University School of Medicine, Kyoto, Japan; [19]Pediatrics, St. Luke's International Hospital, Tokyo, Japan; [20]Pediatric Surgery, Keio University School of Medicine, Tokyo, Japan

Objectives: The objectives of current study are to assess the incidence and risk factors for secondary cancers (SC) in children with malignancies through a nationwide survey in Japan.
Methods: A retrospective cohort study comprising 10,069 children with cancer who were treated between 1980 through 2009 were conducted in 15 Japanese hospitals. The cumulative incidence rate of SC was calculated using competing risk as death and compared by Gray method. The standardized incidence rate ratio (SIR) was defined as the ratio of the number of observed divided by the number of expected cancers using the regional cancer registry data in Japan. The risk factors were analyzed using Cox regression analysis.
Results: One-hundred twenty-nine SC patients (1.3%) were identified in the cohort with a median follow-up of 8.4 years (2 months to 30 years) with total 77,151 person-years observation. The most common SC were acute myeloid leukemia (n = 29) followed by myelodysplastic syndrome (n = 23), brain tumors (n = 17), sarcoma (n = 15), adult-type carcinoma (n = 15), thyroid cancer (n = 12), lymphoid malignancy (n = 7) and others (n = 11). The cumulative incidence rate was 1.1% (95%CI, 0.9-1.4) at 10 years and 2.6% (95%CI, 2.1-3.3) at 20 years after the diagnosis, respectively. The sensitivity analysis limited to 10 years or longer duration survivors (n = 3,155) confirmed these low incidence rates. The SIR of SC was 12.6 (95% CI, 10.5-14.9). In Cox analysis, the hazard ratios for SC were 3.98 in retinoblastoma (95%CI, 1.98-10.0), 3.02 in bone and soft tissue sarcomas (95%CI, 1.57-5.84), 2.27 in allogeneic stem cell transplantation (95%CI, 1.47-3.50), respectively.
Conclusions: The cumulative incidence rate of SC in Japan was not high but SIR was relatively high. Allogeneic stem cell transplantation, and retinoblastoma or sarcoma as a primary cancer were significant risk factors for SC.

LIVER TUMOURS

P-131

DE NOVO MUTATION OF RB1 IN MONOZYGOTIC TWINS WITH HEPATOBLASTOMA

C. Bozkurt[1], F. Trippel[2], T. Kanmaz[3], K. Acarli[3], I. Leuschner[4], G. Sahin[5], T. Schwarzmayr[6], D. Von Schweinitz[2], T.M. Strom[6], R. Kappler[2]

[1]*Pediatric Hematology-Oncology, Dr. Sami Ulus Research and Training Hospital of Women's and Children's Health and Diseases, Ankara, Turkey;* [2]*Pediatric Surgery, Dr. von Hauner Children's Hospital Ludwig-Maximilians-University, Munich, Germany;* [3]*Organ Transplantation Center, Sisli Memorial Hospital, Istanbul, Turkey;* [4]*KielInstitute of Paidopathology Pediatric Tumor Registry, Christian-Albrechts-University, Kiel, Germany;* [5]*Pediatric Hematology-, OncologyDr. Sami Ulus Research and Training Hospital of Women's and Children's Health and Diseases, Ankara, Turkey;* [6]*Institute of Human Genetics, Helmholtz Zentrum München Neuherberg and Technische Universität München, Munich, Germany*

Objectives: Hepatoblastoma (HB) is the most common malignant liver tumor in childhood and characterized by ß-*catenin* mutations in about 80% of patients. However, the genetic basis of the remaining cases still remains elusive. We aimed at identifying genes that caused early-onset HB development in a pair of monozygotic twins lacking *ß-catenin* mutation.
Methods: Genomic DNA of liver tumor tissue and peripheral blood was analyzed by exome sequencing and subsequent Sanger verification. Blood from the parents and the unaffected brother was analyzed as a control. Transcript variants were disclosed by reverse transcription PCR and gel electrophoresis.
Results: Using whole-exome sequencing, we found a heterozygous single nucleotide exchange at the splice-site of intron 21-22 of the *retinoblastoma 1* (*RB1*) gene in a pair of monozygotic twins who developed HB at the age of 8 months. This mutation was detected both in the patients' tumor and blood samples, but was absent in the parents and the unaffected brother, indicating a *de novo* occurrence either in the germ cell of one of the parents or the fertilized egg. On the RNA level, the splice-site mutation gave rise to transcripts skipping exon 21 and/or 21/22, which were expressed in parallel to the wild-type transcript. The patients are alive and disease free eight months after liver transplantation and now closely monitored for retinal pathologies.
Conclusions: This is the first study reporting a point mutation affecting *RB1* integrity in HB. These data advocate the screening of *ß-catenin*-unmutated HB patients for *RB1* mutations.

P-132

INTRAOPERATIVE DETECTION OF MICRO-SIZED PULMONARY METASTASES OF HEPATOBLASTOMA USING INDOCYANINE GREEN FLUORESCENT IMAGING

N. Kitagawa[1], M. Shinkai[1], K. Mochizuki[1], H. Usui[1], H. Miyagi[1], Y. Tanaka[2], M. Tanaka[2], H. Goto[2], M. Kusano[3], S. Otsubo[4]

[1]*Department of Surgery, Kanagawa Children's Medical Center, Yokohama, Japan;* [2]*Department of Pathology, Kanagawa Children's Medical Center, Yokohama, Japan;* [3]*Department of Surgery, Kushiro Rosai Hospital, Kushiro, Japan;* [4]*Department of Oral and Maxillofacial Surgery, Kushiro Rosai Hospital, Kushiro, Japan*

Objectives: We previously demonstrated that thorough surgical resection of the pulmonary metastatic lesions improves the prognosis of patients with hepatoblastoma. We have introduced intraoperatively indocyanine green (ICG) fluorescent imaging to visualize non-palpable small lesions in 2011. We herein present the usefulness of this modality to complete a thorough resection.
Methods: Five patients with hepatoblastoma associated with multiple lung metastases underwent metastasectomy guided by this method. Their age ranged from 1 to 6 years old. Intraoperative ICG fluorescence imaging was done as follows: ICG (0.5mg/kg) was administered intravenously 24 hours before the operation. Through a thoracotomy, a fluorescent detector combined with an infrared ray radiator (Photodynamic Eye^{R}, Hamamatsu Photonics, Japan) was used to visualize metastatic lesions. All resected lesions were examined histopathologically, and some lesions were examined by a fluorescent microscope specifically made for ICG fluorescence observation. The size of lesions was measured by a microscope.
Results: Thirty-seven lesions in total were detected as fluorescent-positive and resected. Among them, 11 were CT-negative and 5 were non-palpable. All lesions were diagnosed as hepatoblastoma histopathologically. The smallest diameter of the lesion was 0.062mm. On the other hand, 7 fluorescent-negative and palpable lesions were also resected. All of these lesions were diagnosed as benign histology. Fluorescent microscopy revealed that the fluorescence was observed in the cytoplasm of the tumor cells, and in a case, small blood thrombus was also detected as an origin of fluorescence.
Conclusions: Our results suggested ICG fluorescence imaging was valuable for identifying CT-negative or non-palpable micro-sized pulmonary lesions. But we should pay attention to possibility of false positive originating from thrombus.

P-133

HISTOPATHOLOGICAL STUDY OF PRE- AND POST-CHEMOTHERAPEUTIC HEPATOBLASTOMA FOCUSING ON THE SIGNIFICANCE OF IMMATURE-LOOKING CELLS

M. Tanaka[1], M. Yoshida[1], R. Ijiri[1], H. Goto[2], N. Kitagawa[3], M. Shinkai[3], Y. Tanaka[1]

[1]*Department of Diagnostic Pathology, Kanagawa Children's Medical Center, Yokohama, Japan;* [2]*Department of Oncology, Kanagawa Children's Medical Center, Yokohama, Japan;* [3]*Department of Surgery, Kanagawa Children's Medical Center, Yokohama, Japan*

Objectives: Comparative histopathological study on hepatoblastoma of pre- and post-chemotherapy has not been carried out sufficiently. Degrees of post-chemotherapeutic histological alternation differ in each case. A subset of hepatoblastomas contain so called 'immature-looking cell' (ILC), described by Zimmermann, which consist of small round cells with marked nuclear expression of beta-catenin and low proliferative activity. However, significance of ILC has not been yet clarified. We verified the histopathological correlation of pre- and post-chemotherapy, and the property of ILC in hepatoblastoma.
Methods: Fourteen hepatoblastomas with pre-chemotherapeutic biopsied specimens and post-chemotherapeutic resected specimens, were collected from archives of our institute. Histological subtype and presence of ILC for pre-chemotherapeutic specimens, and histological pattern of residual tumor and the ratio of necrosis/fibrosis/osteoid for post-chemotherapeutic specimen, were reviewed. Immunohistochemical study were performed for beta-catenin, LEF1, hepatocyte specific marker, AFP, DLK1, glypican-3, and Ki67.
Results: Histological diagnosis of biopsied specimens included one fetal subtype, eleven combined fetal and embryonal type, and two mixed epithelial and mesenchymal type (MEM). Among 14 cases, 5 biopsied specimen, including two MEM, contained foci of ILC (ILC+). Among 5 ILC+ cases, four contained osteoid in the post-chemotherapy specimen, and the remaining one showed extensive fibrosis. In addition, foci of squamous epithelia were observed after chemotherapy in 2 ILC+ cases. Osteoid was also observed in 6 of 9 post-chemotherapeutic ILC- cases. Ratio of necrosis/fibrosis/osteoid area in the tumor after chemotherapy was more than 90% in three (all ILC+ cases), 50%-90% in six (2 ILC + cases), 10%-50% in four, and less than 10% in one.
Conclusions: The results suggested that ILC might be related to the histological alternation including mesenchymal differentiation and/or necrosis/fibrosis, deviating from hepatic cells.

P-134

IMPROVING SURVIVALS OF HEPATOBLASTOMA IN DVELOPING COUNTRIES -A CASE SERIES FROM INDIA

S. Siddaiahgari[1], D. Makadia[1], H. Jayaram[2], C. Vvs[2], R. Kancharla[2]

[1]*Pediatric Hematology-Oncology, Rainbow Childrens Hospital, Hyderabad, India;* [2]*Pediatric Surgery, Rainbow Childrens Hospital, Hyderabad, India*

Objectives: To describe overall survival rates of children managed with hepatoblastoma at tertiary care Children's Hospital in India
Methods: Eighteen children who were diagnosed with hepatoblastoma, in the age group of 2 months to 10 years from October 2007 to 2013 March were analysed. It is 3 years prospective and 2 nad half years retrospective descriptive study.
Results: Majority of patients were between 2 months to 2 years of age (13/18). 10/18 are females. Most common presenting symptom (15/18) was abdominal distention. Two cases were picked up during vaccination visit. None of them had syndromic association. All underwent ultrasound as initial investigation followed by CT abdomen & chest, along with bone scan. Renal functions, liver function, clotting were assessed along with alfa fetoprotein (AFP) levels. AFP was elevated in 16/18 cases, in the range of 44,000 to 5 lakhs. Two had normal AFP levels. Out of 18, 5 had inoperable tumors and 13had gone through the surgery. Before surgery they received 4 to 6 cycles chemotherapy PLADO (Cisplatin and Doxorubicin) followed by tumor excision through lobectomy. Post op chemotherapy 2-3 cycles given as per AFP levels. All children who had gone through surgical resection are off treatment in the range of 4.2 yrs to 1 year, overall survival is 72%. Out of 5 children with inoperable tumor one child is alive 1.7 years off chemotherapy. Two died secondary to relapsed tumor after initial response. Two died with progressive tumor.
Conclusions: Hepatoblastoma is chemosensitive tumor, results are good even in developing countries when surgery is combined with chemotherapy and good supportive care.

P-135

RHABDOID TUMORS OF THE LIVER: REPORT OF 5 PEDIATRIC CASES TREATED AT A SINGLE INSTITUTE.

M. Cornet[1], G. de Lambert[1], F. Guérin[1], V. Fouquet[1], S. Franchi-Abella[2], C. Guettier[3], H. Martelli[1], S. Branchereau[1]

[1]*Pediatric Surgery, Bicetre hospital, Le Kremlin Bicetre, France;* [2]*Pediatric Radiology, Bicetre hospital, Le Kremlin Bicetre, France;* [3]*Pathology, Bicetre hospital, Le Kremlin Bicetre, France*

Objectives: Rhabdoid tumors (RTs) of the liver are rare, aggressive and non-secreting malignancies mainly occurring during the first year of life. The definition of RT is histological and relies on characteristic morphology and on the inactivation of the hSNF1/INI1 tumor suppressor gene which encodes a subunit of the SWI/SNF chromatin remodeling complex. The aim of this study was to analyze clinical data, treatments and outcomes in our patients.
Methods: We report retrospectively the cases of 5 patients treated in our institution for RT of the liver between January 2007 and December 2013. Examined variables included age at diagnosis, tumor stage, variable treatment and long-term survival.

Results: Median age at diagnosis was 6 months (range: 4-23). Four patients had diagnosis by percutaneous biopsy and one by laparoscopic biopsy. All patients presented a loss of INI1 expression. Normal or minimally increased serum AFP levels were observed in all patients. No patient presented metastasis at diagnosis. Median follow up was 9 months (range: 9-80). All patients received chemotherapy, with variable regimens, completed by surgical treatment. Two patients (40%) died of disease. They both were mistaken for non secreting hepatoblastomas at diagnosis and had recurrence shortly after completion of treatment. Three patients (60%) are long-term survivors. All of them received multimodal therapy including chemotherapy according to protocol EpSSGNRSTS with doxorubicin and complete surgical removal of the tumor performed within 3 months after diagnosis. One patient had adjuvant radiotherapy.
Conclusions: According to our results, search of INI1 mutation in non secreting hepatoblastomas is mandatory to exclude RT. Chemotherapy with doxorubicin and an aggressive and early surgical treatment seems justified to improve long term survival.

LYMPHOMAS

P-136

PD1+ CELLS IN PEDIATRIC CLASSICAL HODGKIN LYMPHOMA IS ASSOCIATED WITH BETTER OUTCOME

M. Barros[1], P. Segges[2], R. Hassan[2], G. Niedobitek[1]

[1]Institute for Pathology, Unfallkrankenhaus Berlin, Berlin, Germany; [2]Brazilian National Cancer Institute, Bone Marrow Transplantation Center, Berlin, Germany

Objectives: Classical Hodgkin lymphoma (cHL) is characterized by few neoplastic cells in a background of inflammatory cells. Many studies have described the T cell composition of tumour microenvironment in adult cases and we have demonstrated differences between pediatric and adult cHL in this respect. Two studies recently described that high numbers of PD1+ cells were associated with worse survival in adult cHL. PD1 is a receptor expressed by CD8+ and CD4+ T cells upon activation, as well as by T follicular helper cells, exhausted CD8+ T cells and effector memory CD8+ T cells. The objective of this study was to evaluate PD1+ cells in 100 paediatric cHL cases (3 to 18y, median: 14y).
Methods: PD1+ cells were identified by immunohistochemistry and the numbers of these cells were evaluated using computer assisted microscopical analysis. The results were compared with the other T-cell populations as determined in our previous study of these cases.
Results: A median of 5 PD1+ cells/mm^2 was observed (1 to 363 cells/mm^2), while 40% of cases did not show any PD1+ cell. A direct correlation was observed between the numbers of PD1+ and CD4+ cells ($P = 0.018$), as well as PD1+ and CD8+ cells ($P = 0.02$). Higher numbers of PD1+ cells were observed in cases with cytotoxic microenvironment profile ($P = 0.016$), as disclosed by the ratio TIA1+ cells/FOXP3+ cells > 1.5. The numbers of PD1+ cells were not associated with age group or EBV-status. Cases with higher numbers of PD1+ cells (> 5 cells/mm^2) were associated with better 5-years overall survival ($P = 0.019$).
Conclusions: Our results suggest that the majority of PD1+ cells in the tumour microenvironment of paediatric cHL may contribute to the immune response against the neoplastic cells. A more detailed characterization of these cells is in progress.

P-137

PATHOGENESIS OF PAEDIATRIC LYMPHOMA: POLYCOMB PROTEIN ANALYSIS

M. Ramaglia[1], A. Iannotta[1], V. D'Angelo[1], G. Pecoraro[1], E. Pota[1], C. Fusco[1], M. Di Martino[1], D. Di Pinto[1], M. Oreste[1], C. Indolfi[1], E. Boccieri[1], P. Indolfi[1], F. Casale[1]

[1]Women Child and General Specialized Surgery, Second University of Naples, Naples, Italy

Objectives: Polycomb genes are a set of epigenetic effectors in multimeric repressive complexes. EZH2 is the catalytic subunit of Polycomb repressive complex 2 (PRC2), which methylates histone H3 lysine 27, thereby silencing several tumor-suppressor genes. EZH2 expression is required in the bone marrow for progression of pro-B cells into pre-B cells. Therefore, genetic inactivation of EZH2 leads to an accumulation of cells at the pro–B-cell stage. However, if EZH2 is inactivated after this phase, additional maturation steps are not hindered, suggesting that EZH2 functions early in B-cell differentiation. EZH2 has been reported to harbour a gain-of-function mutation affecting exon 15 that replace the tyrosine 641 (Y641) residue in 22% of diffuse large B-cell lymphomas (DLBCLs) and 7% of follicular lymphomas (Fls) in adult patients. Aim of our study was to evaluate EZH2 expression and Y641 mutation to estimate its role in paediatric patients with Lymphoma.
Methods: We analysed by Real Time PCR and Western Blotting the expression levels of EZH2 in 20 lymph node biopsies of paediatric patients with Hodgkin/non-Hodgkin lymphoma. We have also studied the EZH2/Y641 mutation by Sanger sequencing.
Results: Our analysis revealed one DLBCL paediatric sample with heterozygous Y641N mutation. Furthermore, a significant increase (75%) in EZH2 mRNA was observed in the patients with advanced stages of Hodgkin lymphoma. Protein expression of EZH2 was detected in 45% of the samples, in particular a higher level of expression in the sample with Y641 mutation.
Conclusions: Our preliminary data showed that EZH2 in paediatric lymphomas, to date not yet been analysed, it seems to have a role in the pathogenesis of these cancer. Further investigations to gain better insight into the dependence of cancer growth on EZH2 is warranted, particularly to unravel the complexity of the protein's capacity to induce both pro-oncogenic and tumor-suppressive effects.

P-138

SERUM TARC LEVELS IN A COHORT OF PEDIATRIC PATIENTS WITH HODGKIN LYMPHOMA (HL): A PROMISING BIOMARKER?

E. Schiavello[1], M. Terenziani[1], A. Mazzocchi[2], S. Catania[1], V. Biassoni[1], M. Podda[1], S. Chiaravalli[1], N. Puma[1], L. Bergamaschi[1], M. Casanova[1], A. Ferrari[1], R. Luksch[1], C. Meazza[1], D. Polastri[1], F. Spreafico[1], M. Massimino[1]

[1]Department of Pediatrics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Unit of Transfusion Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Objectives: TARC (thymus and activation-regulated chemokine) is expressed by Hodgkin Reed-Sternberg cells detectable in serum. TARC seems to have a correlation with adult HL prognosis but there are no data published in pediatrics.
Methods: TARC serum level was prospectively tested in 23 consecutive patients, considering pathological level >500 pg/ml, after report on healthy controls: 20 naïve (Group1); 2 at relapse after autologous stem-cell-transplantation (autoSCT) and one primary-refractory (Group2). In group1 TARC samples were collected at diagnosis, after the 2nd cycle, and at treatment end; in group2 every 2 cycles, after auto-alloSCT, and during follow-up. Patients' characteristics were: median age 13 years (range 5-18), stage III-IV 10, B-symptoms 11, bulky disease 13, extranodal involvement 6.
Results: Basal TARC level (median 51223pg/ml) was high in 21/23patients (range 344-184833pg/ml) and significant higher in bulky disease ($p = 0.03$), higher but not significant in Bsymptoms/stage III-IV patients. In Group1only two patients had a normal value at diagnosis (1 with stage IIB nodular/lymphocyte predominant variety, the other with stage IIA classical variety), 18 had a significant decline ($p = 0.0001$) after the 2nd cycle, normalization persisted during follow-up; 1 patient (stage IVB) had a significant decrease without reaching normalization while in CCR. Two primary refractories had TARC increasing (>1000 pg/ml) at relapse as compared to remission values. In Group2 two were monitored for TARC during reinduction: one patient had PD with concomitant increasing TARC, the other had TARC normalization while in PR before subsequent allo-SCT. After transplantation, TARC increased before radiological detection of relapse. The primary refractory patient had TARC decrease correlated with PR status.
Conclusions: This preliminary study shows a correlation between TARC both with some clinical risk factors and radiological response. Our first pediatric series needs to be validated in a larger cohort to confirm the clinical application of TARC monitoring.

P-139

IBRUTINIB SIGNIFICANTLY ALTERS CELL PROLIFERATION AND APOPTOSIS IN BL AND PMBL: IBRUTINIB MAY BE A POTENTIAL ADJUVANT THERAPY IN THE TREATMENT OF BL AND/OR PMBL

T. O'Connell[1], C. Yin[1], M. Barth[2], R. Miles[3], J. Ayello[1], L. Harrison[1], C. van de Ven[1], P. Galardy[4], S. Goldman[5], M. Lim[6], M. Hermiston[7], L. McAllister-Lucas[8], L. Roth[9], S. Perkins[3], S. Lee[1], M. Cairo[1]

[1]Pediatrics, New York Medical College, Valhalla, USA; [2]Pediatrics, University of Buffalo, Buffalo, USA; [3]Pathology, University of Utah, Salt Lake City, USA; [4]Pediatrics, Mayo Clinic, Rochester, USA; [5]Pediatrics, Texas Oncology, Dallas, USA; [6]Pathology, University of Michigan, Ann Arbor, USA; [7]Pediatrics, University of California San Francisco, San Francisco, USA; [8]Pediatrics, University of Pittsburgh, Pittsburgh, USA; [9]Pediatrics and Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, USA

Objectives: BL and PMBL are two common subtypes of B-cell non-Hodgkin Lymphoma in children and adolescents (Miles/Cairo, BJH 2012). Children with relapsed or progressive BL develop chemotherapy-resistant disease and can rarely be cured with salvage therapy (Cairo et al, JCO 2012). Previously, we reported a significant decrease in EFS among pediatric PMBL patients compared with stage III non-PMBL pediatric DLBCL patients following FAB/LMB-96 therapy (Gerrard/Cairo et al, Blood 2013). Bruton's tyrosine kinase (BTK) is a regulator of normal B-cell development and is a component of BCR signaling. Chronic active BCR signaling through BTK activation can be inhibited by the selective and covalent BTK inhibitor, ibrutinib, which recently gained FDA approval in adults with relapsed CLL and MCL. We hypothesize that ibrutinib may be a therapeutic agent in the treatment of BL and PMBL.
Methods: Rituximab-sensitive (Raji, Ramos) and -resistant (Raji 2R) BL cells and PMBL-derived Karpas-1106P cells were exposed to ibrutinib (0-50uM) for 24 hours and evaluated for cell proliferation. Raji, Ramos, and Karpas-1106P were also evaluated for apoptosis and phospho-BTK expression. Ibrutinib was generously provided by Janssen Pharmaceuticals, Inc.
Results: Ibrutinib significantly decreased proliferation in Raji (25uM, 0.622 ± 0.020, $p = 0.0005$, $IC50 = 25.9$uM), Ramos (15uM, 0.418 ± 0.040, $p = 0.015$, $IC50 = 11.59$uM), Raji 2R (50uM, 0.409 ± 0.165, $p = 0.001$, $IC50 = 31.48$uM), and Karpas-1106P (25uM, 0.348 ± 0.035, $p = 0.006$, $IC50 = 16.44$uM) cells vs. control. Significant increases in caspase 3/7 activities were observed in ibrutinib-treated Raji (25uM, 1.477 ± 0.133, $p = 0.013$),

Ramos (15uM, 2.453 ± 0.053, p = 0.008), and Karpas-1106P (25uM, 7.409 ± 1.345, p = 0.008) vs. control. Significant decreases in phospho-BTK expression were observed in ibrutinib-treated Raji (5uM, 0.067 ± 0.009, p = 0.002), Ramos (5uM, 0.127 ± 0.006, p = 0.002), and Karpas-1106P (5uM, 0.166 ± 0.003, p = 0.001) vs. control.
Conclusions: Ibrutinib significantly inhibits cell proliferation in Raji, Ramos, Raji 2R, and Karpas-1106P, and increases apoptosis with a concomitant decrease in phospho-BTK expression in Raji, Ramos, and Karpas-1106P. Ibrutinib may be a potential therapeutic agent in BL and PMBL.

P-140

CHARACTERIZING STANDARDIZED UPTAKE VALUES ON DIAGNOSTIC PET/CT SCANS ACCORDING TO PEDIATRIC LYMPHOMA SUBTYPES

J. Halparin[1], S.R. Rassekh[1], H.R. Nadel[2]

[1]Pediatric Hematology/Oncology, BC Children's Hospital, Vancouver, Canada; [2]Radiology, BC Children's Hospital, Vancouver, Canada

Objectives: ^{18}Fluorodeoxyglucose Positron Emission Tomography / Computerized Tomography (FDG PET/CT) is being used increasingly in pediatric lymphoma for diagnostic staging, assessment of treatment response, and identification of relapsed disease. PET / CT measures tissue metabolic activity in terms of the Maximum Standardized Uptake Value (SUV max). Whether SUV max at diagnosis is related to pathologic subtype of lymphoma is unknown. The purpose of this study was to characterize SUV max in pre-treatment FDG PET/CT scans in pediatric lymphoma according to pathologic subtype.
Methods: This was a retrospective chart review. Subjects included all patients diagnosed with lymphoma at a tertiary children's hospital from 2005 – 2012 who had a PET/CT scan at the time of diagnosis. Data collected for each subject included the initial SUV max and pathologic subtype of lymphoma. Descriptive statistics were used to summarize the data.
Results: A total of 69 subjects were included, with pathologic diagnoses of Hodgkin Lymphoma (HL), Anaplastic Large Cell Lymphoma (ALCL), Burkitt Lymphoma (BL), Diffuse Large B Cell Lymphoma (DLBCL), B-Lymphoblastic Lymphoma (BLL), and T-Lymphoblastic Lymphoma (TLL). The results are as follows:

	Lymphoma pathologic subtype					
	HL	**ALCL**	**BL**	**DLBCL**	**BLL**	**TLL**
Number of subjects	40	3	7	12	2	5
SUV max range	2.2 - 26.8	14.4 - 48.4	13 - 36.8	2.2 - 26.8	2.1 - 5.6	8.2 - 16.4
SUV max mean	8.8	29.3	21.1	16.5	3.9	11.6
SUV max median	11	25.1	16.6	16.1	3.4	11
95% confidence interval	14.4 - 18.5	9.2 - 49.4	14.7 - 27.5	14.4 - 18.5	2.5 - 5.3	9.5 - 12.5

Conclusions: This data suggest that different subtypes of pediatric lymphoma are characterized by different SUV max on pre-treatment FDG PET/CT scans. However, there appears to be significant overlap in ranges of initial SUV max across subtypes. Larger prospective studies are needed to validate this data, and to investigate whether SUV max and change in SUV max with treatment are related to outcomes in pediatric lymphoma.

P-141

OUTCOME OF SPANISH PATIENTS OUTSIDE EURONET-PHL-C1

A. Fernandez-Teijeiro[1], D. Hasenclever[2], A. Echebarria[3], C. Garrido[4], J.L. Vivanco[5], A. Carboné[6], M. Guibelalde[7], I. Rodriguez[8], M. Coronado[9], S. on behalf of SEHOP[10]

[1]Pediatric Oncology Unit, Hospitales Universitarios Virgen Macarena y Virgen del Rocío, Sevilla, Spain; [2]Institut für Medizinische Informatik Statistik & Epidemiologie (IMISE), Universität Leipzig, Leipzig, Germany; [3]Pediatric Onco-Hematology Unit, Hospital Universitario de Cruces, Baracaldo-Vizcaya, Spain; [4]Pediatric Onco-Hematology Unit, Hospital Universitario Gregorio Marañón, Madrid, Spain; [5]Pediatric Onco-Hematology Unit, Hospital Universitario Doce de Octubre, Madrid, Spain; [6]Pediatric Onco-Hematology Unit, Hospital Universitario Miguel Servet, Zaragoza, Spain; [7]Pediatric Onco-Hematology Unit, Hospital Universitario Son Espases, Palma de Mallorca, Spain; [8]Radiotherapy Service, Hospital Universitario La Paz, Madrid, Spain; [9]Nuclear Medicine Service, Hospital Universitario La Paz, Madrid, Spain; [10]Sociedad Española, de Hematología y Oncología Pediátricas, Madrid, Spain

Objectives: In November-2008 Spanish hospitals started accrual to the Euronet-PHL-C1 trial. Due to local difficulties in completing legal requirements some patients from different hospitals were treated outside the trial according to the standard arm and did not benefit from the national pathology review and the central imaging review in Halle for staging and early response assessment.
Objective: Compare outcome of Spanish patients treated outside the trial according to standard arm of Euronet-PHL-C1 trial and those in the trial.
Methods: Patients from Spanish hospitals treated inside Euronet-PHL-C1 trial and those to standard arm of the trial from November 2008 to October 2012. Descriptive statistics. Event free survival Kaplan-Meier estimates. Log-rank test.
Results: From November 2008 to October 2012 103 Spanish patients from 19 hospital entered the Euronet-PHL-C1 trial (C1-Spain), accounting for 5% of the 2018 C1 patients. From September-2008 to October-2013 36 Spanish patients from 10 hospitals were treated according to standard arm (noC1-Spain). Treatment group distribution:C1-Spain, TG1-40 (39%), TG2-24 (23%), TG3-39 (38%); noC1-Spain, TG1-15 (42%), TG2-15 (42%), TG3-6 (16%);other C1: TG1-657 (34%), TG2-431 (22%), TG3-827 (43%). EFS at 36 months for C1-Spain is similar to that of other C1-countries (93 vs 88% p = 0.45). EFS at 36 months for noC1-Spain is lower than C1-Spain (93 vs 78%, p = 0,074).
Conclusions: Outcome of Spanish patients registered into Euronet-PHL-C1 trial is similar to those of other C1-countries. Although numbers are small, understaging may explain the worse outcome trend in Spanish patients treated outside the trial. Participating in prospective international randomized trials with reference pathology and central image review should be encouraged in all Spanish hospitals. National and regional authorities and parents' associations must be made aware of these results in order to facilitate and encourage participation in clinical trials.

P-142

ASSESSMENT OF TREATMENT OUTCOMES AMONG CHILDHOOD ENDEMIC BURKITT LYMPHOMA AT JARAMOGI OGINGA ODINGA TEACHING AND REFERRAL HOSPITAL, KENYA

G.C. Buckle[1], E.O. Mick[2], P. Omollo[3], J. Oyombe[3], D. Omenah[3], J.A. Otieno[4], A.M. Moormann[1]

[1]Department of Pediatrics, University of Massachusetts Medical School, Worcester, USA; [2]Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, USA; [3]Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya; [4]Pediatrics, Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu, Kenya

Objectives: To evaluate clinical characteristics and treatment outcomes of children diagnosed with endemic Burkitt lymphoma (eBL) at Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH), a regional referral center for pediatric oncology in western Kenya, and to identify factors that are associated with long-term survival.
Methods: A retrospective analysis was conducted for children diagnosed with eBL at JOORTH from 2003 - 2011. Patients were treated with a dose-modified cytotoxic regimen including cyclophosphamide, vincristine, adriamycin, prednisone and intrathecal methotrexate. Kaplan-Meier method and multivariate Cox proportional hazards model were used to evaluate survival probabilities and identify prognostic factors. Age, gender, body surface area (BSA), Plasmodium falciparum malaria infection, hemoglobin levels, tumor staging and deviations from recommended cytotoxic dosing were all evaluated.
Results: Four hundred eight-eight children were included in the analysis; 265 (61%) were male. Mean age at diagnosis was 7.5 years. Murphy stage distribution was stage I, 155 (36%); II, 224 (52%); III, 45 (10%); and IV, 9 (2%). Cyclophosphamide, vincristine and methotrexate dosing deviated by >15% of the recommended dose based on BSA in 13%, 12% and 15% of patients, respectively. Overall in-hospital survival was 67% with an average of 52 days on the ward. Tumor stage and cyclophosphamide dosing emerged as independent factors influencing prognosis. Tumor stage of II or higher, and overdosing with cyclophosphamide were both associated with a significantly increased risk of death, with hazard ratios of 1.9 (95% CI 1.2-3.2, p = 0.007) and 3.4 (95% CI 1.4-7.9, p = 0.004), respectively.
Conclusions: Our findings suggest: i) advanced stage of presentation remains a barrier to improving long-term survival among children with eBL, ii) lower doses of cytotoxic agents may be better tolerated in settings with limited supportive care, and iii) insufficient pharmacy and nursing support may contribute to treatment failure, particularly with the administration of complex chemotherapeutic regimens.

P-143

CLINICAL OUTCOME OF CHILDREN WITH ANAPLASTIC LARGE CELL LYMPHOMA WHO UNDERWENT IN POLAND ALLOGENEIC OR AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN YEARS 2000-2013

D. Kulej[1], G. Wrobel[1], N. Adrianowska[2], I. Daniluk[3], E. Dudkiewicz[4], R. Debski[5], K. Drabko[4], E. Gorczynska[1], E. Latos- Grazynska[1], B. Kazanowska[1], E. Kamienska[6], A. Koltan[5], T. Luszawska- Kutrzeba[7], L. Maciejka- Kapuscinska[8], J. Owoc-Lempach[1], M. Rapala[9], M. Ussowicz[1], J. Wachowiak[10], O. Wegner[2], M. Woszczyk[11], O. Zajac- Spychala[10], K. Kalwak[1]

[1]Peadiatric Heamatology Oncology and BMT, Medical University, Wroclaw, Poland; [2]Peadiatric Heamatology and Oncology, Medical University, Lodz, Poland; [3]Peadiatric Heamatology and Oncology, The Children's Memorial Health Institute, Warsaw, Poland; [4]Peadiatric Heamatology Oncology and BMT, Medical University, Lublin, Poland; [5]Peadiatric Heamatology Oncology and BMT, Medical University, Bydgoszcz, Poland; [6]Peadiatric Heamatology and Oncology, Medical University, Szczecin, Poland; [7]Peadiatric Heamatology Oncology and BMT, Polish- American Institute of Pediatrics Jagiellonian University, Krakow, Poland; [8]Peadiatric Heamatology and Oncology, Medical University,

Gdansk, Poland; [9]Peadiatric Surgery, Marciniak Hospital, Wroclaw, Poland; [10]Peadiatric Heamatology Oncology and BMT, Medical University, Poznan, Poland; [11]Peadiatric Heamatology and Oncology, Medical University, Chorzow, Poland

Objectives: Risk of relapse and progression of disease in children with anaplastic large cell lymphoma (ALCL) remains very high (28%). Here we report the clinical characteristics and outcome of patients (pts) with relapsed ALCL, who underwent either autologous or allogeneic haematopoietic stem cell transplantation (HSCT).
Methods: Twenty-seven pts with ALCL were registered in Polish Paediatric Leukemia/ Lymphoma Study Group (PLLSG) in years 2000-2013. 25of them (28,7%) developed relapses during or after the 1st line treatment (7F/18M). Clinical stages: II/4, III/11, IV/10;risk groups: standard/4, high/21. All relapsed pts were treated according to the ALCL-Relapse 2004 protocol. After 2nd or 3rd line of treatment 17pts achieved CR,8pts died of disease progression (DOD). 13pts with relapsed ALCL underwent 15 transplantation: 4/autologous (autoHSCT), 3/matched sibling donor (MSD), 8/matched unrelated donor (MUD), 2pts had to be retransplanted due to relapse after auto-HSCT (1/MUD,1/MSD), the transplantation center were:9/Wroclaw, 6/others: Poznan, Lublin, Bydgoszcz). Median age at HSCT:12.08 years (range3.4-18.8). The source of stem cells were: bone marrow (BM) (n = 2), peripheral blood stem cells (PBSC) (n = 13). Primary conditioning regimen for transplant procedures: auto-HSCT: BEAM (BCNU+VP-16+Melphalan+ARA-C), allogeneicHSCT: MUD/MSD:TBI, Thiotepa+VP-16+/-ATG. ATG was used in all MUD transplant recipients as a GvHD/graft rejection prophylaxis.
Results: All of 13pts engrafted and achieved CR after HSCT,2pts after auto-HSCT relapsed and underwent subsequent allogeneic HSCT. Outcome after 15 HSCT in 13pts: 5pts died due to TRM: 1pt/cardiac and renal dysfunction 26days after HSCT, 3pts/GvHD late posttransplant (6,6.5 and 24 months after HSCT), 1pt/pulmonary aspergillosis 14months after HSCT. 8pts remain alive in CR after HSCT: 7/without any transplant-related complications, 1/chronic GvHD (liver, skin) and pulmonary aspergillosis. 2/4pts after auto-HSCT remain alive in 2nd CR, 2pts relapsed and achieved persistent CR after allogeneicHSCT but died due to TRM.
Conclusions: As the risk of relapse for pediatric ALCL is very high (28%) the use of allogeneicHSCT seems to be a potentially curative option. Reduction of toxicity leading to TRM is essential to improve the overall results of allogeneic HSCT.

P-144

ANESTHETIC MANAGEMENT OF CHILDREN WITH ANTERIOR MEDIASTINAL LYMPHOMAS (AML)

A. Narciso[1], C. Tognon[2], M. Pillon[3], A. Todesco[3], R. Alaggio[4], S. Metrangolo[2], M. Grazzini[2], N. Zadra[2], G. Cecchetto[1], P. Dall'Igna[1]

[1]Pediatric Surgery, University-Hospital of Padua, Padova, Italy; [2]Pediatric Anesthesia, University-Hospital of Padua, Padova, Italy; [3]Pediatric Hematology-Oncology, University-Hospital of Padua, Padova, Italy; [4]Pediatric Pathology, University-Hospital of Padua, Padova, Italy

Objectives: Children with aML may experience serious complications during general anesthesia, due to compression of trachea/bronchi, hearth and main vessels. In our Institution, specific guidelines for anesthesia have been used since 2004 and recognize three groups of patients:
Methods: Groups A (no respiratory symptoms, no compression of trachea/hearth/main vessels): 27 patients Group B (mild respiratory symptoms, no vascular compression, tracheal compression <50%): 15 patients Group C (severe respiratory symptoms and/or vena cava syndrome and/or tracheal compression >50%): 15 patients
Results: Group A. Six, cooperative, underwent supra-clavicular/cervical lymph-node biopsy (CLNb) with local anesthesia (LA); 14, non cooperative, underwent CLNb using mild sedation (midazolam, ketamine, alfentanyl); 2 underwent CLNb and 5 Chamberlein procedure under general anesthesia (GA) with tracheal intubation, spontaneous ventilation, and without using muscle relaxant drugs. Median MMR (mediastinal mass to chest diameter ratio) was 0.36. Group B. Two underwent CLNb with LA; 5 underwent Chamberlein procedure and 1 CLNb under GA as above; 7 had CLNb or trucut of the mass under LA and anxiolytic medications (midazolam): in 2/7, since diagnosis was not obtained, a Chamberlein procedure and CLNb were necessary under GA. Median MMR was 0.42. Group C. Four underwent CLNb, 1 trucut biopsy of the mass, 5 Chamberlein procedure under LA and anxiolytic medications; 4 had CLNb under LA; 1 patient was treated with steroids before the biopsy. In 3 cases, mild episodes of cardiorespiratory breakdown occurred, requiring a change of the patients' position during the procedure. Median MMR was 0.47.
Conclusions: The anesthesiologic risk in patients with aML always needs to be carefully calculated and discussed in a multidisciplinary setting, including children' parents. In our recent experience, since the use of these guidelines, which combine a thorough preoperative assessment, less invasive anesthesiologic methods, whenever feasible, and a possible rapid surgical procedure, we could obtain the correct diagnosis, without severe complications.

MYELOID LEUKEMIAS, MYELODYSPLASTIC SYNDROMES, MYELOPROLIFERATIVE SYNDROMES

P-145

EVALUATION OF AN ESTABLISHED TREATMENT RELATED MORTALITY RISK SCORE FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN IN A SINGLE CENTER OVER A TWENTY YEARS PERIOD

A. Farrag[1], T. Vraetz[1], A.M.J. Peters[1], A. Yoshimi[1], P. Noellke[1], C.M. Niemeyer[1], B. Strahm[1]

[1]Division of Pediatric Hematology and Oncology Department of Pediatrics and Adolescent Medicine, University of Freiburg, Freiburg, Germany

Objectives: Matthes et al. [1] described a risk score for 1year treatment related mortality (1-TRM) after hematopoietic stem cell transplantation in children. Age ≥10 years, advanced disease, and donors other than matched sibling donors (MSD) were characterized as risk factors. We evaluated this risk score in patients transplanted over a 20 year period at our center which is a reference center for myelodysplastic/myeloproliferative syndromes (MDS/MPS) including juvenile myelomonocytic leukemia (JMML).
Methods: Data from 265 consecutive patients transplanted between 1994 and 2011 were analyzed retrospectively.
Results: Median age at transplantation was 8.6 (0.3-21.0) years. Diagnosis included MPS/ MDS (n = 98), other malignancies (n = 88), and non-malignant disorders (n = 79). Most patients received a myeloablative preparative regimen (76.6%), had a matched unrelated donor (62%) and received a bone marrow graft (66%). The 5-year overall survival was 69% (63-75). 1-TRM occurred in 41 (15.5%) patients. 1-TRM was 6.4%, 17.5%, 13.4% and 37.5% for patients with a risk score of 0, 1, 2 and 3, respectively, thus not demonstrating a steady increase of 1-TRM with increasing risk score. However, 1-TRM increased according to the risk score and was comparable to the results of Matthes in the earlier time period (1994-2003). This observation may reflect the decline in 1-TRM in patients transplanted from an unrelated donor due to better HLA-Typing. Due to our center's specialization, several diagnoses, like JMML and advanced MDS were overrepresented. Adapting the risk score by considering these disorders as advanced disease the score system worked well.
Conclusions: The 1-TRM score of Matthes has to be adjusted when patient subgroups are heavily overrepresented in cohorts studied as compared to the reference cohort.
1. Matthes-Martin, S., et al., *Risk-adjusted outcome measurement in pediatric allogeneic stem cell transplantation*. Biol Blood Marrow Transplant, 2008. 14 (3): p. 335-43.

P-146

THE +3010G-G AND +3142C-C HOMOZYGOUS HAPLOTYPES AT THE HLA-G 3' UNTRANSLATED REGION ARE ASSOCIATED WITH DECREASED OVERALL AND EVENT-FREE SURVIVAL IN CHILDHOOD ACUTE MYELOID LEUKEMIA

N. Lucena-Silva[1], R. Santos[1], R.G. Gomes[1], A.M.L. Ramos[2], E.A.V. Marques[2], T.C. Fonseca[2], G.T.N. Diniz[3], F. Pedrosa[2], E.A.V. Donadi[4]

[1]Imunologia, Centro de Pesquisas Aggeu Magalhães-FIOCRUZ, Recife, Brazil; [2]Oncologia Pediátrica, Instituto de Medicina Integrl Professor Fernando Figueira, Recife, Brazil; [3]Laboratório de Métodos Computacionais, Centro de Pesquisas Aggeu Magalhães-FIOCRUZ, Recife, Brazil; [4]Divisão de Imunologia Clinica Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil

Objectives: HLA-G, a major histocompatibility complex class 1b molecule, exhibits immunomodulatory functions with a role in cancer and allotransplantation, but much controversy has arisen regarding its role in leukemia. We aim to evaluate the possible association of the *HLA-G* 3'untranslated region (UTR) alleles with Acute Myeloid Leukemia (AML), to measure soluble HLA-G (sHLA-G) levels in bone marrow of children with AML, and assessed HLA-G features of childhood AML according to overall and event-free survival.
Methods: A hundred and nine consecutive unselected children with AML referred to the Instituto de Medicina Integral Professor Fernando Figueira in Recife, Northeastern Brazil, from 2005 to 2012, were studied. At diagnosis, the leukemia was characterized by blast morphology, phenotyping and genetic abnormalities. Polymorphic sites at the 3'UTR of the *HLA-G* gene were investigated in 97 AML and 91 healthy unrelated children by gene amplification and sequencing. Allelic and genotypic frequencies were estimated using Genepop and Arlekin softwares. sHLA-G was measured in leukemia and normal free-cell bone marrow by ELISA. Statistical analyses were done using R-software.
Results: AML patients were classified into non-APL (n = 76), APL (n = 25) and secondary AML (n = 8). In non-APL, children exhibiting the +3010C-C/+3142G-G diplotype showed a worsened overall survival in relation to those exhibiting the +3010G-G/+3142C-C diplotype ($P = 0.058$; hazard = 2.06; 41% x 24% deaths) and in relation to patients exhibiting the heterozygous +3010C-G/+3142C-G diplotype ($P = 0.051$; hazard = 1.94; 41% x 35% deaths). The majority of AML patients exhibited low bone marrow sHLA-G levels (mean = 120.44 ± 160.21 units/mL and median = 44.16 units/mL). The variance of sHLA-G levels in children exhibiting +3010G-G/+3142C-C homozygous haplotype was different compared with children carrying +3010C-C/+3142G-G or +3010C-G/+3142C-G haplotypes ($P = 0.0098$).
Conclusions: Down regulation of bone marrow' sHLA-G might be involved in childhood AML pathogenesis, and disease outcome.

P-147

CYTOGENETIC PROFILE OF ACUTE MYÉLOBLASTIC LEUKAEMIA IN TEENAGERS AND YOUNG ADULTS: A SINGLE CENTER EXPERIENCE

N. Khoubila[1], M. lamchaheb[1], N. Hda[2], M. Quachouh[1], M. Rachid[1], A. Madani[1], S. Benchekroun[1], A. Quessar[1]

[1]Hematology and pediatric oncology, 20 August Hospital IBN ROCHD University Hospital, Casablanca, Morocco; [2]Biology, Analysis Laboratory HDA, Casablanca, Morocco

Objectives: At present, cytogenetic aberrations detected at the time of acute myeloblastic leukaemia (AML) diagnosis constitute the most common basis for predicting clinical outcome. There have been minimal data on the cytogenetic profile of AML in young adults in low-income countries. The objective was to analyze the cytogenetic characteristics of young patients with the novo AML.
Methods: From 25/1/04 to 1/12/10, eligible patients aged between 15 and 30 years old with de novo AML were included to the AML-MA2003 protocol. Were excluded patients with Acute Promyelocytic Leukemia (APL), secondary AML and AML with myélodysplasia.
Cytogenetic analysis was done at diagnosis. We separate our cytogenetic findings into three broad prognostic categories: favourable, intermediate and adverse*. Treatment included two inductions and two consolidations.
Results: 989 patients with AML were followed in our department. 236 patients were aged between 15 and 30. 24 patients were excluded, 14 had APL. 212 patients with de novo AML were included. AML subtype 2 was the most frequent in 74 (35%) patients. Karyotype was done in 189 (89%) patients and Cytogenetic analysis failed in 8 cases (4%). 23 (11%) patients didn't have a cytogenetic study. There were 181 patients with cytogenetic analysis results were eligible. Cytogenetic findings were divided into three groups:- Favorable: 51 (28%), 44 (24%) had t (8;22) and 7 (4%) had Inv 16.- Intermediate: 103 (57%), 60 (33%) had a normal caryotype.- Adverse: 27 (15%).
176 patients were treated. The OS rate among favourable, intermediate and adverse group was respectively at 36% 28% and 22%.
Conclusions: Our cytogenetic profile reveals some particularities: the High range of t (8,21) at 24% probably due to the young age of our patients and a majority of intermediate group (67%). The challenge of our future studies is to determine the prognosis significance of normal caryotype with molecular technical such as FLT3 and NPM1.

P-148

SOMATIC THROMBOPOIETIN (TPHO) GENE MUTATIONS IN CHILDHOOD MYELOID LEUKEMIAS

M. Houwing[1], R. Kersseboom[2], S.L.M. Gooskens[1], A.C.H. de Vries[1], D. Reinhardt[3], J. Stary[4], V. de Haas[5], R.O.B. Pieters[6], M. Zwaan[1], M.M. van den Heuvel-Eibrink[1]

[1]Department of Pediatric Hematology and Oncology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Department of Clinical Genetics, Erasmus University Medical Center, Rotterdam, Netherlands; [3]Department of Pediatric Oncology/Hematology, Medical School, Hannover, Germany; [4]Department of Pediatric Oncology/Hematology, Charles University and University Hospital Motol, Prague, Czech Republic; [5]Dutch Childhood Oncology Group, Dutch Childhood Oncology Group, The Hague, Netherlands; [6]Department of Pediatric Hematology and Oncology, Prinses Maxima Center/Erasmus University Medical Center - Sophia Children's Hospital, Utrecht/Rotterdam, Netherlands

Objectives: We report, for the first time, a non-syndromic infant with a myeloproliferative condition that harbors a germline hereditary thrombopoietin (*THPO*) gene mutation. Our patient was from a Dutch family with a G>C mutation at the splice donor site of intron-3 of the *THPO* gene, which is known to induce familial thrombocytosis (FT) at increasing age, involving the regulation of megakaryopoiesis. FT is generally characterized by sustained proliferation of megakaryocytes resulting in elevated platelet counts.
The five known mutations in the *THPO* gene are located in the 5'untranslated region (5'UTR) of the *THPO* gene. These mutations lead to increased translation of *THPO* by inhibiting or removing the upstream open reading frames (uORFs). The monocytic hyperproliferation at infant age of our patient seemed to occur in conjunction to her germline*THPO* mutation, which could suggest that THPO is involved in hyperproliferation of the monocytic progenitor and -cell lineage. It was recently suggested that gain-of-function mutations in the *THPO* gene might predispose to adult acute myeloid leukemia, myelofibrosis and multiple myeloma. In contrast, the occurrence of somatic *THPO* mutations in sporadic pediatric AML patients was never described.
Methods: We performed a mutation screening of a representative and well-characterized cohort of pediatric AML ($n = 264$), ML-DS ($n = 16$) and JMML ($n = 47$) samples by amplifying the 5'UTR region of *THPO*.
Results: The screening revealed 1/327 case with a gain-of-function mutation, in the exon-3 intron-3 splice site (c. 13+3 G>A) in a 7-year-old AML patient (inv16).
Conclusions: We conclude that somatic mutations in the *THPO* gene seem to be rare in sporadic childhood myeloid malignancies. Nevertheless, a germline *THPO* mutation may be considered in an infant with a TMD-like disease, without dysmorphic features and cytogenetic aberrations, as this diagnosis may have important implications for clinical course, treatment and genetic counseling.

P-149

FLT3 INTERNAL TANDEM DUPLICATION AND NPM1 MUTATIONS IN PAEDIATRIC AML: A SINGLE CENTRE EXPERIENCE

V. Gupta[1], D. Bourne[2], N. Bown[2], S. Samarasinghe[3], S. Bailey[1], R. Skinner[1]

[1]Paediatric and Adolescent Oncology/BMT, Great North Children's Hospital Newcastle Upon Tyne Hospital NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom; [2]Northern Genetics Service, Newcastle Upon Tyne Hospital NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom; [3]Department of Heamatology and Oncology, Great Ormond Street Hospital, London, United Kingdom

Objectives: FLT3 internal tandem duplications (ITD) and high alleleic ratio are associated with high relapse risk in AML, although additional NPM1 mutations may reduce the risk. Relatively little paediatric data about treatment and outcome is available. To date, no therapy is of proven benefit. FLT3 inhibitor, sorafenib and haematopoetic stem cell transplantation (HSCT) are treatment options. We present our experience of FLT3 and NPM1 mutations in paediatric AML.
Methods: Retrospective data analysis was carried out to identify children with FLT3/ITD with/without NPM1 mutation. Clinical profile, response to chemotherapy and outcome was noted. Treatment was according to UK guidelines.
Results: FLT3-ITD and NPM1 mutations were evaluated in 48 paediatric patients (age $\leq$ 18 years) with AML since year 2008. Eight patients, median age 9 years (range 7-17 years), were identified with FLT3/ITD giving a frequency of 16.6% in this cohort. Four patients entered remission after one course of ADE. One of these had isolated skin relapse immediately before planned HSCT. Second remission was achieved with clofaribine, DaunoXome, sorafenib followed by transplant. Another relapsed 3 months after completing chemotherapy and died of refractory diseases despite FLA-X and sorafenib. Three patients had refractory disease after first course of ADE. Sorafenib and FLA-IDA was used in second course. One patient with additional NPM1 mutation had pharyngeal granulocytic sarcoma without marrow involvement and responded well to chemotherapy. Six patients were transplanted successfully (5 unrelated including one double cord and one matched sibling), 5 in CR1 and one in CR2. All remain in remission, median 441 days (range 80-2081 days).
Conclusions: Inspite of small numbers, this experience is consistent with previous reports that children with FLT3 ITD have an aggressive course of AML often with poor response to first course of chemotherapy. Longer follow up is required to see whether HSCT improves disease control and overall survival.

P-150

BASELINE HIGH RESOLUTION CT SCAN (HRCT) THORAX FOR DETECTING RESPIRATORY INFECTION IN PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML) AT PRESENTATION

N. Tandon[1], S. Banavali[1], B. Arora[1], S. Kembhavi[2]

[1]Medical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Radiology, Tata Memorial Hospital, Mumbai, India

Objectives: Intensive chemotherapy in AML increases infectious complications; especially pulmonary (bacterial and fungal) leading to dismal prognosis. The aim of this study was to assess the incidence of baseline pulmonary infection by HRCT chest in AML patients before starting induction.
Methods: This is a prospective, observational, single centre study of consecutive pediatric ($<$ or $=$ to 21 years) AML (excluding APML) patients who were treated at Tata memorial centre from 1st June 2013 to 31st January 2014. All eligible patients underwent baseline HRCT thorax before initiating induction; which were centrally reviewed by the radiologist.
Results: Out of 40 patients enrolled, the mean age was 12 years (1-21); 82.5% were males; 80% had fever; 30% had respiratory symptoms; 7.5% had abnormal chest examination; 75% had good and intermediate; and 25% had poor risk cytogenetics. Their mean symptom duration was 2 months. Twenty two patients (55%) had an abnormal HRCT thorax. Among these, 5 (22.7%) had possible bacterial; 12 (54.5%) had fungal infection and 10 (45.4%) had miscellaneous findings like tuberculosis, pneumocystis carinii and non specific nodules. On univariate analysis, the presence of fever ($p = 0.007$), respiratory symptoms ($p = 0.018$), and poor risk cytogenetics ($p = 0.01$) were significantly correlated with abnormal HRCT scan. However, on multivariate analysis, only respiratory symptoms and poor risk cytogenetics were statistically significant ($p = 0.023$ each).
Conclusions: HRCT Chest is an excellent imaging modality in AML to detect baseline pulmonary infection and should be included in diagnostic work up in centres with significant rate of infection. This would help to choose antifungal prophylaxis versus treatment thereby improving morbidity and mortality during intensive AML induction.

P-151

UNDERLYING UNDIAGNOSED INHERITED MARROW FAILURE SYNDROMES AMONG CHILDREN WITH CANCER

F. Alabbas[1], Y. Dror[1], R. Grant[1], D. Malkin[1], O. Abla[1], S. Weitzman[1], E. Bouffet[1]

[1]Hematology and Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: To determine the prevalence of children with cancer who have an underlying inherited bone marrow failure syndrome (IBFMS)
Methods: A retrospective review of medical records of newly diagnosed pediatric cancer patients at The Hospital for Sick Children from June 2009 to May 2010 was conducted. Clinical, laboratory and radiologic parameters were extracted from the patient charts focusing particularly on findings suggestive of possible underlying IBMFS.

Table I. Findings suggestive of underlying IBMFS in newly diagnosed cancer patients

Family history of cancer at age < 50 years
Associated physical anomalies (on physical or radiological examination)
History of previous cytopenia
Elevated MCV
Elevated hemoglobin F
Severe toxicities from chemotherapy or radiation treatment.

Results: Records of 276 patients were reviewed. Five candidate patients (1.8%) were identified. Three presented with acute leukemia. Two presented with kidney malformations and elevated MCV and elevated hemoglobin F was seen in one patient. One patient developed grade 4 toxicities in response to chemotherapy. The fourth patient presented with a brain tumor, later developed severe toxicities to chemotherapy (prolonged pancytopenia) and his father was diagnosed with nasopharyngeal carcinoma in his 30s. The fifth patient presented with Wilms tumor, congenital anomalies and elevated hemoglobin F.
Conclusions: Our data suggest that a small fraction of patients with cancer have clinical features that indicate an investigation to rule out underlying IBMFSs. Careful evaluation of indicators of IBMFSs is helpful to personalize treatment, minimize toxicity and provide appropriate family counseling and prognosis. Prospective studies are necessary to accurately determine the prevalence of IBMFSs among newly diagnosed cancer patients.

NEUROBLASTOMA

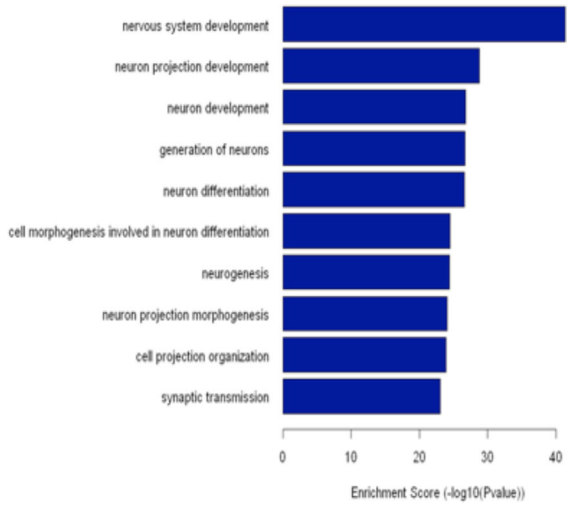
P-152

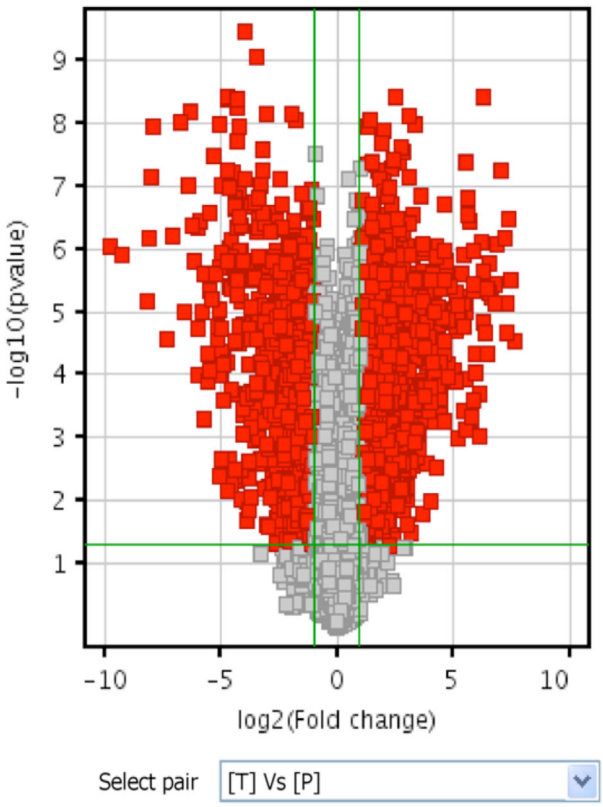
LNCRNA EXPRESSION SIGNATURES OF NEUROBLASTOMA REVEALS THE POTENTIAL ROLE OF LNCRNA IN CONTRIBUTING TO NEUROBLASTOMA PATHOGENESIS

T. Weitao[1], D. Kuiran[1], C. Ximao[1], L. Gongbao[1], Z. Shan[1]

[1]The Pediatric Surgery, Children' Hospital of Fudan University, Shanghai, China

Objectives: Long non-coding RNAs (lncRNAs) are broadly defined as transcribed RNA molecules greater than 200nt in length and lacking an open reading frame of significant length (less than 100 animo acids). The purpose of our study is to investigate the differentially expressed lncRNAs in neuroblastoma.
Methods: The tumor tissues and para-tumor tissues were collected and stored in the past two years (2011.12-2013.12). In this study, lncRNA microarray (Human LncRNA Microarry V3.0) was used to investigate the differentially expressed lncRNAs in 12 samples (6 tumor tissues, 6 para-tumor tissues).
Results: There were 4802 lncRNAs and 5130 mRNAs differentially expressed between the tumor tissues and para-tumor tissues (tumor VS para-tumor, 3098 lncRNAs and 2526 mRNAs up-regulated, while 1704 lncRNAs and 2604 mRNAs down-regulated). In Gene ontology (GO) analysis, there were 1609 differentially expressed genes, involved in 728 biological processes, up-regulated (341 genes' fold enrichment ≥ 2, $P < 0.05$) while 1698 genes that involved in 943 biological processes down-regulated (456 genes' fold enrichment ≥ 2, $P < 0.05$) in tumor tissues. By comprehensively analyzing, 140 enhancer-like lncRNAs and 325 nearby coding genes had been demonstrated to express differentially meanwhile (fold change ≥ 2, $P < 0.05$). Especially, the RP11-204E9.1 lncRNA up-regulated (fold change = 7.112, $P < 0.01$) with the nearby coding gene SOX4 up-regulated synchronously (fold change = 28.1, $P < 0.01$) in tumor tissues. Those findings were comfirmed by the subsequent PCR results in 30 neuroblastoma samples and 10 para-tumor tissues.





Conclusions: Our experiments provide a list of differentially expressed lncRNAs and mRNAs in neuroblastoma that could be useful for further study. The novel lncRNA RP11-204E9.1 maybe play an important role in neuroblastoma pathogenesis by regulating its nearby coding gene SOX4.

P-153

COPY NUMBER VARIATIONS (CNVS) CAN DEFINE THE PROGNOSIS IN NEUROBLASTOMA PATIENTS

A. Druy[1], E. Shorikov[1], G. Tsaur[1], S. Tuponogov[2], A. Popov[1], A. Solodovnikov[3], L. Saveliev[4], L. Fechina[1]

[1]Pediatric Oncology and Hematology Center, Regional Children's Hospital/Research Institute of Medical Cell Technologies, Yekaterinburg, Russia; [2]Pediatric Oncology and Hematology Center, Regional Children's Hospital, Yekaterinburg, Russia; [3]Pediatric Oncology and Hematology Center, Research Institute of Medical Cell Technologies, Yekaterinburg, Russia; [4]Chair of Laboratory Medicine, Ural State Medical University, Yekaterinburg, Russia

Objectives: 1p, 11q deletions, *MYCN* amplification (MNA) are known to be adverse prognostic markers in neuroblastoma, while significance of many other CNVs is unclear.
Methods: We analyzed 108 neuroblastomas by MLPA for loci 1p,2p,3p,11q,17q and 100 tumors for 4p,7q,9p,12q,14q. Prognostic significance was estimated by overall (OS) and event-free survival (EFS) with median of follow-up time 28 months (range 1-166 months).
Results: In 29 patients (26.9%) 1p deletion was revealed and had prognostic impact (EFS 0.33 ± 0.10 vs. 0.67 ± 0.06, $p = 0.002$, OS 0.46 ± 0.10 vs. 0.73 ± 0.06, $p = 0.003$). 17q gain was detected in 54 patients (50.0%) and led to decreased survival rates (EFS 0.42 ± 0.08 vs. 0.71 ± 0.07, $p < 0.001$, OS 0.48 ± 0.09 vs. 0.80 ± 0.06, $p = 0.002$). Both 1p deletion and 17q gain retained prognostic significance in *MYCN* non-amplified patients. 2p24 gain including *MYCN* was observed in 15 patients (13.9%) and showed prognostic significance in patients under 1 year (EFS 0.53 ± 0.25 vs. 0.96 ± 0.04, $p = 0.047$). 4p gain detected in 8 patients (8.0%) decreased EFS in patients under 1 year (0.00 vs. 0.88 ± 0.06, $p = 0.055$). Gain of both 7p and 7q (6 patients, 6.0%) led to reduced EFS in the whole group (0.33 ± 0.19 vs. 0.56 ± 0.06, $p = 0.053$) and in *MYCN* non-amplified patients (0.40 ± 0.22 vs. 0.64 ± 0.06, $p = 0.044$). In 8 patients (8.0%) 9p deletion was found. Presence of this aberration resulted in dramatic decreasing of survival rates: both EFS and OS were 0.00 vs. 0.60 ± 0.06 and 0.68 ± 0.06 correspondingly, $p = 0.035$, $p = 0.014$). In multivariate analysis of OS performed by stage, age, MNA, 1p, 9p deletions and 17q gain as covariates patients with stage IV ($p = 0.042$), MNA ($p = 0.049$) and 9p deletion ($p = 0.041$) had significantly poor survival.

Conclusions: In our cohort of patients MNA, 1p, 9p deletions and 17q gain demonstrated negative prognostic significance. MNA and 9p deletion were defined as independent molecular adverse factors. Presence of 2p24 and 4p gains led to decreased EFS in the group of patients below 1 year.

P-154

ROLE OF LMO1 IN NEUROBLASTOMA INITIATION AND MAINTENANCE: ANALYSIS IN THE ZEBRAFISH MODEL OF CHILDHOOD NEUROBLASTOMA

S. Zhu[1], A. Wood[2], G. Yang[1], X. Zhang[1], N. Weichert[3], S. He[3], T. Tao[3], D. Oldridge[2], J. Maris[2], T. Look[3]

[1]Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, USA; [2]Division of Oncology and Center for Childhood Cancer Research, Children's Hospital of Philadelphia, Philadelphia, USA; [3]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: Neuroblastoma, an embryonic tumor of the peripheral sympathetic nervous system (PSNS), accounts for 10% of all childhood cancer deaths. We recently developed a robust zebrafish model of neuroblastoma and demonstrated that activated ALK synergizes with MYCN by inhibiting a developmentally-timed apoptotic response that is otherwise induced by MYCN. We have now used this model to provide evidence in support of the results of a genome-wide association study (GWAS) conducted by Dr. John Maris's group. Their study revealed that inherited common single nucleotide polymorphisms (SNPs) within the LIM domain-only 1 (LMO1) gene locus are highly associated with the development of advanced neuroblastoma. In children with a higher risk of developing neuroblastoma, LMO1 is overexpressed without alteration of the coding sequences.
Methods: Accordingly, we developed two independent transgenic lines in which the human *LMO1* gene is overexpressed in the PSNS under control of the zebrafish dopamine-beta-hydroxylase (d(h) promoter. Both lines were bred to heterozygous transgenic fish overexpressing MYCN-EGFP in the PSNS under the control of the d(h promoter.
Results: Our recent results show that overexpression of LMO1 in the zebrafish model markedly accelerates the onset and increases the penetrance of MYCN-induced neuroblastoma, providing in vivo evidence for the role of LMO1 overexpression in the initiation of neuroblastoma. LMO1 accelerates tumorigenesis primarily by increasing the proliferative rate of MYCN expressing sympathetic neuronal progenitors. In addition, we found that coexpression of LMO1 with activated ALK induced neuroblastoma, which is the first time that neuroblastoma has been induced in the zebrafish system without MYCN overexpression.
Conclusions: Thus, the zebrafish model system appears to be ideal for "functional genomics analysis" to provide in vivo evidence and investigate mechanisms and pathways underlying new associations emerging from GWAS, tumor genome resequencing and other genome-wide technologies that are currently under intense investigation in human cancers.

P-156

PROTEIN SIGNATURES IN THE SERUM OF PATIENTS WITH NEUROBLASTOMA

S. Ragg[1], M. Key[1], F. Rankin[1], T. Vik[1], M. Hogarty[2]

[1]Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [2]Pediatrics, University of Pennsylvania, Philadelphia, USA

Objectives: Neuroblastoma is a very heterogeneous tumor with outcomes ranging from excellent survival to high risk of failure. With the goal of developing better prognostic indicators, the Children's Oncology Group (COG) has collected serum samples from a large number of subjects at the time of diagnosis. These samples can be used to characterize protein signatures in the blood indicative of tumor type, response to therapy, and relapse post treatment.
Methods: We measured the relative concentration of 103 low abundance proteins with a customized human cytokine antibody array (Raybiotech, Inc.) in 50 subjects with osteosarcoma, 50 subjects with Wilms tumor, and 87 subjects with neuroblastoma (30 with stage 2 favorable histology, 30 with stage 4 MYCN amplified, and 27 with stage 4 MYCN-non-amplified). Sera were collected at diagnosis locally and through the COG. These samples were compared to 150 age- and gender-matched samples from healthy subjects using a mixed effects model. Several standard statistical learning approaches were used to classify the serum of children with neuroblastoma versus those of healthy controls.
Results: In comparison to healthy control samples, 34 proteins were differentially abundant in samples of subjects with MYCN amplification and high risk neuroblastoma, and 13 proteins were differentially abundant in samples of subjects with low risk neuroblastoma. Samples of subjects with MYCN amplification and high risk neuroblastoma contained 22 proteins differentially abundant when compared to sera from subjects with Wilms tumor or osteosarcoma, with 4 proteins differentially abundant for both and 9 unique to each. The classification results were consistent across the five classification algorithms used, with an average specificity of 90% and an average sensitivity of 74%.
Conclusions: This study demonstrates that multiple low abundance proteins form an accurate signature that can distinguish healthy and diseased subjects as well as different cancer types.

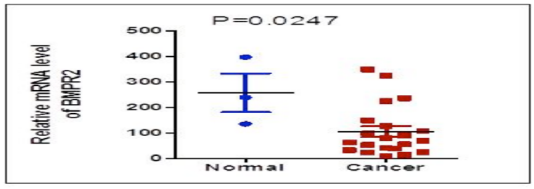
P-157

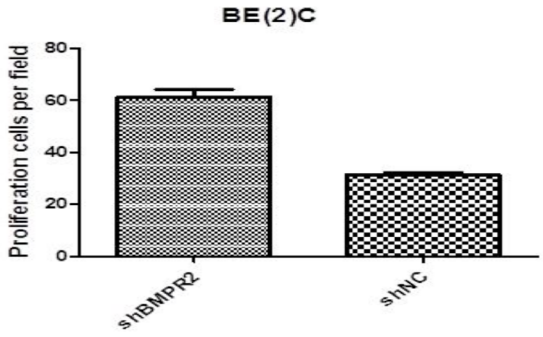
BONE MORPHOGENETIC PROTEIN RECEPTOR II SUPPRESS NEUROBLASTOMA PROLIFERATION IN VITRO AND IN VIVO

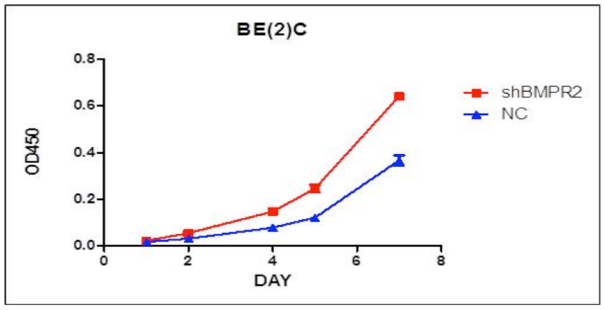
X. Cui[1], K. Dong[1], D. Jia[2], R. Dong[1], K. Li[1], X. Xiao[1], W. Yao[1], G. Liu[1]

[1]pediatric surgery, Children's Hospital of Fudan University, Shanghai, China; [2]Shanghai Medical College, Fudan University, Shanghai, China

Objectives: BMPR2, Bone morphogenetic protein receptor II, encodes a member of the bone morphogenetic protein receptor family of transmembrane serine/threonine kinases. The aim of this study was to determine whether the different expression of BMPR2 will affect neuroblastoma cell proliferation.
Methods: Specimens of neuroblastoma were obtained from hospital. The BMPR2 shRNA vector was transfected to NB cell lines SK-N-BE (2) and KP-N-NS, the BMPR2 overexpression vector was transfected to NB cell lines IMR-32, SK-N-SH and SH-SY5Y. The efficiency of gene silence or overexpression was confirmed by Quantitative real-time PCR and western-blot. Cell proliferation ability was measured by Cell-Counting Kit and colony formation assay. Cells were injected subcutaneously into the nude mice. The tumor size was quantified in two dimensions using calipers. Immunohistochemical staining was used for BMPR2 expression. The statistical analysis and graphical presentation were performed using GraphPad Prism 5.0.
Results: Quantitative real-time PCR and immunohistochemical staining showed the expression levels of BMPR2 in neuroblastoma were higher than that of non-tumor adrenal tissues ($P < 0.05$). The CCK-8 assays and colony formation assays showed that disruption of BMPR2 gene expression had a positive effect on the proliferation of neuroblastoma cells. On the contrary, overexpression of BMPR2 had a negative effect. In vivo, we found that BMPR2 could inhibit neuroblastoma cells growth in mouse models.







Conclusions: The data presented here indicate a significant role of BMPR2, which could suppress proliferation of neuroblastoma both in vitro and in vivo.

P-158

NLRR2 IS INVOLVED IN CELL SURVIVAL AND DIFFERENTIATION THROUGH JNK PATHWAY IN NEUROBLASTOMA

A. Sheikh[1], A. Takatori[1], M.S. Hossain[1], M.K. Hasan[1], Y. Nakamura[1], A. Nakagawara[1]

[1]Childrens Cancer Research Center, Chiba Cancer Center Research Institute, Chiba, Japan

Objectives: Neuronal Leucine-rich repeat protein 2 (NLRR2) is a transmembrane protein of human NLRR gene family. Of NLRR family, NLRR1 is associated with unfavorable prognosis, while NLRR3 is correlated to favorable outcome of neuroblastoma (NB). However, the clinical significance and function of NLRR2 in NB are still uncovered. In the present study, we were interested to investigate the functions and the transcriptional regulation of *NLRR2* in NB.
Methods: We evaluated the NLRR2 and c-Jun expression in SK-N-BE, TGW and SMS-SAN cells by RT-PCR, quantitative real time PCR and western-blot. Retinoic acid (RA) was used to induce neuronal differentiation in NB cells. *NLRR2* promoter activity and c-Jun recruitment were analyzed by dual luciferase and ChIP assays respectively. SK-N-BE cells were used for tumor xenograft study.
Results: We have found that enforced expression of NLRR2 increased NB cell growth. The knockdown of NLRR2 significantly reduced NB cell growth *in vitro* and *in vivo*. In *NLRR2* knockdown cells, RA-mediated differentiation was significantly enhanced. After the RA treatment, NLRR2 expression was increased which was correlated with the upregulation of c-Jun, a member of activator protein-1 (AP-1) family. Interestingly, the treatment of JNK inhibitor reduced the expression of c-Jun and NLRR2. Promoter analysis revealed that RA treatment enhanced *NLRR2* transcription which was suppressed by JNK inhibitor. The AP-1 binding site was identified in the *NLRR2* promoter region and c-Jun recruitment was confirmed by ChIP assay. Moreover, the knockdown of c-Jun reduced *NLRR2* expression, suggesting that *NLRR2* is an inducible gene regulated by JNK pathway with the functions to enhance NB cell survival and inhibit cell differentiation.
Conclusions: Accumulated evidences suggest that NLRR2 acts as a negative feedback regulator for RA-mediated differentiation. NLRR2 might play a role in NB drug resistance and could give us a possible therapeutic approach to treat aggressive NB.

P-159

COMPARING 123I-MIBG SCINTIGRAPHY WITH MRI-STIR IN PATIENTS WITH STAGE 4 NEUROBLASTOMA TO INVESTIGATE BONE AND BONE MARROW METASTASES

G. Bleeker[1], A. Smets[2], E. Deurlo[2], B. Van Eck-Smit[2], H. Caron[1], G. Tytgat[1]

[1]Department of Paediatric Oncology, Academic Medical Center, Amsterdam, Netherlands; [2]Department of Radiology and Nuclear Medicine, Academic Medical Center, Amsterdam, Netherlands

Objectives: To compare radionuclide 123-Iodide-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy with magnetic resonance imaging (MRI) with short tau inversion recovery (STIR) to investigate bone and bone marrow metastases in neuroblastoma.
Methods: Diagnostic ^{123}I-MIBG-scans and MRI-STIR images from 10 patients with stage 4 neuroblastoma were evaluated to assess metastatic spread in 14 skeletal segments. First presence or absence of lesions were scored. Then morphological characteristics of the lesions were compared: with 'focal', being sharply demarcated, limited to one location in the skeletal segment or 'diffuse', indistinct margins, dispersed throughout the skeletal segment.
Results: A total of eighty-nine skeletal segments were evaluated with both modalities. In 36 segments, lesions were visible both MIBG^{pos}/MRI-STIR^{pos}. In 33 segments, discrepancies were seen: 26 lesions were ^{123}I-MIBG^{neg}/MRI-STIR^{pos} and 7 ^{123}I-MIBG^{pos}/MRI-STIR^{neg}. The morphological investigation revealed that ^{123}I-MIBG-scintigraphy showed focal lesions in 12 segments, diffuse in 30 and a combination of both in 1 segment. MRI-STIR showed focal lesions in 30 segments, diffuse in 10, and a combination of both in 22. Concordant morphological findings were seen in 30 segments: 10 focal, 19 diffuse and in 1 segment both types of lesions. In 36 segments morphological discordant findings were found. MRI-STIR^{pos}/^{123}I-MIBG^{neg} lesions were: 22 focal and 4 both. Discordant ^{123}I-MIBG^{pos}/MRI-STIR^{neg} were diffuse lesions in 7 segments. In eight affected segments (in 3 patients), cortical destruction was seen on MRI-STIR. These lesions were all of the diffuse type on ^{123}I-MIBG-scans; on MRI-STIR 5 were of the diffuse type and 3 were focal.
Conclusions: MRI-STIR showed more affected skeletal segments than ^{123}I-MIBG-scintigraphy. Because all included patients were stage 4, these findings did not affect staging. Discrepancies were most ^{123}I-MIBG^{neg}, but also MRI-STIR^{neg}. Morphological investigation indicated that MRI-STIR showed more focal and ^{123}I-MIBG-scintigraphy more diffuse lesions.

P-160

FEASIBILITY OF I131-MIBG AND TOPOTECAN THERAPY FOLLOWED BY CONSOLIDATION WITH BUSULFAN, MELPHALAN AND AUTOLOGOUS STEM CELL TRANSPLANTATION FOR REFRACTORY METASTATIC NEUROBLASTOMA

I. Ferry[1], G. Schleiermacher[2], D. Valteau-Couanet[3], S. Proust[4], P. Chastagner[5], J. Michon[6], A. Oudoux[7], A.S. Defachelles[1]

[1]Unité de Pédiatrie, Centre Oscar Lambret, LILLE, France; [2]Département de pédiatrie, Institut Curie, Paris, France; [3]Département de pédiatrie, Institut Gustave Roussy, Paris, France; [4]Unité d'hémato-oncologie pédiatrique, Centre Hospitalier Universitaire, Angers, France; [5]Unité d'hémato-oncologie pédiatrique, Centre Hospitalier Universitaire, Nancy, France; [6]Département de Pédiatrie, Institut Curie, Paris, France; [7]Unité de médecine nucléaire, Centre Oscar Lambret, Lille, France

Objectives: To evaluate the safety of MIITOP (MIBG therapy with topotecan) followed by busulfan and melphalan (BuMel) with ASCT in patients with refractory metastatic neuroblastoma.
Methods: In this retrospective analysis, toxicity data from patients with refractory neuroblastoma enrolled in the MIITOP protocol followed by BuMel were assessed. During MIITOP, patients received an activity of 12 Mci/kg of ^{131}I-mIBG combined with topotecan. In vivo dosimetry was used to calculate a second activity of ^{131}I-mIBG to be given on day 21 to deliver a total whole-body dose of 4 Gy, with a second course of topotecan. ASCT was performed on day 32. After MIITOP, patients without progressive disease could receive BuMel consisting of IV busulfan on days -7 to -3 (0.8-1.2mg/kg according to body weight strata), melphalan (140 mg/m2) on day -2 with ASCT on Day 0. Toxicity was assessed after MIITOP and after Bu-Mel.
Results: Seven patients completed MIITOP followed by BuMel/ASCT (median interval 11 weeks after MIITOP). Immediate tolerance of MIITOP was good with grade 3 non-hematologic toxicity limited to two patients (fever of unknown origin (FUO)). Two patients developed late complications: 1 grade 4 adrenal insufficiency and 1 grade 2 hypothyroidy. After BuMel, two patients developed bacterial sepsis and five FUO. Grade 3 and 4 mucositis occurred in five patients. One patient developed grade 4 sinusoidal obstructive syndrome that recovered on day 32. Median duration of neutropenia and thrombocytopenia was 12 and 36 days respectively. One patient had a persistent thrombocytopenia 140 days post ASCT. At the end of treatment, there were one complete remission, five stable diseases and one progressive disease.
Conclusions: BuMel can be safely administered 11 weeks after MIITOP therapy (MIBG up to 24 mCi/kg with topotecan) in refractory metastatic neuroblastoma. The impact on survival of this treatment combination should now be evaluated in a phase II trial.

P-161

UTILITY OF 18F-FDG PET-CT IN PAEDIATRIC NEUROBLASTOMA AND COMPARISON WITH 131I-MIBG SCINTIGRAPHY: SINGLE INSTITUTIONAL EXPERIENCE

V. Dhull[1], P. Sharma[1], C. Patel[1], S. Agarwala[2], V. Bhatnagar[2], S. Bakhshi[3], C. Bal[1], R. Kumar[1]

[1]Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India; [2]Paediatric Surgery, All India Institute of Medical Sciences, New Delhi, India; [3]Medical Oncology, All India Institute of Medical Sciences, New Delhi, India

Objectives: To evaluate the utility of ^{18}F-FDG PET-CT in patients with paediatric neuroblastoma and compare the results with that of ^{131}I-MIBG scintigraphy.
Methods: Data of 44 patients (male: 35, female: 9) with histopathology proven neuroblastoma who underwent ^{18}F-FDG PET-CT (staging-23, restaging-21) was retrospectively evaluated. ^{131}I-MIBG scintigraphy was available for 30/44 patients (mean interval 15 days). ^{131}I-MIBG scintigraphy and ^{18}F-FDG PET-CT images were independently evaluated by two nuclear medicine physicians and in separate sessions 1 week apart to minimize recall bias. Histopathology (n = 53 lesions) and/or clinical/imaging follow-up (n = 92 lesions) were taken as reference standard.
Results: Patient wise sensitivity, specificity, PPV, NPV and accuracy of ^{18}F-FDG PET-CT were 100%, 57.14%, 92.50%, 100% and 93.18% respectively. A total of 145 lesions (primary-40, lymph node-32, bone-51, bone marrow-15, and others-7) were detected on ^{18}F-FDG PET-CT in 44 patients. In 30 patients undergoing both the modalities, sensitivity, specificity, PPV, NPV and accuracy of ^{18}F-FDG PET-CT were 100%, 66.67%, 92.31%, 100% and 93.33% respectively and that of ^{131}I-MIBG were 95.83%, 66.67%, 92%, 80% and 90% respectively. In these 30 patients, ^{18}F-FDG PET-CT detected 108 lesions (primary-26, lymph node-22, bone/bone marrow-56 and others-4) and ^{131}I-MIBG detected 75 lesions (primary-25, lymph node-5, and bone/bone marrow-45). On patient wise comparison there was no significant difference between ^{18}F-FDG PET-CT and ^{131}I-MIBG, but ^{18}F-FDG PET-CT detected more lesions than ^{131}I-MIBG. While no difference was noted for primary lesion, PET-CT was significantly better than ^{131}I-MIBG scintigraphy for the detection of lymph nodal and bone/bone marrow lesions.
Conclusions: ^{18}F-FDG PET-CT is a highly accurate modality in patients with neuroblastoma and detects more lesions as compared to ^{131}I-MIBG scintigraphy in such patients.

P-162

123I-MIBG SCINTIGRAPHY AND 18F-FDG-PET (-CT) IMAGING FOR DIAGNOSING NEUROBLASTOMA: A COCHRANE DIAGNOSTIC TEST ACCURACY REVIEW

G. Bleeker[1], G. Tytgat[1], J. Adam[2], H. Caron[1], L. Hooft[3], L. Kremer[1], E. van Dalen[1]

[1]Department of Pediatric Oncology, Academic Medical Center, Amsterdam, Netherlands; [2]Department of Nuclear Medicine and Radiology, Academic Medical Center, Amsterdam, Netherlands; [3]Dutch Cochrane Centre, Academic Medical Center, Amsterdam, Netherlands

Objectives: Many studies reporting on the diagnostic accuracy of Iodine-123-metaiodo-benzylguanidine (^{123}I-MIBG) -scintigraphy in neuroblastoma patients, are very heterogeneous in number of included patients and performance of the imaging methods. Still, prognosis, treatment and response of patients are based on extension-scoring of ^{123}I-MIBG-

scans. Therefore, we assessed the diagnostic accuracy of ^{123}I-MIBG and that of a possible add-on test: Fluorine-18-fluorodeoxy-glucose (^{18}F-FDG) positron emission tomography (-computed tomography) (PET (-CT)).
Methods: We searched databases of MEDLINE/PubMed (1945-September 2012) and EMBASE/Ovid (1980-September 2012), reference lists of relevant articles and reviews, conference proceedings and contacted experts. Inclusion criteria: cross-sectional studies comparing results of ^{123}I-MIBG-scintigraphy, ^{18}F-FDG-PET (-CT), or both with the reference standards or with each other; diagnostic design; children 0-18 years old; neuroblastoma of any stage at first diagnosis or at recurrence. Two review authors independently selected studies, extracted data and assessed methodological quality.
Two-by-two tables were used to calculate sensitivity and/or specificity for each study and, if possible, forest plots were generated.
Results: Of 4,693 references, we included 11 studies with 621 eligible patients. The pooled mean sensitivity of ^{123}I-MIBG-scintigraphy was 92.4% (95% confidence interval 84.6-96.4%; 95% prediction interval 63.0-98.9% (in 608 patients)). The specificity was 85% in 115 lesions in 22 patients, described in one study. The sensitivity of ^{18}F-FDG-PET (-CT) alone and compared to ^{123}I-MIBG-scintigraphy was reported in one study as 100%. The specificity could not be calculated. None of the studies provided outcome data on the diagnostic accuracy of ^{18}F-FDG-PET (-CT) in patients with negative ^{123}I-MIBG-scintigraphy. All studies had methodological limitations.
Conclusions: The pooled sensitivity of ^{123}I-MIBG-scintigraphy was 92.4%, analysis of the specificity was difficult, because only one study provided data on false positive and true negative results. Although currently not enough evidence is available, a possible add-on test is ^{18}F-FDG-PET (-CT) for ^{123}I-MIBG negative tumours.

P-163

THE ROLE OF CHEST COMPUTED TOMOGRAPHY (CT) AS A SURVEILLANCE TOOL IN CHILDREN WITH NEUROBLASTOMA

S.M. Federico[1], S.L. Brady[1], A.S. Pappo[1], J. Wu[1], S. Mao[1], V. McPherson[1], R.A. Kaufman[1], S.C. Kaste[1]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA

Objectives: The amount and frequency of imaging in children with neuroblastoma varies among institutions. This study examines the value of chest CT in a cohort of pediatric patients with high-risk neuroblastoma.
Methods: Medical records and imaging of 88 patients with high-risk neuroblastoma, diagnosed at St. Jude Children's Research Hospital between January, 2002 and December, 2009, were reviewed. Surveillance imaging was conducted through 2013. Ten patients with thoracic disease at diagnosis were excluded. Event free survival (EFS) and overall survival (OS) were estimated using the method of Kaplan and Meier. Size specific dose estimates for CT scans of the chest, abdomen, and pelvis were used to estimate absolute organ doses to 23 organs. Organ dosimetry was used to calculate cohort effective dose.
Results: Seventy-eight patients underwent 2,489 CTs, including 872 chest, 857 abdomen, and 760 pelvis scans. The 5 year OS and EFS were 48.8% $\pm$ 7% and 49.4% $\pm$ 7% respectively. Forty-two (54%) patients progressed/recurred and 37 (47%) died of disease. Eleven patients (14%) developed thoracic disease progression/recurrence identified by chest CT (1 with pulmonary nodules, 1 paraspinal mass, and 9 nodal). MIBG (metaiodobenzylguanidine) scans confirmed thoracic disease in 6 of these patients. Five of the 11 had normal MIBG scans of the chest; 2 had symptomatic disease, 2 were asymptomatic with normal chest MIBG scans but avid bone disease and 1 had bone/chest pain with a normal MIBG, but abnormal positron emission tomography scan. The estimated radiation dose savings from gender neutral CT surveillance without chest imaging was calculated as 33%, a relative risk reduction of 43%.
Conclusions: Neuroblastoma progression/recurrence in the chest is rare and often presents with symptoms or is identified using non-CT imaging modalities. For patients diagnosed with high-risk neuroblastoma, who lack thoracic disease initially, omission of chest CTs from on-therapy/surveillance imaging can save approximately 33% of the radiation burden without compromising disease detection.

P-164

FEASIBILITY OF THERAPEUTIC I131 METAIODOBENZYLGUANIDINE (MIBG) PREVIOUS TO BLOOD STEM CELL COLLECTION AS "PURGING IN VIVO " FOR HIGH-RISK NEUROBLASTOMAS (HRNB)

V. Odone-Filho[1], M.T.A. Almeida[1], C. Buchpigel[2], A.M.P. Azambuja[1], C.S.C. Vince[3], M. Brumatti[3], N.S.H. Neves[3], G.L.F. Batista[1], P.T. Maluf Jr[4], L.M.C. Cristofani[1]

[1]Oncologia Pediátrica, ITACI - Instituto de Tratamento do Câncer Infantil, Sao Paulo, Brazil; [2]Medicina Nuclear, ICESP - Instituto de Câncer do Estado de São Paulo, Sao Paulo, Brazil; [3]Hematologia e Oncologia, Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [4]Oncologia, Hospital Sírio Libanês, Sao Paulo, Brazil

Objectives: To estimate the feasibility of MIBG as 'purging in vivo' for HRNB.
Methods: Starting in 199**5 (ASCO Proceedings, 1996/XXXII Annual Meeting, Philadelphia/PA/USA, v.15, p.353/T1037), 44** children with HRNB underwent high-dose chemotherapy with autologous hematopoietic stem cell support (AHSCS), being the cell collection proceeded by exposure to I^{131} MIBG (8–12 mci/kg). Data related to 30/44 of these procedures (all children whose follow up as outpatients was done exclusively at ITACI), focusing mainly on their feasibility and toxicity, are here presented. Conditioning regimen included CBDCA/ETO/MEL in 26/30 (86.7%) and BU/MEL in 4/30 (13.3%) children.
Results: Peripheral blood stem cells (PBSC) sufficient for allowing hematological recovery ($\geq$ 2.0 CD34+ cells X 10^6/kg) were obtained in 28/30 (93.3%) children (requiring**:** median of 5 apheresis), **whose transplantation was done** only with PBSC support. 2 additional children received either PBSC + marrow support (MS) (1) or exclusive MS (1). No stable ANC $>$ 500/mm^3**was obtained** before the 19th day after cell reinfusion; only 11/30 (36.7%) and 14/30 (46.7%) children respectively achieved stable platelet counts $\geq$ 20,000/mm^3 before the 27th day and independence of red cell transfusions before the 44th day after AHSCS. Most relevant immediate toxicities were**:** death secondary to sepsis in 2/30 (6.7%) children and 1 episode (3.3%) of severe, non-fatal VOD. Late toxicities included 2/28 (7%) secondary neoplasia (1 thyroid carcinoma and 1 fatal abdominal NHL). Within 15 survivors, 2 (13.3%) require thyroid hormone supplementation (oral iodine **was given** at the time of MIBG exposure). Considering the patients whose procedures were done after January/2010, when cell collections with previous I^{131}MIBG (10 mci/kg) became a routine step within ITACI, 9/11 children are surviving, being the EFS (death/progression/2nd neoplasia) of 68.6% $\pm$ 18.6%.
Conclusions: Therapeutic use of I^{131}MIBG before cell collection for AHSCS is feasible and deserves analysis regarding its potential usefulness for treating HRNB.

P-165

CHARACTERTICS OF IMAGE DEFINED RISK FACTORS (IDRFS) IN PATIENTS ENROLLED THE LOW RISK PROTOCOL (JNB-L-10) FROM THE JAPANESE NEUROBLASTOMA STUDY GROUP (JNBSG)

A. Yoneda[1], T. Tajiri[2], T. Iehara[3], M. Kitamura[4], A. Nakazawa[5], H. Takahashi[6], T. Takimoto[7], A. Nakagawara[8]

[1]Pediatric Surgery, Osaka Medical Center and Research Institute for Maternal and Child Health, Izumi, Japan; [2]Pediatric Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan; [3]Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan; [4]Radiology, National Center for Child Health and Development, Tokyo, Japan; [5]Pathology, National Center for Child Health and Development, Tokyo, Japan; [6]Clinical Trial and Clinical Epidemiology, Tsukuba University, Tsukuba, Japan; [7]Clinical Research, National Center for Child Health and Development, Tokyo, Japan; [8]Biochemistry and Innovative Cancer Therapeutics, Chiba Cancer Center Research Institute, Chiba, Japan

Objectives: The Japanese Neuroblastoma Study Group (JNBSG) has been conducted the protocol (JNB-L-10) for low risk patients to minimize treatment complications using Image Defined Risk Factors (IDRFs) as the main factor for treatment decision. In this preliminary report, we analyzed IDRF results in JN-L-03 protocol in order to clarify characteristics of IDRF in low risk neuroblastoma (NB) patients.
Methods: IDRFs were evaluated at diagnosis, as well as at the time after 3, 6, 9 courses of chemotherapy in JN-L-03 protocol (2010-2013 registry). Three low dose chemotherapy protocols were included in this study, such as LI-A (VCR / CPA), LI-B (VCR / CPA / THP-ADR), LI-C (VCR / CPA / CBDCA). If no IDRFs were present, the patient underwent surgery. If any IDRFs were present, the patient underwent further chemotherapy. IDRF results from 60 localized NB patients enrolled in JN-L-03 were collected. We analyzed the relationship between IDRF results and tumor location as well as INSS.
Results: IDRF results were available in 58 of 60 patients. Twenty-nine of 58 patients were identified. IDRFs present at the onset of disease. Two of 4 tumors originated from neck, 9 of 12 tumors from mediastinum, 7 of 29 tumors from adrenal gland, 8 of 9 tumors from retroperitoneal, 1 of 1 tumor from kidney, 2 of 3 tumors from pelvis had IDRFs at diagnosis. None of 24 INSS stage 1 tumors, 13 of 15 stages 2A tumors, 4 of 5 stage 2B tumors, all of 10 stage 3 tumors had IDRFs at diagnosis.
Conclusions: IDRFs were present in 50% of low risk patients with NB at diagnosis. Tumors originated from mediastinum or retroperitoneum and INSS stage 2A, 2B, 3 tumors more likely have IDRFs compared to the tumors originated from adrenal grand and stage 1 tumors.

P-166

A SYSTEMATIC REVIEW OF THE LITERATURE REVEALS NO UNIFORM DEFINITIONS ON DIAGNOSTIC IMAGING FOR BONE AND BONE MARROW METASTASES IN NEUROBLASTOMA PATIENTS

G. Bleeker[1], D. Heijkoop[1], E. van Dalen[1], L. Kremer[1], A. Smets[2], B. Van Eck-Smit[2], E. Deurlo[2], H. Caron[1], G. Tytgat[1]

[1]Department of Paediatric Oncology, Academic Medical Center, Amsterdam, Netherlands; [2]Radiology and Nuclear Medicine, Academic Medical Center, Amsterdam, Netherlands

Objectives: Since the presence of bone and/or bone marrow (BM) metastases correlates with bad prognosis, it is important to have clear and uniform definitions. The objectives of this review were: 1. To identify all definitions of bone and BM metastases used in imaging studies; and 2. To determine diagnostic accuracies for bone and/or BM metastases of all imaging tests.
Methods: We searched MEDLINE/PubMed (1945-April 2013) and EMBASE/Ovid (1980-April 2013) and bibliographies of relevant articles. Studies were included if they reported on diagnostic imaging of patients with suspected metastatic neuroblastoma and defined bone and/or BM metastases. Two review authors selected studies, extracted data and assessed

methodological quality. Disagreements were resolved by discussion. Sensitivity and/or specificity were calculated using data in two-by-two-tables.
Results: Thirty of 400 identified studies were eligible for inclusion. The main exclusion reason was not providing a definition for bone and/or BM metastases (n = 52).
Of the 30 included studies 9 defined bone, 13 defined BM and 8 defined both metastases (objective 1). Definitions of bone and BM metastases varied widely between included studies. Bone metastases were frequently defined as focal lesions or hotspots on scintigraphy and as osteolytic lesions with periosteal reaction on radiography; BM metastases as diffuse lesions on MRI and on scintigraphy (with or without focal lesions). BM metastases on MRI were additionally defined as: low-intensity on T1- and high-intensity on T2-weighted-images.
Fourteen studies reported data on diagnostic accuracy (objective 2). Sensitivity and specificity values varied enormously between studies for both bone and BM metastases.
Conclusions: Despite the fact that many studies report on outcome data of patients with bone and/or BM metastases, the majority do not provide definitions. Furthermore, in the studies that do provide definitions, both the definitions and the diagnostic accuracy varied so widely that no conclusions can be drawn.

P-167

PATTERNS OF RELAPSE IN HIGH-RISK NEUROBLASTOMA PATIENTS

R. Li[1], M. Sridharan[2], W. London[2], S. Lee[1], S. Shusterman[2], K. Marcus[2]

[1]Department of Radiation Oncology, Brigham and Women's Hospital, Boston, USA; [2]Department of Pediatric Oncology, Dana Farber/Boston Children's Cancer and Blood Disorder Center, Boston, USA

Objectives: We performed a retrospective review of pediatric patients treated for high-risk neuroblastoma to identify whether patients relapsed at original sites of disease or previously disease-free sites, with particular emphasis on the impact of radiotherapy to metastatic sites.
Methods: All patients from 1994-2008 who relapsed after treatment for stage IV neuroblastoma were included in our cohort. Sites of disease, as defined by anatomic location of MIBG avidity, were compared at diagnosis and at first relapse. Fisher's exact test was performed to determine relationship between radiation therapy technique and relapse at previously involved sites.
Results: Forty-five patients with relapse of high-risk neuroblastoma were included. 62% of patients were male, and the median age at diagnosis was 3.6 years old. 44% of patients were treated with total body irradiation (TBI), and 56% were treated without TBI, instead using local radiation to the primary site with or without focal radiation to metastases. Median time from diagnosis to relapse was 1.9 years, with 67% relapsing in at least one previously MIBG avid site and 16% of patients relapsing in a previously irradiated site. 11% of patients had involvement of the primary site at relapse. When grouped by radiation technique, 50% of patients treated with TBI (n = 20) relapsed in previously involved sites compared with 80% of patients treated without TBI (n = 25) (p = 0.05).
Conclusions: Overall, the majority of neuroblastoma patients relapsed in at least one site of previous MIBG-avid disease, with a small number relapsing in previously irradiated locations. Patients who did not receive TBI were significantly more likely to relapse in a previously involved disease site.

P-168

HEALTH-RELATED QUALITY OF LIFE IN A POPULATION-BASED SAMPLE OF SURVIVORS OF ADVANCED NEUROBLASTOMA IN CANADA

C. Portwine[1], C. Rae[2], T. Schecter[3], V. Lewis[4], J. Davis[5], D. Mitchell[6], D. Wall[7], P. Teira[8], R. Barr[1]

[1]Pediatrics, McMaster University, Hamilton, Canada; [2]Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada; [3]Hematology Oncology and Transplantation, Hospital for Sick Children, Toronto, Canada; [4]Hematology Oncology and Transplantation, Alberta Children's Hospital, Calgary, Canada; [5]Hematology Oncology and Transplantation, BC Children's Hospital, Vancouver, Canada; [6]Hematology Oncology and Transplantation, Montreal Children's Hospital, Montreal, Canada; [7]Pediatric Hematology Oncology and Transplantation, University of Manitoba/Cancer Care Manitoba, Winnipeg, Canada; [8]Pediatric Hematology Oncology and Transplantation, Hopital Ste. Justine, Montreal, Canada

Objectives: To examine the health related quality of life (HRQL) of survivors of advanced neuroblastoma (AN) who underwent intensive chemotherapy followed by myeloablative therapy with autologous stem cell transplant (SCT).
Methods: A national population-based survey was conducted in survivors of AN treated between 1991 and 2010. Parents of survivors completed a proxy Health Utilities Index (HUI) questionnaire, scored on a scale of 0.00 to 1.00. Comparative data for other clinical groups were obtained from previous studies and for the general population from Statistics Canada. Differences $\geq$0.03 in overall HRQL scores and $\geq$0.05 in single attribute scores are considered clinically important.
Results: Data were collected from 13/17 pediatric centres, including all 6 SCT centres, with 99 of 105 questionnaires returned being complete for scoring. The overall mean HRQL utility score was 0.84 (SD = 0.18); significantly less than that of children (5-12 years of age) in the general population (0.96; $p < 0.001$). There was no significant difference (p = 0.660) in mean overall HRQL between survivors of AN treated with SCT (mean age at dx 3.6yrs) and those treated without transplant (n = 20; mean age at dx 1.2yrs). However a clinically important (0.06) difference was observed in the attribute of hearing, with greater morbidity reported in the SCT group. Survivors of ALL (0.90; p = 0.009), and Wilms tumour (0.93; p = 0.002) had significantly better HRQL than survivors of AN, with substantially lower morbidity in the attribute of hearing ($p < 0.0001$). Survivors of AN experienced better HRQL than survivors of brain tumours (0.81); a difference considered to be clinically important.
Conclusions: In survivors of AN, HRQL is no worse with than without transplant. The differential effect on hearing reflects additional exposure to platinum-based chemotherapy in the SCT group. AN survivors enjoy better HRQL than survivors of brain tumours but have poorer HRQL than survivors of ALL and Wilms tumour.

P-169

VALIDITY AND RELIABILITY OF IMAGE-DEFINED RISK FACTORS IN LOCALIZED NEUROBLASTOMA: A REPORT FROM 2 TERRITORIAL CENTERS IN JAPAN

S. Fumino[1], K. Kimura[1], T. Iehara[2], N. Motoki[3], N. Satoaki[3], R. Souzaki[4], A. Nishie[5], T. Taguchi[4], H. Hosoi[2], T. Tajiri[1]

[1]Department of Pediatric Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan; [2]Department of Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan; [3]Department of Radiology, Kyoto Prefectural University of Medicine, Kyoto, Japan; [4]Department of Pediatric Surgery, Kyushu University, Fukuoka, Japan; [5]Department of Clnical Radiology, Kyushu University, Fukuoka, Japan

Objectives: The Japanese Neuroblastoma Study Group (JNBSG) has been employing a protocol using image-defined risk factors (IDRFs) for localized neuroblastoma to minimize surgical complications since 2010. However, the report from the INRG Project (Radiology, 2011) supplemented the description of renal vessels, in which even isolated contact is considered IDRFs-positive. The aim of this study was to evaluate the validity and reliability of IDRFs by comparing the previous and new guidelines.
Methods: Medical records of patients with localized neuroblastoma, who were treated at 2 centers in West Japan from 2002 to 2013, were retrospectively reviewed and classified as having IDRFs or not at diagnosis by radiologists. Before 2009, the indication of surgery was based on the surgeon's judgment.
Results: A total of 47 patients were enrolled, and their median age was 13 months (0 - 78). Primary tumor locations were the abdomen (adrenal gland and retroperitoneum) in 38, pelvis in 2, and mediastinum in 7. For all sites, IDRFs was present in 22/47 (46.8%) using the previous guideline (PG), and 38/47 (80.9%) using the new guideline (NG). For abdominal neuroblastomas, IDRFs was present in 15/38 (39.5%) usign PG, and 31/38 (81.6%) using NG. Moreover, the IDRFs-positive rate increased from 26.7% (4/15) to 80.0% (12/15) in 15 cases diagnosed at mass screening. Of IDRFs-positive cases, complete primary resection was achieved in 2/15 (13.3%) usign PG and 17/31 (54.8%) using NG. There was only one major surgical complication (renal atrophy) occurring in an IDRFs-positive case using either guideline.
Conclusions: Although it was expected that the IDRFs-positive rate would increase and resection rate would decrease according to NG, IDRFs could be not used to predict precisely the surgical risk in our limited series. NG might overestimate surgical risks and lead to unnecessary chemotherapy and a prolonged hospital stay.

P-170

RECENT TRENDS AND DISPARITIES IN HIGH-RISK NEUROBLASTOMA SURVIVAL IN THE UNITED STATES: A POPULATION-BASED PERSPECTIVE

J. Marron[1], K. Ribeiro[2], L.R. Diller[1]

[1]Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Social Medicine, Santa Casa School of Medicine, Sao Paulo, Brazil

Objectives: Recent changes in treatment for children with high-risk neuroblastoma have led to significant increases in survival. Patients who receive the full complement of therapy (chemotherapy, radiation, surgery, autologous bone marrow transplant, and immunotherapy) now experience a two-year event-free survival of 66% (NEJM 2010). Using publicly available registry data, we examined whether outcome improvements for patients >12 months of age have been consistent across racial, ethnic, and socioeconomic groups. Given the complexity of new treatment modalities, we hypothesized that access limitations could lead to disparities in survival gains.
Methods: We analyzed the 3-year relative survival of neuroblastoma patients diagnosed at >12 months of age between 1992 and 2007 in the 13 cancer registries of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program according to individual characteristics such as race and ethnicity and county-based measures such as education, income, and immigration status.
Results: Survival rates improved for all analyzed populations between 1992 and 2007, with an annual percent change (APC) in relative survival of 2.01% per year (p = 0.032), but these gains were experienced disproportionately by some populations. Greater survival improvements were seen in counties with few immigrants than in those with many immigrants (APC

2.03% vs 0.92%, p = 0.032), in low-poverty counties than in high-poverty counties (APC 2.42% vs 1.53%, p = 0.032), and in highly-educated counties than in less-educated counties (APC 2.74% vs 1.54%, p = 0.002). Disparities were also found according to race, ethnicity, metropolitan residency, and language isolation, but these findings did not reach statistical significance.
Conclusions: Recent improvements in survival for children with neuroblastoma diagnosed at >12 months of age have preferentially benefited some racial, ethnic, and socioeconomic groups. This may be due to disproportionate access to advanced treatment modalities by some patient populations. As care for children with cancer becomes more complex, addressing disparities in access will require further research and resources.

P-171

CHYLE LEAK FOLLOWING SURGICAL MANAGEMENT OF NEUROBLASTOMA: AN UNDERRATED COMPLICATION

E. Rent[1], S. Qureshi[1], P. Rent[2], M. Bhagat[1], N. Singhal[1]

[1]Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Public Health, Tata Institute of Social Science, Mumbai, India

Objectives: Surgery is a mainstay in the management of neuroblastoma in children. While the incidence of complications like infection and organ dysfunction are documented, literature on chyle leak is lacking. We have attempted to fill this void by evaluating the incidence, risk factors and implications of chyle leak following surgical management of neuroblastoma.
Methods: We retrospectively analysed the prospectively collected data on 150 patients who underwent surgery for neuroblastoma over a period of ten years. The possible risk factors including stage, lymph nodes dissected, side and site of disease was analysed. To determine the oncological implications we evaluated the hospital stay and the delay in further treatment.
Results: Chyle Leak was documented in 30 (20%) of the patients. It was more commonly seen in lesions arising from the adrenal gland (24% VS 13%), higher stage disease, previous chemotherapy and left sided disease (25% VS 13%). However none of these reached statistical significance. The only risk factor that showed a statistically significant increase in chyle leak was number of lymph nodes dissected with a 11% leak rate for patients with less than 5 lymph nodes sampled and 24% if more than 5 lymph nodes were sampled. (p = 0.028). All patients were managed conservatively. The duration of hospital stay was prolonged by 5 days compared to those without chyle leak however adjuvant chemotherapy was not compromised.
Conclusions: Chylous ascites is a common and under reported complication following surgical management of intra-abdominal neuroblastoma which settles with conservative management. It does not compromise the further oncological treatment and hence should not be a deterrent to aggressive surgery. Vigilance in detection however is advisable.

NEW DRUGS/EXPERIMENTAL THERAPEUTICS

P-172

IMMUNOTHERAPY OF ACUTE LEUKEMIAS WITH CHIMERIC ANTIGEN RECEPTORS (CARS) -ENGINEERED CYTOKINE INDUCED KILLER (CIK) CELLS BY SLEEPING BEAUTY SYSTEM

C.F. Magnani[1], N. Turazzi[1], F. Benedicenti[2], S. Tettamanti[1], G.M.P. Giordano Attianese[1], E. Montini[2], L.J.N. Cooper[3], A. Aiuti[2], A. Biondi[1], E. Biagi[1]

[1]Centro Ricerca Tettamanti Clinica Pediatrica, Università Milano Bicocca Osp. San Gerardo/ Fondazione MBBM, Monza (MB), Italy; [2]San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET), Ospedale San Raffaele, Milano, Italy; [3]University of Texas, MD Anderson Cancer Center, Houston, USA

Objectives: T cell engineering with CARs has been recently proved to be effective in redirecting effector activity towards leukemic blasts. Since the profile of efficacy, safety and feasibility of cell manufacturing and gene therapy by viral vectors still remain major concerns, we explored here the use of Sleeping Beauty (SB) Transposon-mediated gene transfer in CIK cells for targeting Acute Leukemias.
Methods: With an optimized clinical-grade stimulation protocol, we genetically modified CIK cells to express two distinct CARs specific for myelogenous leukemia (AML) CD123+ or acute lymphoblastic leukemia (ALL) CD19+ blasts.
Results: The nucleofection minimally affected the phenotype of CIK cells, and the optimized protocol was effective in inducing T-cell expansion, with a fold increase sufficient to be translated into clinical protocols. Modified CIK cells displayed stable expression of CD123. CAR or CD19. CAR with a frequency of 51.4% ± 2.9 (n = 13) and 48.8% ± 6.8 (n = 7), respectively, and exerted efficient lysis of leukemic primary blasts. Interestingly, CAR triggering by the antigen expressed by leukemic cells promoted specific cytokine secretion and proliferation that was restricted to the modified fraction of CIK cells. The loss of the expression of transposase during the differentiation was assessed to assure the genome stability of the cellular product by absolute quantification through RT-PCR. Finally, preliminary insertion-site analysis by LAM-PCR confirmed that the integrations in the genome of SB system do not correlate with the genes-enriched regions.
Conclusions: SB system together with an optimized method of differentiation efficiently expand CD123. CAR+ and CD19. CAR+ CIK cells, redirect their activity towards AML and ALL cells, and retain a safe pattern of integrations in the genome. An easy clinical-grade adoptive cell therapy platform based on an innovative non viral method of gene transfer will be fundamental to improve the range of applications of immunotherapy to control relapse in leukemic patients.

P-173

A PHASE I DOSE-ESCALATION STUDY OF PEGCRISANTASPASE ADMINISTERED BY INTRAVENOUS INFUSION IN ADULT PATIENTS WITH RELAPSED OR REFRACTORY HEMATOLOGICAL MALIGNANCIES

G. Salles[1], S. Lepretre[2], S. Le Gouill[3], F. Rigal-Huguet[4], C. Haioun[5], S. Balouet[6], T. Corn[7], X. Thomas[1]

[1]Département d'Hématologie, Hospices Civils de Lyon – Université Claude Bernard Lyon-1, Pierre-Bénite, France; [2]Département d'Hématologie, Centre Henri Becquerel, Rouen, France; [3]Hématologie Clinique, Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]Service d'Hématologie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [5]Lymphoid Malignancies Unit, Centre Hospitalier Universitaire Henri Mondor, Créteil, France; [6]The Lymphoma Academic Research Organisation (LYSARC), Centre Hospitalier Lyon-Sud, Pierre-Bénite, France; [7]Department of Clinical Oncology, EUSA Pharma (An international division of Jazz Pharmaceuticals plc), Oxford, United Kingdom

Objectives: Asparaginase is an important component of chemotherapy to treat acute lymphoblastic leukemia and lymphoma. Hypersensitivity occurs in 10%-30% of patients receiving *Escherichia coli*-derived asparaginases, often necessitating a switch to asparaginase *Erwinia chrysanthemi*. Due to a short half-life, asparaginase *Erwinia chrysanthemi* is administered 3 times a week. To improve pharmacokinetics and reduce immunogenicity, recombinant PEGylation technology was used to create a new *Erwinia chrysanthemi*-asparaginase, pegcrisantaspase. The objective of this open-label, multicenter, dose-escalation study was to determine the maximum tolerated dose, safety, and pharmacokinetics of pegcrisantaspase in patients with relapsed or refractory hematological malignancies.
Methods: Patients aged 18-50 years received pegcrisantaspase intravenously once every 2-4 weeks; initial dose was 500 IU/m^2. Dosing continued until disease progression if judged appropriate by the investigator. Dose escalation was based on the number of patients experiencing dose-limiting toxicity (DLT) within 14 days of first infusion. Patients with active CNS disease or previous hypersensitivity (grade ≥2) to asparaginase *Erwinia chrysanthemi* were excluded.
Results: Ten patients (mean age: 40.6 years) have enrolled to date. All patients had failed multiple therapy regimens. Six and 3 patients dosed at 500 IU/m^2 and 750 IU/m^2, respectively, maintained asparaginase activity >0.1 IU/mL at 14 days. Three patients maintained target activity after week 5 following the second dose of 500 IU/m^2. One DLT was observed with 750 IU/m^2 (neutropenia lasting >7 days). Most common adverse events (>30%) were diarrhea, anemia, hypoalbuminemia, decreased antithrombin III, and nausea. Three deaths occurred following 500 IU/m^2 (1 cerebral hemorrhage; 2 disease progression), and 1 after 750 IU/m^2 (disease progression); none were considered study drug-related.
Conclusions: Pegcrisantaspase 500 IU/m^2 and 750 IU/m^2 provide effective serum asparaginase activity for 14 days following intravenous infusion. Safety data are consistent with the known safety profile of asparaginase treatment and with comorbidities and disease progression in this patient population.
Study funded by Jazz Pharmaceuticals plc or its subsidiaries.

P-174

SFCE METRO-01 FOUR-DRUG METRONOMIC REGIMEN PHASE II TRIAL FOR PEDIATRIC EXTRACRANIAL SOLID TUMOURS

A. Verschuur[1], A. Aschero[2], P. Petit[2], S. Roffe-Vidal[3], P. Chastagner[4], P. Leblond[5], I. Aerts[6], N. Corradini[7], N. Entz-Werle[8], L. Tessonnier[9], N. André[1]

[1]Pediatric Hematology and Oncology, La Timone Children's Hospital, Marseille, France; [2]Pediatric Radiology, La Timone Children's Hospital, Marseille, France; [3]CIC-CPCET, La Timone Children's Hospital, Marseille, France; [4]Pediatric Oncology, Children's Hospital, Nancy, France; [5]Pediatric Oncology, Centre Oscar Lambret, Lille, France; [6]Pediatric Oncology, Institut Curie, Paris, France; [7]Pediatric and Adolescent Oncology, Mothers-Children's Hospital, Nantes, France; [8]Pédiatrie Onco-Hématologie, CHU Hautepierre, Strasbourg, France; [9]Biophysics and Nuclear Medicine, La Timone University Hospital European Center for Research in Medical Imaging, Marseille, France

Objectives: To investigate the anti-tumour activity of a 4-drug metronomic therapy (MT) in relapsing/progressing pediatric extracranial solid tumours (EST). Primary objective was no progression after 2 cycles of therapy.
Methods: Patients of ≥4 to 25 years of age with progressing EST and adequate organ function. Treatment consisted of an 8-week cycle of oral celecoxib BID, weekly vinblastine 3 mg/m2, oral cyclophosphamide 30 mg/m2/d qd for 3 weeks alternating with oral methotrexate 10 mg/m2 twice a week for 3 weeks, with a 2-week rest. Maximum treatment was 2 years. Kepner- Chang two steps model was used with 10 patients in first stage. If primary objective was reached in 2 or more patients, 8 additional patients were included according to 4 groups: Neuroblastoma (NBL), Soft-tissue sarcoma (STS), Bone sarcoma (BS), Miscellaneous (Misc). IRB approval was obtained.

Results: 38 patients were evaluable: 6 STS with 1 SD and 1 MR (angiosarcoma) after 2 cycles: 1 patient with metastatic hemangioendothelioma stabilized and is currently at 16 months of therapy; 8 Misc with no significant stabilization observed; 10 BS (8 osteosarcoma and 2 Ewing) all progressed. In the NBL group the second stage opened with currently 3 out of 14 patients (21%) being stable after 2 cycles. Of the patients with SD, 1 stopped MT after 4 cycles being stable (physician's choice) and 2 patients remained stable for 1 year. Ten patients progressed before cycle 3, 1 not yet evaluated. Median number of cycles was 1.5 (range 0.5-6). Treatment was interrupted temporarily in 8 patients for grade 3/4 toxicity (2 hepatic and/or 6 haematological).
Conclusions: This MT has no activity in BS and Misc and limited though interesting activity in NBL and STS with some patients being stable for > 1 year. (This study was supported by "Enfants et Santé" Foundation and PHRC-grant).

P-175

SFCE METRO 01 FOUR-DRUG METRONOMIC REGIMEN HAS ANTI-TUMOUR ACTIVITY IN PEDIATRIC LOW-GRADE GLIOMA

A. Verschuur[1], P. Dory-Lautrec[2], S. Roffe-Vidal[3], P. Chastagner[4], P. Leblond[5], I. Aerts[6], N. Corradini[7], N. Entz-Werle[8], S. Honoré[9], J.C. Gentet[10], N. André[10]

[1]Pediatric Hematology and Oncology, La Timone Children's Hospital, Marseille, France; [2]Neuroradiology, La Timone Children's Hospital, Marseille, France; [3]CIC-CPCET, La Timone Children's Hospital, Marseille, France; [4]Pediatric Oncology, Children's Hospital, Nancy, France; [5]Pediatric Oncology, Centre Oscar Lambret, Lille, France; [6]Pediatric Oncology, Institut Curie, Paris, France; [7]Pediatric and Adolescent Oncology, Mothers-Children's Hospital, Nantes, France; [8]Pédiatrie Onco-Hématologie, CHU Hautepierre, Strasbourg, France; [9]Department of Clinical Pharmacy, La Timone Children's Hospital, Marseille, France; [10]Pediatric Hematology and Oncology, La Timone Children's Hospital, Marseille, France

Objectives: To investigate the anti-tumour activity of a 4-drug metronomic regimen in relapsing/progressing pediatric brain tumours (BT) as defined as progression-free survival (PFS) after 2 cycles (4 months) of therapy.
Methods: Patients of ≥4 to 25 years of age with progressing BT and adequate organ function. Treatment consisted of an 8-week cycle of oral celecoxib BID daily (D1-D56), 100/200/400 mg according to BW, weekly IV vinblastine 3 mg/m^2, oral cyclophosphamide 30 mg/m^2/d qd for 3 weeks alternating with oral methotrexate 10 mg/m^2 twice a week for 3 weeks, with a 2-week rest period. Maximum treatment was 2 years. Kepner and Chang two-steps model was used with 10 patients in the first stage. If primary objective was reached in 2 or more patients, 8 additional patients were recruited. This regimen was considered efficacious if PFS after 2 cycles was over 34% (alpha 10%, beta 10%). Approval was obtained from IRB and french medical agency.
Results: 16 patients were included: 2 medulloblastoma (MB), 4 high grade glioma (HGG) (2 of which DPIG), 9 low grade glioma (LGG, one BSG), 1 meningioma. One patient with HGG (anaplastic oligodendroglioma) stabilized for 2 years. None of the other HGG or MB were stabilized. Of the 9 patients with LGG, median age was 9 years, median duration of illness at inclusion was 6 years and 7 patients received vinblastine previously. 1 PR was observed, 6 SD, 2 PD (1 BSG) after 2 cycles. Median number of cycles was 4.0 (range 1.0-12). Four patients received at least 1 year of therapy and 7 are alive. Treatment was interrupted temporarily in 4 patients for grade 3/4 toxicity (hepatic and/or hematological).
Conclusions: This metronomic regimen is active in patients with LGG, even if patients had received vinblastine previously. (This study was supported by "Enfants et Santé" Foundation and National PHRC-grant).

P-176

ANALYSIS OF ANGIOGENIC MARKERS DURING SFCE METRO-01 FOUR-DRUG METRONOMIC REGIMEN PHASE II TRIAL FOR PEDIATRIC MALIGNANCIES IN PROGRESSION

A. Verschuur[1], L. Arnaud[2], S. Roffe-Vidal[3], F. Sabatier[2], N. André[1]

[1]Pediatric Hematology and Oncology, La Timone Children's Hospital, Marseille, France; [2]: Laboratory of Hematology and Vascular Biology, La Conception Hospital, Marseille, France; [3]CIC-CPCET, La Timone Hospital, Marseille, France

Objectives: Circulating endothelial cells and progenitors have been suggested as biomarkers indicative of angiogenic activity, with potential clinical value in monitoring of metronomic chemotherapy. This study investigated changes in angiogenic biomarkers during a 4-drug metronomic regimen in relapsing/progressing pediatric solid tumours (ST).
Methods: Patients of ≥4 to 25 years of age with adequate organ function with progressing ST. Treatment consisted of an 8-week cycle of oral celecoxib BID daily (D1-D56), weekly iv vinblastine 3 mg/m2, oral cyclophosphamide 30 mg/m2/d qd for 3 weeks alternating with oral methotrexate 10 mg/m2 twice a week for 3 weeks, with a 2week rest. Venous blood samples were obtained at inclusion, days 22, end of the first and second cycle and at progression. CD34+CD45-7AAD- Endothelial Progenitor Cells (EPC) were enumerated using flow cytometry. Circulating Endothelial Cells (CEC) counts, and Vascular Endothelial Growth Factor (VEGF) levels were determined using CD146-based immune-magnetic separation and ELISA respectively. IRB approval was obtained and patients/parents gave informed consent.
Results: Twenty-one patients were included: 8 with brain tumours and 13 extracranial tumours. EPC and VEGF levels did not significantly vary during the metronomic regimen. At baseline, CEC values were widely distributed with 5 patients having high CEC levels. Metronomic regimen is associated to a trend toward CEC decrease. Interestingly, CEC counts significantly increased at progression compared to value at the preceding time (81 cells/mL +/- 110 vs 9.53 cells/mL +/- 15.61).
Conclusions: Among biomarkers of angiogenesis, changes in CEC may reflect the impact of SFCE METRO-01 four-drug metronomic regimen on neovascularization. Sequential measurement of CEC levels may provide tools for monitoring the response to treatment and/or progression.
(This study was supported by "Enfants-et-Santé" Foundation and PHRC-grant).

P-177

PROGNOSTICATION OF PEDIATRIC ONCOLOGY PATIENTS ENROLLED IN PHASE I CLINICAL TRIALS DESIGNED FOR ADULTS

V. Subbiah[1], F. Corrales-Medina[2], C.E. Herzog[2], K. Hess[3], P.M. Anderson[4], W.W. Huh[5], E. Kleinerman[5], R. Kurzrock[6]

[1]Phase 1 program, UT MD Anderson Cancer Center, Houston, USA; [2]Pediatrics, UT MD Anderson Cancer Center, Houston, USA; [3]Biostatistics, UT MD Anderson Cancer Center, Houston, USA; [4]Pediatric Oncology/BMT/Cell Therapy, Levine Children's Hospital/Levine Cancer Institute, Houston, USA; [5]UT MD Anderson Cancer Center, Pediatrics, Houston, USA; [6]Division of Hematology & Oncology, UC San Diego Moores Cancer Center, San Diego, USA

Objectives: Most pharmaceutical industry sponsored trials excludepatients less than 18 years in phase 1 clinical trials. Even in the era of targeted therapy pediatric patients have to wait for most phases of trials to be completed in adults to enroll in clinical trials in the advanced metastatic and relapsed setting. We report the preliminary analyses of the outcomes of pediatric patients enrolled in phase 1 studies designed for adults at a major cancer center.
Methods: We reviewed the medical records of 40 pts < 18 years treated in ≥ 1 phase I trial at MD Anderson (2005-2012). We used univariate and multivariate analyses to determine which baseline clinicopathologic characteristics, including RMH and MDACC scores, were associated with increased or decreased overall and progression-free survival.
Results: The median overall survival duration from the time of enrollment in a phase I trial was 8.5 months (95% CI, 5.5-13.2 months). In the multivariate analysis, age ≥15 was the only independent factor that predicted increased overall survival (P = 0.0065), and >3 prior therapies (P = 0.053) predicted decreased overall survival. The median progression-free survival duration was 2.8 months (95% CI, 2.3-4.1 months. In the multivariate analysis, independent factors that predicted increased progression-free survival were age ≥15 years (P < 0.001) and prior radiation therapy (P = 0.049); performance status >1 (P < 0.001) and >3 prior therapies (P = 0.002) predicted decreased progression-free survival.
Conclusions: It is feasible to conduct phase I studies in pediatric patients based on adult protocols. There was no mortality related to phase 1 therapy. A composite score using a larger number of patients needs to be developed using the RMH and MDACC scores in future trials. In the era of targeted therapy more trials should allow pediatric patients earlier in the drug development especially if deemed safe in adults in early phase trials.

P-178

SOLID TUMORS OF CHILDHOOD DISPLAY SPECIFIC SERUM MICRORNA PROFILES

M. Murray[1], K.L. Raby[1], H.K. Saini[2], S. Bailey[1], S.V. Wool[3], J.M. Tunnacliffe[3], A. Enright[2], J.C. Nicholson[3], N. Coleman[1]

[1]Department of Pathology, University of Cambridge, Cambridge, United Kingdom; [2]European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI), Cambridge, United Kingdom; [3]Department of Paediatric Haematology and Oncology, Addenbrooke's Hospital, Cambridge, United Kingdom

Objectives: Currently, the diagnosis and risk-stratification of childhood solid tumors is heavily reliant upon histopathological findings. The availability of serum biomarkers would improve the accuracy and timeliness of diagnosis and reduce the need for invasive procedures for patients with these tumors. We hypothesized that the differential expression and/or release of microRNAs by solid tumors of childhood may be detected as altered serum microRNA profiles.
Methods: We undertook global quantitative reverse-transcription polymerase chain reaction (qRT-PCR) microRNA profiling (n = 741) on RNA extracted from 54 serum samples, representing 34 taken from patients at the time of diagnosis of common childhood cancers (including neuroblastoma, Wilms tumor, sarcoma, hepatoblastoma, lymphoma, central nervous system glioma) plus 20 reference samples. Robust quality control steps for RNA extraction and qRT-PCR efficiency using non-human spike-in RNA/DNA and hemolysis assessment were next performed and 53/54 samples (98.1%) were suitable for full profiling. Multiple methods to normalize the global data were assessed, which showed that the 'global mean' approach was optimal. We generated a panel of six top-ranking most stable microRNAs suitable for normalization for microRNA qRT-PCR in pediatric serum samples.

Results: Tumor-specific serum microRNA profiles were identified for each tumor type. Selected microRNAs underwent confirmatory testing using a subset of 17 tumor and four control samples from the profiling set, plus four independent samples from patients with neuroblastoma. Striking findings for *MYCN*-amplified high-risk neuroblastoma (MYCN-NB) were noted, with a panel of microRNAs (miR-124-3p/miR-9-3p/miR-218-5p/miR-490-5p/miR-1538) highly over-expressed compared with the other tumor and control groups, including non-*MYCN*-amplified low-risk neuroblastoma (NB).
Other 'differential diagnosis' panels were also identified for distinguishing an abdominal mass (Wilms tumor *vs*. MYCN-NB/NB), liver mass (hepatoblastoma *vs*. MYCN-NB/NB), subtypes of sarcoma and lymphoma.
Conclusions: This study demonstrates the feasibility of robust diagnostic serum microRNA profiling in solid tumors of childhood, and has identified candidate microRNA profiles for testing in larger, prospective studies.

P-179

CHIMERIC HCMV/HSV-1 IS SUPERIOR TO ICP34.5-DELETED HSV-1 AT INFECTING PEDIATRIC-DERIVED GLIOBLASTOMA XENOGRAFT CELLS INCLUDING CD133+ GLIOMA STEM CELLS IN PHYSIOLOGIC HYPOXIA

G.K. Friedman[1], L. Nan[1], M.C. Haas[1], V.M. Kelly[1], E.A. Beierle[2], J.M. Markert[3], G.Y. Gillespie[3], K.A. Cassady[1]

[1]Department of Pediatrics, University of Alabama at Birmingham, Birmingham, USA; [2]Department of Surgery, University of Alabama at Birmingham, Birmingham, USA; [3]Department of Neurosurgery, University of Alabama at Birmingham, Birmingham, USA

Objectives: Oncolytic engineered herpes simplex virotherapy has emerged as a promising treatment for glioblastoma, however the efficacy of a ($_1$34.5-deleted (ICP34.5-) HSV-1 (C101), similar to viruses previously used in high-grade glioma clinical trials, was reduced in physiologic hypoxia, a hallmark of glioblastoma. Physiologic hypoxia supports and maintains the glioma stem cell (GSC) phenotype and has a vital role in tumor development, invasiveness, and resistance to chemotherapy and radiation. We investigated the ability of a chimeric HCMV/HSV-1 virus (C154), which contains the HCMV *IRS1* gene to improve late viral protein synthesis, to infect and kill tumor cells including CD133+ GSCs in hypoxia from a pediatric patient-derived glioblastoma xenograft. A non-green fluorescence protein (GFP) - expressing version of C154 (C134 HSV) is being prepared for clinical trials.
Methods: D456 tumors, maintained in the flanks of nude mice, were disaggregated, placed under hypoxia (1% oxygen) and maintained as neurospheres in stem cell-defined medium. Relative infectivities of tumor cells and CD133+ GSCs by GFP-expressing C101 and C154 at 10 plaque-forming units (PFU)/cell were quantified 30 hours post-infection by FACS analysis. Virus recovery measured by limiting plaque dilution and cytotoxicity measured by the AlamarBlue assay were determined 48 and 72 hours post-infection, respectively.
Results: By 30 hours post-infection, C154 infected $48.9 \pm 1.2\%$ of cells compared to only $26.4 \pm 0.9\%$ of cells for C101 ($p < 0.0001$). C154 infected significantly more CD133+ cells (1.5x, $p < 0.0001$) than C101. A significantly lower dose of C154 was required to kill 50% of the cells (LD_{50}) than C101 (3.9 ± 0.4 PFU/cell versus 10.7 ± 0.8, $p = 0.0002$). Over 200-fold more C154 virus was recovered than C101 ($p = 0.0004$).
Conclusions: The chimeric HCMV/HSV-1 virus is superior to ($_1$34.5-deleted HSV-1 at infecting a pediatric-derived glioblastoma xenograft under physiologic hypoxic conditions, and may be effective at targeting pediatric high-grade gliomas including chemotherapy and radiation resistant GSCs.

P-180

NATURAL KILLER CELL BASED THERAPIES FOR METASTATIC OSTEOSARCOMA

A. Pérez-Martínez[1], L. Fernandez[2], J. Valentín[1], M. Zalacaín[3], L. Marrodán[3], I. Martínez[4], A. Patiño[3]

[1]Pediatric Hemato-Oncology, Hospital Universitario La Paz.IdiPAZ. Universidad Autonoma de Madrid, Madrid, Spain; [2]Clinical Research Group, Cancer National Research Center, Madrid, Spain; [3]Pediatric Hemato-Oncology, Clínica Universitaria de Navarra, Madrid, Spain; [4]Pediatra. Centro de Salud de Carabanchel Alto. Madrid, Spain

Objectives: Metastatic osteosarcoma has a dismal prognosis despite conventional treatment. New therapeutic approaches are urgently needed to improve survival. Natural Killer (NK) cells are lymphocytes with cytotoxic activity toward malignant cells. Crosstalk between NK cell receptors and tumour cell ligands is necessary for anti-cancer activity. In the present study we explored ex-vivo and in vivo feasibility of NK cell–mediated therapies against primary metastatic osteosarcoma.
Methods: HLA class I, Fas, NKG2D and DNAM-1 ligands expression in 19 metastatic primary osteosarcoma and NK receptors on activated and expanded NK (NKAE) cells were analyzed by multiparametric flow cytometry. NKAE cells were obtained by co culture of peripheral blood mononuclear cells (PBMCs) from donors and patients with the K562mbIL15-41BBL cell line in RPMI supplemented with 10% human AB serum, 100 IU/mL IL-2, and 1% penicillin and streptomycin. We performed ex-vivo cytotoxicity with NK cell receptor blocking antibodies by a conventional 2-h europium-TDA release assay to explore NK cell susceptibility from primary osteosarcoma to be lysed by NKAE. In addition we explored different strategies (irradiation, gemcitabine and spironolactone) to increase osteosarcoma NK cell cytotoxic susceptibility.
Results: We found ULBP3, Fas and CD112 were highly expressed (ratio MFI $\geq$10) in 13/19 of the primary cell lines. Specific antibodies blockade shown Fas-FasL and NKG2D pathways have a main role in the NK cell antitumor activity. We found spironolactone upregulated NKG2D and DNAM-1 ligands expression. Finally we have developed an in vivo orthotopic and metastatic osteosarcoma xenograft to explore successfully ex vivo therapies.
Conclusions: CD112, NKG2D ligands and Fas are expressed in metastatic osteosarcoma cells. Although these tumours shown heterogeneity to NK cell lysis, NKG2D/NKG2DL and Fas/FasL pathways were responsible for NK cell elimination. The upregulation of NKG2D ligands mediated by spironolactone could enhance NK cell mediated lysis ex vivo and in vivo.

P-181

A SIMPLE FORMULA BASED ON CYSTATIN C FOR INDIVIDUAL CARBOPLATIN DOSING IN CHILDREN

H. Blufpand[1], A.J. Wilhelm[2], G.J.L. Kaspers[1], G.J. Peters[3], A. Bökenkamp[4]

[1]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Clinical Pharmacology and Pharmacy, VU University Medical Center, Amsterdam, Netherlands; [3]Medical Oncology, VU University Medical Center, Amsterdam, Netherlands; [4]Pediatric Nephrology, VU University Medical Center, Amsterdam, Netherlands

Objectives: As carboplatin clearance is linearly related to glomerular filtration rate, the principle of renal function-based dosing is widely accepted although not always practiced. The prediction of carboplatin clearance could be improved by adding plasma cystatin C to other patient characteristics routinely used for dosing. We aimed to evaluate the usefulness of cystatin C as a predictor of carboplatin clearance in children and develop a simple model that can be used for dosing.
Methods: We performed a population pharmacokinetic analysis on 78 clearance studies performed in 30 children with a wide spectrum of solid tumors, using non-linear mixed effect modeling. The influence of six covariates (sex, age, body weight, height, BMI, BSA, creatinine and cystatin C) on carboplatin pharmacokinetics was evaluated. The final model was validated using bootstrap analysis.
Results: A two-compartment model was fitted to the time-concentration data. The best equation was: carboplatin clearance = 2.63 x (*cystatin C*/0.695) $^{-0.637}$ x (*body weight*/15.72) $^{0.79}$ with clearance in L/h, cystatin C in mg/L and weight in kilograms. The mean parameters obtained from the 1,000 bootstrap runs were almost identical to the estimates obtained from the original dataset, indicating the model is robust. Observed carboplatin concentrations were accurately predicted by the final model. The correlation between observed and predicted clearance was almost perfect ($R^2 = 0.92$; $P < 0.001$). Bias (%MPE) and imprecision (% MAPE) of the final model were 1.8% and 15.6% respectively.
Conclusions: A model based on cystatin C and weight gives the best prediction of carboplatin clearance in children. This simple model can be used for individualized dosing of carboplatin.

P-182

CARBOPLATIN DOSING IN CHILDREN USING ESTIMATED GLOMERULAR FILTRATION RATE: EQUATION MATTERS

H. Blufpand[1], G.J.L. Kaspers[1], A.J. Wilhelm[2], G.J. Peters[3], A. Bökenkamp[4]

[1]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Clinical Pharmacology and Pharmacy, VU University Medical Center, Amsterdam, Netherlands; [3]Medical Oncology, VU University Medical Center, Amsterdam, Netherlands; [4]Pediatric Nephrology, VU University Medical Center, Amsterdam, Netherlands

Objectives: Renal function-based carboplatin dosing results in more consistent drug exposure than flat dosing. We aimed to validate the Newell dosing equation using estimated glomerular filtration rate (GFR) and study which renal function marker most accurately predicts carboplatin clearance in children.
Methods: In 30 children with a wide spectrum of solid tumours, 78 carboplatin clearance values were obtained from individual fits using NONMEM. Observed carboplatin clearance was compared with predicted clearance calculated according to the Newell dosing equation using three different GFR estimates, one creatinine-based (eGFR-Schwartz), one cystatin C-based (eGFR-CKiD1) and one based on creatinine and cystatin C (eGFR-CKiD2). Bias and precision of the predictions was examined.
Results: Both CKiD equations were accurate with a bias of 1.7 (95%CI -1.7 to 5.1) and -3.3 (95%CI -7.0 to 0.35) ml/min for respectively eGFR-CKiD1 and CKiD2, whereas the bias of eGFR-Schwartz significantly differed from zero (−16.2; 95%CI -21.5 to -10.9 ml/min). eGFR-CKiD1 gave the lowest bias and imprecision, the other two eGFR equations showed overprediction of carboplatin clearance as reflected by negative bias and higher mean prediction error values. The proportion of variance in observed clearance that can be explained by the predicted clearance was lowest for Schwartz ($R^2 = 0.58$), the explained variance was 0.65 for both CKiD equations.
Conclusions: The two cystatin C-based CKiD equations outperform the widely used creatinine-based Schwartz equation in predicting carboplatin clearance. We recommend the use of estimated GFR based on cystatin C for carboplatin dosing in children unless a gold standard GFR measurement is available.

P-183

ASSOCIATION OF HEMORRHAGIC CYSTITIS WITH GSTM1 AND CYP2C9 GENOTYPES IN PEDIATRIC PATIENTS RECEIVING BUSULFAN BASED CONDITIONING REGIMEN PRIOR TO HEMATOPOIETIC STEM CELL TRANSPLANTATION

C.R.S. Uppugunduri[1], M.A. Rezgui[2], P. Huezo-Diaz[1], A. Tyagi[1], J. Rousseau[2], M. Duval[2], H. Bittencourt[2], M. Krajinovic[2], M. Ansari[1]

[1]Department of Pediatrics Onco-Hematology Unit CANSEARCH Research Laboratory, University Hospitals of Geneva, Geneva, Switzerland; [2]Department of Pediatrics CHU Sainte-Justine, Charles-Bruneau Cancer Center, Montreal, Canada

Objectives: One of the complications of Busulfan (BU) based myeloablative conditioning regimen especially in combination with cyclophosphamide (CY) in children prior to hematopoietic stem cell transplantation (HSCT) is occurrence of hemorrhagic cystitis (HC). In this study we explored the association of genetic variants in GSTM1 which is involved in metabolism of BU and CYmetabolites, CYP2C9 (involved in formation of sulfolane and activation of CY), and ALDH3A1 (enzyme detoxifying CY metabolites) in relation to the incidence of HC before day 30 post-transplant.
Methods: Sixty six pediatric patients (33 females, 33 males) recruited at St. Justine's hospital, Canada were retrospectively analyzed. All patients were genotyped for *GSTM1* null, *CYP2C9**2, *3 and *ALDH3A1**2 alleles. HC was defined as the presence of hematuria (both microscopic and macroscopic) for more than a week from the initiation of the conditioning regimen up to 30 days post-transplant. All patients received MESNA as prophylaxis for HC.
Results: Cumulative incidence of HC was 19.7% and BK virus was detected in 85% of the HC cases. We observed higher incidences of HC in carriers of both functional *GSTM1* and *CYP2C9* (36%, n = 25) compared to those carrying non-functional allele in either or both of these genes (9.7%, n = 41). Significant correlation between age, weight and incidence of HC was also seen. In multivariate analysis including conditioning regimen, age, weight, gender, *ALDH3A1**2 genotype, BU steady state concentration levels only combined *GSTM1* and *CYP* genotype status was independently associated with HC with hazards ratio of 4.2 (1.3-13.6).
Conclusions: In view of these observations, we hypothesize that normal *GSTM1* and *CYP2C9* function indicates either higher formation of sulfolane from BU or CY toxic metabolites. Functional *GSTM1* genotypes indicates increased formation of GST conjugates for BU intermediary compounds and simultaneously might deplete GSH levels, to be available for other conjugating enzymes (GSTA1, P1 and T1) predominantly involved in toxic CY metabolites elimination.

P-184

INAPPROPRIATE CARBOPLATIN EXPOSURE IN CHILDREN AFTER FLAT DOSING

H.N. Blufpand[1], A. Bökenkamp[2], G.J.L. Kaspers[1]

[1]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Pediatric Nephrology, VU University Medical Center, Amsterdam, Netherlands

Objectives: Although the concept of renal function-based carboplatin dosing is well-established in children, this dosing method is not routinely practiced. Failure to correct for renal function results in variable carboplatin exposure, with the risk of adverse effects and suboptimal treatment. We set out to determine carboplatin exposure in children after flat dosing and compared this with targeted exposure.
Methods: In 30 children with a wide spectrum of solid tumors, the area under the concentration-time curve (AUC) was calculated after 78 courses of carboplatin using NONMEM. Observed AUC values were compared with target values, calculated as 1.325 mg/mL.min per 100 mg/m^2 of protocol dose. Bias, precision and accuracy within 20% of target AUC were calculated.

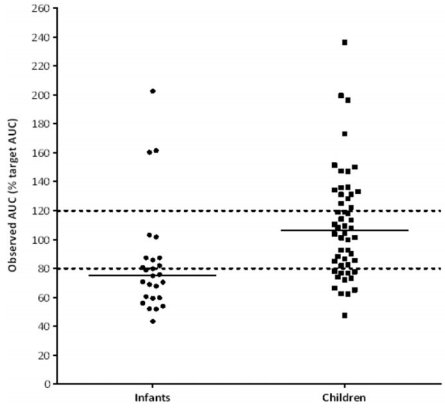


Figure. Observed AUC as percentage of target AUC for infants and older children

Results: Median observed AUC as a percentage of target AUC was 89% (range 43%-236%). AUC within 20% of target was achieved in 42% of courses (Figure). This proportion was slightly lower in infants (27%) than in older children (44%; $P = 0.139$). In infants, most measurements fell below 80% of the target value (62%), as opposed to 23% underestimation in older children ($P = 0.001$).
Conclusions: Dosing based on body surface area or body weight results in highly variable carboplatin exposure, particularly in infants, with the risk of toxicity as well as a lower cure-rate. This once more underscores the importance of renal function-based carboplatin dosing in children.

P-185

NOVEL FORMULATIONS TO TARGET OXIDATIVE STRESS IN PRECLINICAL MODELS OF RETINOBLASTOMA

R. Brennan[1], E. Pritchard[2], E. Stewart[1], C. Bradley[3], B. Freeman[4], W. Caufield[4], M.A. Dyer[3], K. Guy[2]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Chemical Biology and Therapeutics, St. Jude Children's Research Hospital, Memphis, USA; [3]Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis, USA; [4]Preclinical PK Shared Resource, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Overall survival for patients with intraocular retinoblastoma (RB) is excellent; however, globe salvage in advanced disease and survival for patients with metastatic disease remains poor. While whole genome sequencing of retinoblastoma revealed that epigenetic deregulation is essential for tumor development, the presence of double-stranded DNA breaks and G-to-T or C-to-A transversions indicates a possible role for oxidative stress in tumorigenesis. Congruent with this finding, a targeted drug screen of retinoblastoma cells utilizing a library of over 300 anti-neoplastic agents revealed activity of histone deacetylase inhibitors (HDACi). This study evaluated the efficacy of HDACi in preclinical models of RB, optimized the ocular formulation and characterized the pharmacokinetic and toxicity profile of this class of new agents in the retinoblastoma arsenal.
Methods: Panobinostat and vorinostat were selected for characterization. We developed an ocular formulation using FDA approved adjuvants, identifying a topical and intravitreal formulation for ocular delivery. We performed pharmacokinetics and compared the vitreal penetration to systemic dosing. Due to differences in the epigenomic landscape of retinoblastoma mouse models compared with human retinoblastoma, we utilized the human orthotopic xenograft for efficacy studies, monitoring intraocular pressure (IOP) as a proxy for disease progression. Eyes with progressive disease underwent enucleation.
Results: Comprehensive preclinical testing following a standardized approach demonstrated a significant ocular survival advantage with HDACi compared to systemic and subconjunctival chemotherapy. Topical delivery of panobinostat resulted in improved intraocular penetration compared with intravitreal, subconjunctival and systemic dosing. Retinal toxicity following HDACi administration was minimal.
Conclusions: Panobinostat, an HDACi, is a promising targeted therapy for retinoblastoma. Topical application is effective at penetrating the vitreous, and may be useful in a protracted, outpatient dosing regimen. Pediatric phase I testing of oral panobinostat is ongoing and will inform future plans for a clinical trial with this drug in retinoblastoma patients.

NURSING

P-186

PSYCHOSOCIAL CONCERNS EXPRESSED BY CHILDHOOD CANCER SURVIVORS IN ACCRA, GHANA

C.A. Adu[1]

[1]Department of Child Health, Korle Bu Teaching Hospital, Accra, Ghana

Objectives: This study seeks to determine the psychosocial concerns expressed by childhood cancer survivors and what interventions can be instituted by health workers to help address these issues.
Methods: Twenty Ghanaian childhood cancer survivors aged 13 to 35 years were interviewed after consent had been obtained from them. A questionnaire was administered to them during the months of February and March 2014.
Results: Twenty five percent completed treatment less than 5 years ago and 50%, 5-10 years ago. All knew their diagnosis of cancer with 75% having been told at diagnosis. Most support had been from parents and family. Survivors (85%) remember treatment affecting their ability to play and take care of themselves. It affected the finances of all the families with all the mothers having to stay at home to look after them. Over 80% felt stigmatized by friends and it affected their schooling and social life. All the children remember friends who died and this has affected them. All the survivors are concerned about their future ability to marry and have children. 75% of them feel they are stronger and better off than their siblings and peers. Fifty percent still worry about a return of cancer but 50% expressed optimism believing that they were completely healed. 75% felt they were now well adjusted to life.
Conclusions: Easing the financial burden of families in developing countries is a necessity. Clinical psychologists should be involved to help children cope with the psychosocial effects including stigmatization. Measures should be instituted in POUs in developing countries to

address bereavement as these children often suffer from the loss of friends they have made. Age appropriate information should be made available to survivors addressing issues related to sexuality and reproductive health. Clubs where survivors can interact could be set up where possible.

P-187

A TASK FOR THE PHD NURSE IN A TIME OF GREAT TURNOVER OF NURSES IN PEDIATRIC ONCOLOGY

M. af Sandeberg[1]

[1]Pediatric hematology and oncology, Karolinska University Hospital, Stockholm, Sweden

Objectives: The overall aim is to meet the demands of an evidencebased childhood cancer care; to promote good quality of care and patient safety and also greater job satisfaction and lower turnover of nurses.
Methods: A position has been created at the pediatric oncology center and the appointed PhD nurse is initiating quality improvement projects and supervising bedside nurses in performing them.
Results: A number of projects have been performed. For example, since 2002 lidocaine has been given together with the hypotonic, and painful, injection solution of PEG-asparaginase. Despite the change to an isotonic solution in 2008 the same routine continued. A general feeling of parents and staff that lidocaine caused pain resulted in a study aiming to compare children's/parents' perceptions of intramuscular PEG-asparaginase given with and without local anesthesia with lidocaine. All participants (N = 14) preferred to continue without lidocaine and it is no longer given before PEG-asparaginase injections. Another project started due to discussions between nurses and physicians about gastronomies. The opinion of the nurses was that gastrostomies should be offered more often. However, physicians were hesitant referring to the high risk of complications. A retrospective review of medical records identified gastrostomies and gastrostomy-related complications in children and adolescents with cancer at the center. Gastrostomy-related complications were very common, but few were severe. Furthermore, an ongoing project aim to compare milk and molasses enema with the more established enema with docusate sodium and sorbitol regarding efficacy on constipation and the degree of discomfort for the child with cancer.
Conclusions: The new position enables a scientific approach in small quality improvement projects performed by bedside nurses. The competence of the PhD nurse is utilized in nursing care and while care is evidencebased the job satisfaction of bedside nurses is improved.

P-188

INFRINGING ON AUTONOMY – AN ETHICAL CONCERN EXPERIENCED BY NURSING STAFF

C. Bartholdson[1], K. Lützén[1], K. Blomgren[1], P. Pergert[1]

[1]Women and Children's Health, Karolinska Institutet, Stockholm, Sweden

Objectives: A study regarding ethical issues and ways to deal with them has been conducted in pediatric cancer care. Ethical issues are common in pediatric care and arise in connection with value conflicts within an individual and/or between individuals, concerning which of the possible options should be chosen. Each child's specific situation might lead to disagreements about treatment and care. Furthermore, in pediatric care, children's growing autonomy has to be considered.
The purpose of this presentation is to describe one of the ethical concerns which were identified in our study and experienced by nursing staff when caring for children with cancer.
Methods: Physicians, registered nurses and nurse aides working at a children's hospital in Sweden answered a questionnaire. Qualitative content analysis was applied to the open-ended answers.
Results: To infringe on a child's autonomy is not to give the child a chance to decide upon care related concerns by her/himself or to oppose the child's wishes and perform actions and caring procedures that the child does not want. Nurse and nurse aide participants described children's autonomy as something that can be violated and they experienced powerlessness in these situations. Inflicting suffering and limiting truth-telling are subcategories to infringing on autonomy.
Conclusions: Health care professionals' experiences of ethical concerns when, caring for children with cancer, seem to produce strong feelings and moral confusion among nursing staff. Not wanting to inflict suffering on the child and feeling prevented from telling the truth about the circumstances of the child's illness are some examples of nursing care responsibilities that often are connected to medical treatment decisions.

P-189

EXPERIENCE OF PEDIATRIC PROCEDURAL SEDATION AND ANALGESIA IN A TERTIARY CARE HOSPITAL OF PAKISTAN FOR ONCOLOGY PATIENTS

A. Bhimani[1], A. Haque[2], H. Jurair[2], Z. Fadoo[2], S. Imran[1]

[1]Day Care Oncology Unit, Aga Khan University Hospital, Karachi, Pakistan; [2]Pediatrics, Aga Khan University Hospital, Karachi, Pakistan

Objectives: Procedural Sedation Analgesia (PSA) in children is well recognized clinical discipline in developed countries. The aim of this is to describe the experience of PSA from a resource limited country.
Methods: We collected data from our Pediatric PSA database from January 2011 – December 2013. Ketamine and Propfofol IV were used. Success of sedation defined as successful completion of the procedure. Complications defined as hypoxia >1min pulse oximetry less than 90%, apnea>20 sec, cardiac arrest, hallucination & vomiting. All procedures were done according to ASA & AAP guidelines.
Results: 1900 diagnostic and therapeutic procedures performed under PSA. Indication were Intra-thecal (IT) 1287, Bone marrow aspiration (276), Intra-thecal (IT) + Bone marrow aspiration + tryfine (261), PIC line insertion (71) and Abdominal mass biopsy (5). Median dose of Ketamine was 0.5mg/kg and Propofol was 3mg/kg respectively.1880 procedures was successfully performed. Adverse events occurred in 20 (0.88%) patients. Complications were 10 transient de-saturation (0.44%) which resolved by increase flow of O2 and repositioning of airway. 6 apnea (0.26%) which resolved by bag mask ventilation & 3 post sedation hallucination (0.13%) which recorded. 1 sedation failure (0.044%) No cardiac arrest or need of endotracheal intubation.
Conclusions: The Co-administration of small dose of Ketamine and Propofol were found to be safe and effective in children requiring PSA.

P-190

THE LIFE OF THE PRESCHOOL AGED CHILD WITH CANCER IN SWEDEN

L. Darcy[1], M. Björk[1], S. Knutsson[1], K. Enskär[1]

[1]CHILD, School of Health Sciences, Jönköping, Sweden

Objectives: The majority of children who receive a cancer diagnosis are in the 1-to-6 year age group. Survival rates are high, roughly 75%, but treatment is aggressive and requires long and frequent hospital admissions and causes adverse side effects. Health care focus is shifting from surviving childhood cancer to living with it on a daily basis. The young child's experiences are crucial to providing evidence based care. The aim of this study was to explore the everyday life of preschool aged children as expressed by the child and their parents during the first year post diagnosis
Methods: Interviews were conducted with children and their parents connected to a paediatric oncology unit in Southern Sweden. A qualitative content analysis of interview data from three time points, shortly after diagnosis, six months and one year post diagnosis were made.
Results: A dramatic change in the young child's everyday life was described, with experiences of feeling like a stranger, under attack and lonely. Experiences over time of gaining control, making a normality of the illness and treatment and feeling lonely were described. This process may be seen as a striving for an everyday life.
Conclusions: Nurses have a major role to play in the process of striving the child goes through by giving and updating information, making them participary in their care and assuring access to both parents and peers. Ongoing contact with preschool is vital. Addressing these issues and updating them regularly can assist the young child in their transition to living with cancer. Longitudinal studies with young children are vital in capturing their variety of experiences through the cancer trajectory and necessary to ensure quality care.

P-191

THE EFFECTIVENESS OF INTERVENTION ON CHEMOTHERAPY-INDUCED ORAL MUCOSITIS IN HOSPITALIZED PEADIATRIC ONCOLOGY PATIENTS: A SYSTEMIC REVIEW

J. Chen[1], W. Wu[2]

[1]Hematology and oncology department, Shanghai Children's Research Hospital, Shanghai, China; [2]Nursing, Australlian Catholic University, Brisbane, Australia

Objectives: The objective of this review was to determine the best available evidence of vitamin E and granulocyte-macrophage colony-stimulating factor on chemotherapy-induced oral mucositis in hospitalized paediatric oncology patients.
Methods: Databases were searched from 1979 till July 2013. The databases to be searched for published studies in English included: Academic Search Complete, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register of Controlled Trials, EBSCO Medline, EMBASE, PubMed, Science Direct, Proquest, Scopus Database and Proquest dissertation and theses. Two reviewers used standardized critical appraisal instruments from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument to independently evaluate methodological validity of these papers.
Results: The review included five articles that were published from 1976 to 2013 with a total of 314 participants. The five included articles were four RCTs and one quasi-experimental study. The average percentage of topical applied vitamin E was 4.1% in three studies the intervention with topical application of vitamin E had the lowest proportion of severe oral mucositis. Two of five articles presented the results in number of participants with oral mucositis, and other three articles counted the days with oral mucositis. The results of the duration of oral mucositis were not comparable in intervention groups of five included studies.

Conclusions: This review identified five articles that tested the topical application and systemic application of vitamin E and GM-CSF on chemotherapy-induced oral mucositis in hospitalized paediatric oncology patients. It demonstrated that topical application of vitamin E was effective on relieving of oral pain and treating of severe oral mucositis caused by chemotherapy.

P-192

THE NARRATIVE EXPERIENCE OF CHILDHOOD CANCER: A SYSTEMATIC REVIEW AND CRITICAL APPRAISAL

L. Croal[1], L.A. Jibb[1], V. Cheung[2], J.N. Stinson[3]

[1]Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Leadership Sinai Centre, Mount Sinai Hospital, Toronto, Canada; [3]The Peter Gilgan Centre for Research and Learning, The Hospital for Sick Children, Toronto, Canada

Objectives: With improvements in childhood cancer outcomes has come increased interest in the experience of the child under treatment. However, an analysis of the qualitative literature across health-care institutions is lacking. We sought to
systematically review and appraise evidence describing narrative experiences of children receiving cancer treatment to identify gaps in understanding and inform interventions to improve quality of life (QOL).
Methods: Electronic searches were conducted in PsycINFO, MEDLINE, EMBASE, and CINAHL (from database inception to June 2013) for primary qualitative studies. Article inclusion criteria were (1) patient population (0-21 years) receiving active cancer treatment and (2) cancer experience described by the patient. Two independent reviewers assessed articles for relevance and methodological quality, and extracted data.
Results: Of the 3,103 articles identified, 16 with 254 children from 8 countries were included in analysis. Five overarching themes were identified: a family turned upside down (the changed child, the changed family, a changed trajectory); coping strategies (social support, normalization, sustaining hope, spirituality); child in flux (awareness of mortality, protector of loved ones, need for autonomy, reorganization of priorities); managing treatment (information needed, negotiating lifestyle changes, negotiating treatment effects, managing hospitalization); and fluctuating realities (preparing for the worst while hoping for the best, celebrating high-points amidst of low-points, fighting treatment and not cancer).
Conclusions: Cancer has profound impacts on the lives of children living with the disease. The current qualitative evidence suggests day-to-day life, interactions with family, and developmental trajectories are affected. Qualitative research related to intimate relationships and living with uncertainty is needed to broaden understanding of the impact of cancer on children. Age-appropriate and innovative interventions within a culturally diverse and primarily out-patient treatment environment may address identified child psychosocial and educational needs to improve QOL. Interventions should focus on relationships, normalize the child experience, address long-term effects, and better direct healthcare providers.

P-193

ADVANCING NURSING EDUCATION, PRACTICE, AND RESEARCH: THE ROLE AND FUTURE DIRECTIONS OF THE PEDIATRIC ONCOLOGY GROUP OF ONTARIO (POGO) NURSING COMMITTEE IN ONTARIO, CANADA

M.J. De Courcy[1], B. DiMonte[2], C. Bennett[2], C. Armstrong[3], D. Mills[3], J. Volpe[3], J. Lappan[4], P. Bambury[5], M. Gibson[6], A. Tsimicalis[7]

[1]Pediatric Hematology/Oncology, Children's Hospital London Health Sciences, London, Canada; [2]Nursing, Pediatric Oncology Group of Ontario, Toronto, Canada; [3]Pediatric Hematology/Oncology, Hospital for Sick Children, Toronto, Canada; [4]Pediatric Hematology/Oncology, McMaster Children's Hospital HHS, Hamilton, Canada; [5]Children's Outpatient Clinic, Grand River Hospital, Kitchener, Canada; [6]Pediatric Oncology, Cancer Centre of Southeastern Ontario, Kingston, Canada; [7]Ingram School of Nursing, McGill University, Montreal, Canada

Objectives: In 1989, the POGO Pediatric Oncology Nursing Committee was formed to address issues in the delivery of childhood cancer care, and to facilitate professional development activities. Ongoing evaluation is iterative, with aims to ensure accountability, stimulate partnerships, and timely accomplishment of goals. The objective of this presentation is to provide an overview of the Committee's activities and future directions.
Methods: Led by the Chair, the Committee and its taskforces meet in person, correspond via email and telephone, and participate in various POGO-led projects. The committee relies on active participation of its members, knowledge exchange, and sharing of local resources. Each member may lead or provide feedback on any Committee project. Data for this evaluation were collected through follow-up with current Committee/taskforce members as well as selected POGO Staff and Fellows; and through a retrospective review (1989 to 2014) of the nursing roles, meeting minutes, email communications, publications, and research database.
Results: To date, 50 nurses have served as Committee members. Collectively, they have led 5 research projects (e.g. workforce, telepractice); planned 6 education events; and contributed to numerous clinical projects (e.g. drug safe handling; symptom management; and nursing role/curriculum development). The Committee has published 2 peer reviewed articles, developed 7 guidance documents, and presented at 11 peer reviewed conferences. The Committee also promotes research opportunities. Presently, 5 nurses have been awarded PhD Fellowships or seed grants, which have produced 9 peer reviewed publications. Nurses have taken a leadership role in 16 studies related to the delivery of care. Future directions include recruiting new members, planning and implementing additional projects, and strengthening translation efforts and collaborative networks.
Conclusions: The POGO Nursing Committee has been instrumental in advancing the role of nurses in Ontario. These collective efforts may serve as an example to others seeking to optimize the delivery of childhood cancer care.

P-194

NURSING MANAGEMENT FOR PREVENTING OF PERIPHERAL CHEMOTHERAPEUTIC EXTRAVASATION: EVALUATING AN INTERVENTION PROGRAM ON THE EDUCATIONAL OUTCOMES OF NURSES CARING OF ONCOLOGY CHILDREN

N. Elsherif[1], S. Al-Rafay1[2]

[1]Pediatric, Ain Sham University, Cairo, Egypt; [2]Nursing Faculty, Ain Sham University, Cairo, Egypt

Background
There is a growing understanding that good nursing practice is the cornerstone in preventing of extravasation when administrating chemotherapy; one of the shortcomings is lack of understanding or practice of oncology nurses; causes the devastating complication of extravasation. Therefore, good oncology nursing care for children and close monitoring of complications is essential for successful Chemotherapy. This study evaluated the theoretical and practical requirements of the oncology nurses, and the clinical implication of the intervention program as a training for nurses to eliminate the weak points related to safe administration of chemotherapy and prevention of extravasation.
Methods: The study was conducted in the Pediatric Oncology Department at Children Hospital, Ain Shams University Hospital in Cairo, Egypt, using a quasi- experimental research design with pre/post intervention assessments. Data was collected using a self-administered questionnaire sheet and an observation checklist (pre/post format) and developed an intervention educational program about nursing management and for reducing the risks of chemotherapeutic extravasation in oncology children.
Results: Most of the nurses in the study sample were in the age group 25 to less than 30 years (40.0%) and the majority (60.0%) have a nursing school diploma. Only nine nurses (17.0%) have previously attended training courses. the program had a significant positive impact on nurses' knowledge and performance, especially in relation to objectives for minimizing extravasation, types of chemotherapy extravasation, and precautions to follow. Conversely, after application of the program. Meanwhile, no statistically significant increases were noticed in the scores of knowledge related to recommended documentation of extravasation.
Conclusions: The study demonstrated that implementation of an intervention program about preventing chemotherapy extravasation had led to a higher educational and practical outcomes during administration with preventive measures of extravasation as a complication of chemotherapeutic administration among cancer children.

P-195

HOSPITAL INFANTIL TELETON ONCOLOGIA (HITO) AND DANA-FARBER/ BOSTON CHILDREN'S CANCER AND BLOOD DISORDERS CENTER NURSES PARTNER TO IMPROVE PEDIATRIC ONCOLOGY CARE

M. Green[1], M. Noriega Garcia[1], R. Mintor[1], S. Barajas Edid[1], S. Espinoza Manjarres[1], L. Morrissey[1], P. Campillo[1], C. Costello[1], L. Camacho Estrada[1], C. Nixon[1], A. Vargas[1], B. Cuccovia[1], J. Gouthro[1], K.E. Houlahan[1], P. Branowicki[1]

[1]Dana-Farber/Boston Children's Cancer and Blood Disorders Center Nursing, Boston, USA

Purpose/Objective
Nurses are the largest workforce in health care and have a significant influence on patient outcomes. Research has demonstrated the positive association between specialized nursing education and lower mortality rates among children with cancer (1). Nursing partnerships, such as the collaboration between Hospital Infantil Teleton Oncologia (HITO) and Dana-Farber/Boston Children's Cancer and Blood Disorders Center (DF/BCHCC), promote optimal patient care through specialized nursing education and clinical training. The transfer of knowledge between nursing at HITO and DF/BCHCC via an observership exchange program model has proven to be effective.
Materials and Methods
An ongoing collaboration of nursing staff between HITO and DF/BCHCC consists of a formal curriculum tailored to roles of the nurse leader, staff nurse and other specialties. Nurses from HITO spent three months at DF/BCHCC conducting site assessments and observation of practice throughout key areas prior to HITO opening in December 2013. Nursing staff from DF/BCHCC travel to HITO to provide training and education. Nurses specialized in Oncology, Hematopoietic Stem Cell Transplant, Intensive Care, Emergency Care, Infection Control, Surgery, Leadership and Education partnered to develop a program to meet the needs of HITO staff and provide on-site teaching and mentorship.
Results: Data is being collected through voluntary surveys from nurses who have and are participating in the collaboration. To sustain the training and education model, a combination of online, teleconferencing and ongoing exchange visits will be conducted.

Conclusions: Educational programs for oncology nurses throughout developing countries can improve pediatric cancer care and build capacity through ongoing partnerships. HITO and DF/BCHCC nursing programs are committed to continue to exchange information and pursue initiatives to ensure optimal nursing care.
Reference: Aiken LH, Clarke SP, Cheung RB, et al. Educational levels of hospital nurses and surgical patient mortality. *JAMA*. 2003; 290: 1617-1623.

P-196

ROLE OF NURSING CARE IN MANAGEMENT OF RELAPSED HODGKIN LYMPHOMA PATIENTS DURING HIGH DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANT- SINGLE CENTER EXPERIENCE FROM PAKISTAN

H. Hamsar[1], H. Khan[1], M. Khan[2]

[1]Pediatric Oncology Nursing, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan; [2]Pediatric Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan

Objectives: The main objective of this study was to assess the nursing care issues in pediatric patients of relapsed hodgkin lymphoma (rHL) during their inpatient stay for high dose chemotherapy (HDC) and autologous stem cell transplant (ASCT).
Methods: We retrospectively reviewed nursing notes of all pediatric patients of rHL treated at Shaukat Khanum Memorial Cancer Hospital Lahore during April 2011 to March 2014. All of them were treated with BEAM chemotherapy (BCNU, etoposide, cytarabine and melphalan). Strict protective isolation was observed during admission. Data including age, gender, paying status and duration of hospital stay were recorded. Common problems encountered during hospitalization were thoroughly studied.
Results: Of 16 patients reviewed, 13 were male. Median age at diagnosis of rHL was 15 years. All patients except one received free treatment. Patient to nurse ratio during hospitalization was 1:1. Median duration of hospital stay was 24 days (range: 20-38 days). Symptoms persisting for 7 days or more included diarrhea (56%), oral mucositis (44%), nausea (31%) and fever (6%). Oral intake was markedly reduced in 56% patients (n = 9), main contributing factors were oral mucositis (n = 8), nausea/vomiting (n = 8), abdominal discomfort (n = 4) and disliking for hospital food (n = 3). Consistent nursing practices included regular oral care and motivational counseling for dietary improvement. Psychological disturbances were encountered by 62% patients (n = 10), notable reasons were isolation, home sickness, fear of disease progression and side effects of chemotherapy. Frequent counseling sessions by attending nurses were conducted with active listening, employing play therapy (n = 8) and provision of animated movies (n = 8) and story books (n = 7).
Conclusions: This study elaborated physical and psychological issues faced by pediatric patients while undergoing HDC and ASCT. Individual assessment and dedicated efforts by nursing staff can facilitate these patients to cope with the problems encountered during prolonged hospitalization for intensive chemotherapy.

P-197

THE ROLE OF PEDIATRIC ONCOLOGY NURSE AS AN EDUCATOR IN THE "ANYO HOUSE " A HOUSE FOR SHELTER AND EDUCATION

Y. Hanaratri[1]

[1]Education Development Program, Indonesian Anyo Foundation, Tangerang, Indonesia

Objectives: Pediatric oncology nurses are knowledgeable resources for healthcare providers caring for children with cancer. We describe a pediatric oncology nurse educator developed program in Indonesia that aims to provide information to all stakeholders and reinforce important components of the children's care. This educational program is an important element of the child's pediatric oncology treatment.
Methods: Since June 2013, a monthly formal structured learning activity was designed and executed, coordinated by a pediatric oncology nurse educator. This free educational program was presented to families of children with cancer and members of the health sector: nurses, dieticians, medical students, pediatric nurses, and a donor. The educational venue was the 'Rumah Anyo' (Anyo House) of the Indonesian Anyo Foundation. Speakers represent several disciplines i.e., medical oncologist, dietician, pediatrician, general medicine, senior oncology nursing and also a cancer survivor.
Results: Topics included food for healthy life style, optimization of early detection of child development, myths and facts about breast milk, bio energy power, palliative care, effects of chemotherapy in children with cancer, and the optimization of nutrition in children receiving cancer treatment. Teaching was provided in an hour blocks including lectures, discussion, open-ended questions, and questions and answers. At the end of each session, participants completed a checklist evaluation.
Conclusions: From the results of the educational sessions that the nurse coordinated, guidelines have been created through consultation and discussion with the child's health practitioner for managing chemotherapy side effects and providing good nutrition for children during treatments. There has also been collaboration with a donor to develop motivation and continued education for children who stay in 'Rumah Anyo'. There remain several family support-related strategies that should be improved in the development of this education program in this special community setting and are being addressed by the nurse educator.

P-198

HOSPITAL-BASED HOME CARE PROGRAM FOR CHILDREN WITH CANCER: DEVELOPING PALLIATIVE CARE AT HOME

H. Hansson[1], K. Schmiegelow[1], I. Hallström[2]

[1]Paediatric and Adolescent Medicine, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark; [2]Department of Health Sciences Division of Nursing, Faculty of Medicine, Lund, Sweden

Objectives: A hospital-based home care program for children with cancer was established in 2008 to develop and provide medical treatment and nursing care in the children's own homes. Since 2011, the hospital-based home care program also delivers palliative care including end-of-life care, to ensure the quality and continuity of care for the child at home according to the families' needs. Providing palliative care is a complex and challenging task and our purpose is to describe the feasibility of delivering hospital-based palliative care at home.
Methods: Children with any type of cancer and who lives within a radius of 50 kilometres from the hospital are eligible for the hospital-based home care program. Two nurses employed at the department provide the home visits e.g. intravenous chemotherapy, supportive and palliative care. Descriptive analysis was performed on hospital records.
Results: Between January 2012 and December 2013, a total of 107 children received home visits and 14 (9 females) of these received palliative care at home (median age 9 years; range 2-20 years). Ten children with brain tumor, 4 children with solid tumor and one child had ALL. Number of home visits per child were 6 (median; range 1-22) and lasted for 30-40 minutes (median; range 10 to more than 60 minutes). Six children died at home. When needed, the home care nurse provided the home visits in collaboration with the nurse and doctor responsible for the child's treatment, a community-nurse, and a nurse-specialist in pain relief. Evaluation will be performed in 2014 by assessing quantative data and qualitative interviews with the families and the health care professionals.
Conclusions: It is feasible to provide hospital-based palliative care to children in their own homes. The results can be useful when considering the provision of palliative care based at a hospital department.

P-199

INVESTIGATION AND ANALYSIS OF SPECIALIZED NURSING KNOWLEDGE OF NURSES IN DEPARTMENTS OF PEDIATRIC HEMATOLOGY AND ONCOLOGY IN 14 CHINESE HOSPITALS

M. He[1], H. Lu[2], N.P. Shen[2]

[1]Hematology and Oncology, Shanghai Children's Medical Center, Shanghai, China; [2]Nursing, Shanghai Children's Medical Center, Shanghai, China

Objectives: To investigate the present specialized nursing knowledge of nurses in departments of pediatric hematology and oncology in 14 Chinese hospitals and analyze its influence factors.
Methods: Researchers designed investigation form based on literature review, enrolled 182 nurses from 14 Chinese 3A hospitals by convenient sampling, and collected data through SurveyMonkey online investigation system (http://www.surveymonkey.com/).
Results: The average scores of 63.6% parts of specialized nursing knowledge were higher than 3.5, which mean 'less understanding'. Nurses with different experiences and titles demonstrate different levels with respect to total score, disease-related, therapy-related, symptom-related, operation-related, occupational protection-related and nursing education-related knowledge ($p < 0.05$).
Conclusions: Nurses in departments of pediatric hematology and oncology show a relatively lower level of specialized nursing knowledge, especially in the palliative care-related knowledge. Nurses with different background demonstrate different acquisition of specialized nursing knowledge. Researchers suggest paying more attention to the importance of specialized nursing knowledge, in order to substantiate the connotation of nursing, elevate the nursing value, and promote the professional care of children with hematology and oncology.

P-200

NURSING CONSIDERATIONS IN THE TREATMENT OF DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG) WITH VINORELBINE AND NIMOTUZUMAB

P. Hernandez[1], A. Hernandez Alomso[1], P. Garcia Prada[1], R. Olaiz Campos[1]

[1]Hematology and Pediatric Oncology Unit, Hospital Universitario Madrid Monteprincipe, Madrid, Spain

Objectives: Brain tumors are the leading cause of mortality in childhood cancer. The DIPG is a tumor that affects the brainstem. It manifests exclusively in children and teenagers. These patients have a survival rate, after one year of diagnosis, under 10%, with median survival of 6-9 months. Radiation therapy is the standard palliative treatment, because of its location, surgical management is not indicated. Without radiotherapy, the median survival of these patients is 20 weeks. The objetive of this study is to evaluate tolerance and acute side

effects in patients who suffer DIPG, and are under ambulatory treatment with Nimotuzumab and Vinorelbine.
Methods: Review the cases of patients treated in our unit with Nimotuzumab and Vinorelbine, as well as radiotherapy.
Results: Concomitant use of Nimotuzumab plus Vinorelbine along with radiotherapy (weekly during induction treatment, and every two weeks during maintenance period) has shown a decrease in the number of hospital admissions, increased quality of life and survival rate (up to 24 months, with progression-free survival after six months, in 90% of patients).
Conclusions: Combination of radiotherapy and Nimotuzumab plus Vinorelbine is well tolerated by patients, and can be administered on ambulatory basis without the need for hospital admissions due to neutropenia, fever, nausea and vomiting, etc.

P-201

COMPLICATIONS IN SURGICAL WOUND HEALING IN CHILDREN AND TEENAGERS WITH BRAIN TUMORS UNDER TREATMENT WITH BEVACIZUMAB (AVASTIN®) AND DEXAMETHASONE

P. Hernandez[1], A. Hernandez Alonso[1], P. Garcia Prada[1], R. Olaiz Campos[1]

[1]Hematology and Pediatric Oncology Unit, Hospital Universitario Madrid Monteprincipe, Madrid, Spain

Objectives: During treatment of brain tumors, with surgery and/or radiotherapy, it is necessary to combine drugs, in order to control symptoms and working towards eradication. Dexamethasone is a drug frequently used when dealing with cerebral edema, but its long-term administration produces Cushing Syndrome, causing increased skin fragility.
New therapies look to inhibit angiogenesis of these tumors. Bevacizumab causes regression of tumor vascularization, normalized residual tumor vasculature and inhibits tumor neo-vascularization, preventing tumor growth. Because of this, healing time is longer.
The objective of this study is to present management and results, from nursery experience, in complications observed during healing process in surgical wounds in three patients treated in our unit. They were treated with Avastin® and Dexamethasone at the same time.
Methods: Cases of patients treated with Avastin® and long-term Dexamethasone were registered and reviewed. It was found that three of them had dehiscensia in surgical wound. One case presented worn septum. Diagnosed diseases were disseminated Oligodendroglio-matosis craniospinal progression (1 case) and Diffuse Intrinsic Pontine Glioma (2 cases).
Results: In two of these cases, after one month of treatment with Avastin®, there was abdominal dehiscensia and catheter head was exposed. Treatment with silver sulphadiazine and povidone iodine ointment helped, but it was necessary to complete healing with surgery closure. In one case, Vacuum Assisted Closure was used and considerably improved until success. In another patient, worn septum unabled the possibility to rebuild tissue.
Conclusions: Bevacizumab has been a breakthrough in clinical practice. The effects are observed after short time and after a single dose treatment. That is why its use is well accepted, as it has been very useful in the improvement of the neurological symptoms of our patients, although it is not free of significant side effects.

P-202

BIOMARKERS OF OXIDATIVE STRESS IN CHILDREN TREATED FOR LEUKEMIA

M. Hockenberry[1], P. Gundy[2], O. Taylor[3], D. Montgomery[2], I. Moore[2]

[1]Nursing, Duke University, Durham, USA; [2]Nursing, University of Arizona, Tuscon, USA; [3]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: Central nervous system (CNS) treatment for children with acute lymphocytic leukemia (ALL) is necessary to prevent disease recurrence in the brain, but associated with cognitive problems in almost 40% of survivors. CNS biomarkers that can identify children most at risk could increase our understanding of treatment-related neurotoxicity. The purpose of this study was to investigate relationships among F_2-Isoprostanes, a well-established biomarker of oxidative stress, and two oxidized glycerophospholipids [phosphatidylcholine (PC) and phosphatidylinositol (PI)] in the cerebral spinal fluid (CSF) in children with ALL.
Methods: A within subjects repeated measures design was used to investigate relationships among the CSF biomarkers during the first 18 months of ALL treatment. Seventy-nine newly diagnosed children with ALL, and treated on Children's Oncology Group protocols participated. CSF samples were collected with each lumbar puncture required per protocol for intrathecal chemotherapy.
Results: F2 isprostanes and glycerophospholipids increased significantly during CNS treatment compared to diagnostic CSF levels. The highest concentration of F_2-Isoprostanes during induction was significantly correlated with highest levels of oxidized PC ($r = 0.320$, $p = 0.003$) at the same treatment phase. During post-induction the highest concentration of F_2-Isoprostanes was significantly correlated with oxidized PC ($r = .356$, $p = 0.001$) and oxidized PI ($r = 0.290$, $p = 0.005$). Highest concentration of F_2-Isoprostanes during continuation was also significantly correlated with oxidized PC ($r = 0.420$, $p < 0.001$) and oxidized PI ($r = 0.319$, $p = 0.003$).
Conclusions: The significant increase in F2-isoprostanes and oxidized PC and PI provides evidence for their use as measures of oxidative stress in the brain. Both oxidized PC and PI were significantly correlated with F2 Isoprostanes, an established biomarker of oxidative stress. In the future these measures may become important markers of underlying methotrexate-induced neurologic injury.

P-203

PORTFOLIO OF ENHANCING RESILIENCE FOR ADOLESCENTS AND YOUNG ADULTS WITH CANCER

A. Akiko Ishibashi[1], K. Kamibeppu[2]

[1]Department of Children and Infants Nursing, Japanese Red Cross Kyushu International College of Nursing, Fukuoka, Japan; [2]Department of Family Nursing, Graduate School of Health Sciences and Nursing, Tokyo University, Hongo, Bunkyo-ku, Tokyo, Japan

Purpose: The purpose of this study was to evaluate the adolescents and young adults (AYAs) with cancer' views of the usefulness of portfolios to improve their resilience.
Methods: Each patient's portfolio included two sheets to find self and project their goal of the future. The examples of the portfolio were shown to get them an idea of what was expected. One of the authors supported them to work with the questions in the sections that built the content in the portfolio. The Resilience Scale was used before and after the portfolio.
Results: A total of 14 patients aged 12 to 21 years were participated. We found that most of them were middle and high levels of resilience and about a half of them increased their inner resilience score ("I am" factor), a person of hope, faith, confidence, and optimism. All of them found the portfolios worthwhile and useful. The rest of the participants show that they were no change or the low level of resilience after the portfolio.
Conclusions: Using a portfolio can be enabling tool in pediatric oncology nursing to help the AYAs with cancer enhance their resilience. Some of them may need to support for finding self and having their purpose. Future studies are needed to improve the validity of this research.
Acknowledgements: The authors would like to thank Okinawa Prefectural Nanbu Medical Center & Childrens Medical Center and Japanese Red Cross Kumamoto Hospital. Thanks are also to the individuals who participated in this study.

P-204

DELIVERING END OF LIFE CARE FOR CHILDREN AND YOUNG PEOPLE IN A RURAL COMMUNITY

R. Jones[1], J. Thomas[2]

[1]Paediatric Oncology, Hywel Dda University Health Board, Carmarthen, United Kingdom; [2]Paediatric Palliative Care, Hywel Dda University Health Board, Carmarthen, United Kingdom

Objectives: The aim was to develop a Paediatric Palliative Care Nurse Bank (PPCNB) to deliver end of life care for children and young people dying from malignant disease.A previous audit had shown that 50% of parents caring for their dying child in the hospital setting would have taken them home if 24hour nursing support could have been provided. The initiative involved the development, education and training of a nursing bank to provide a fast and flexible response to support families who wish their child to die at home.
Methods: The first step in the process involved explaining our ideas at a senior nurses meeting and gaining management support. Interested paediatric nurses were then recruited in order to to develop a database of staff. Education and Training consisted of an initial series of Study Days followed by a rolling programmme of continuing education and debriefing sessions enabling staff to improve their knowledge and skills in palliative care and symptom management.
Results: The service has so far been utilised for 3 families caring for their dying child at home. The feedback from families and the nurses has been extremely positive. Families have described feeling more in control and reassured by the presence of familiar, experienced nursing staff. The training element of this development has ensured that nurses have supplemented their core skills. These skills have been transferrable to their own areas of practice.
Conclusions: The vision and commitment has been that children, young people and families have safe, accessible, sustainable, high quality end of life care in the home. The development of the PPCNB as a unique service in rural Wales has improved care for families at a vulnerable time and increased confidence, knowledge and skills for nursing staff.

P-205

EMOTIONAL EXPERIENCES OF PARENTS CARING FOR THEIR CHILDREN WITH CANCER

C. Kawakami[1], K. Ideno[1], J. Ogawa[2], R. Amano[1], K. Harada[3], N. Morita[3], F. Ishikawa[4]

[1]Faculty of Nursing, Toho University, Tokyo, Japan; [2]School of Nursing and Nutrition, Shukutoku University, Chiba, Japan; [3]Pediatrics, Toho University Omori Medical Center, Tokyo, Japan; [4]School of Health Sciences, Kyorin University, Tokyo, Japan

Objectives: The Japanese government decided to improve relationships with pediatric cancer centers in 2013. This resulted in 15 centers cooperating with regional hospitals. However, the

system has just started and almost all pediatric cancer patients still receive medical examinations in neighborhood hospitals. Childhood cancer results in considerable stress on families. These stressful events are usually unparalleled in importance to those facing them. The support of professionals is essential for families to adapt to their new lifestyles. Thus, the purpose of this study was to explore the emotional experiences of parents caring for their children with a cancer diagnosis.
Methods: Data were collected through semi-structured interviews and analyzed using qualitative inductive methods. Participants were recruited from a pediatric oncology hospital in Japan. The local ethics committee approved this study.
Results: Eleven parents (9 women and 2 men) were interviewed. At the time of diagnosis, parents commonly experienced very strong emotions such as feelings of shock, disbelief, anger, loneliness, and powerlessness. It was difficult for the parents to appreciate the implications of their child's disease immediately; however, over time, they managed to grasp the reality of their child's health condition. The timing of when the information is delivered to the parent is one of the most important things to consider. It is also necessary for medical professionals to assess the parents' health simultaneously in order to provide care for both the child and the family.
Conclusions: Pediatric nurses have an important role to play in the provision of information, and they need to be vigilant regarding the individual needs of parents. Medical professionals need to provide comprehensive information that meets the needs of all of the individuals concerned. Better care of ill children needs to be accompanied by lasting relationships between parents and health-care professionals.

P-206

JOB ANALYSIS IN ONCOLOGY NURSING AND TASK FORCE PLAN IN THE AMBULATORY CHEMOTHERAPY UNIT: IS AUTOMATING CHEMOTHERAPY PREPARATION WITH ROBOTIC TECHNOLOGY USEFUL?

A. Karapinar[1], I. Kebudi[2], V.Z. Yenen[3], R. Kebudi[4], F. Yaman Agaoglu[5]

[1]Oncology Nursing, Istanbul University Oncology Institute, Istanbul, Turkey; [2]Student in Advanced Placement Microeconomics, Hisar Schools High school, Istanbul, Turkey; [3]Department of Business Administration Division of Hospital Administration, Beykent University Institute of Social Sciences, Istanbul, Turkey; [4]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute, Istanbul, Turkey; [5]Radiation Oncology, Istanbul University Oncology Institute, Istanbul, Turkey

Objectives: To analyse the time spent and efficacy with nursing procedures in the ambulatory chemotherapy unit, after the establishment of the automated chemotherapy preparation with Robotic technology.
Methods: In 2012, 16.661 chemotherapy applications were performed in 177 working days, (94 patients/day) in the 'Ambulatory Chemotherapy Unit' (Monday-Friday, 8a.m.-4p.m.) of the Istanbul University, Institute of Oncology. Since July 2012, automated chemotherapy preparation with Robotic technology have been used. Eight nurses worked in the unit. In June 2012, on 6 different days, on three time periods during the day (8-10a.m., 10 a.m.-1p.m., 1-4p.m.), the time spent in nursing procedures were assessed in detail (21 variables) by two independent observers using a chronometer. The median number of patients recieving ambulatory chemotherapy/day during the study period was 78. All nurses were educated for all procedures previously and interviewed.
Results: Using the Robotic technology, all 8 nurses were actively involved in nursing procedures. Prior to robotic technology, 2 of the 8 nurses were involved only in preparation of chemotherapy drugs with no active patient procedures. The median time spent specifically for nursing procedures before, during and after chemotherapy was 31 min, 32 sec./patient, this increased to a median of 2 hours 31 min 48 sec if an adverse reaction occurred. Excluding lunch/specified breaks, each nurse was expected to work actively for 6 h 25 min/day. The median time spent by a nurse for each patient was 40 minutes. For 78 patients/day, each nurse had to actively work for 6 hours 45 min; 20 minutes more than expected. However the extra time of active work was less than prior to robotic technology.
Conclusions: The robotic technology helped increase the safety and accuracy of chemotherapeutic drugs and increased the time spent by a nurse in active nursing procedures of each patient, which led to a better satisfaction of the patients.

P-207

MULTIDISCIPLINARY PEDIATRIC ONCOLOGY TRAINING IN BOTSWANA

D. Kollar[1], J. Hesselgrave[2], A. Slone[1], P. Semetsa[3], M. Raletshegwana[3], W. Oaitse[4], M.T. Mokotedi[5], J.S. Slone[1], P.S. Mehta[1]

[1]Texas Children's Cancer and Hematology Centers, Baylor College of Medicine, Houston, USA; [2]Texas Children's Cancer and Hematology Centers, Texas Children's Hospital, Houston, USA; [3]Paediatrics, Princess Marina Hospital, Gaborone, Botswana; [4]Paediatrics, University of Botswana, Gaborone, Botswana; [5]School of Nursing, Boitekanelo College, Gaborone, Botswana

Objectives: About 80% of the 160,000 children who develop cancer live in low & middle income countries (LMIC) where survival is considerably less than in resource-rich settings. A major challenge in treating pediatric cancer in LMIC is a lack of trained providers. Baylor College of Medicine (BCM) and Texas Children's Cancer and Hematology Centers (TXCH) have had a partnership with Princess Marina Hospital (PMH) since 2007 as the only center in Botswana treating children with cancer. PMH has a full time pediatric oncologist and a care coordinator from BCM/TXCH. Staff including nurses, pharmacists, dieticians and social workers receive very little, if any, pediatric cancer-specific training.
Methods: We conducted a multidisciplinary workshop to improve cancer care in Botswana. Two nurses and one pediatric resident from PMH were invited to BCM/TXCH for intensive training prior to the workshop. They served as instructors along with the pediatric oncologist, care coordinator, a local nursing instructor and two visiting educators from TXCH. The novel curriculum designed for this workshop included: an overview of pediatric cancer and treatment; supportive care; chemotherapy safety and administration; pain management; family-centered care; and palliative care. Training strategies included case studies, didactic lectures and open forum discussion.
Results: The one week workshop was attended by 28 participants representing eight public and private institutions from throughout Botswana. Eight disciplines were represented including physicians, surgeons, pathologists, nurses, social workers, dieticians, pharmacists and nursing instructors. Pre and post-tests demonstrated the curriculum's effectiveness in relaying key principles to learners. Participant evaluations strongly supported the need for this type of training.
Conclusions: Training opportunities in pediatric oncology are limited in LMIC. Standardized, sustained multidisciplinary education is vital to providing the highest level of oncology care. This curriculum can be adapted to other LMIC. Long term success is dependent on local capacity building of all aspects of pediatric cancer care.

P-208

CANCER – LIFE CHANGES AND SO DO THE RULES

A. Möller[1], A. Richter[1]

[1]Pediatric Hematology and Oncology, University Children's Hospital Münster, Münster, Germany

Objectives: The diagnosis of cancer and immunosuppressive cancer treatment requires a thorough change of lifestyle from patients and their families. Outside the hospital, where professionals provide a sense of security, parents need to know how to protect their child and themselves without overly restricting everyday life. This is where the hospital staff steps in with a structured instructional program designed to provide security in caring for the patient at home and raise awareness for signs of potential emergency situations.
Methods: For about four years now, nurses at our hospital have been running once-weekly formal instructional sessions, the nursing clinic, to be attended when a patient is about to be discharged from hospital after the first in-patient stay. Sessions last about 1-2 hours. If needed, instructions may also be arranged outside the clinic hours. The nursing staff is trained to integrate instructions into their nursing routine.
Results: The program has been well accepted; e.g., out of a total of 124 newly diagnosed patients in 2013, 62% have taken advantage of the nursing clinic, while 38% represent patients who had no systemic chemotherapy and some families who declined. Ideally, both parents take part in the instructional session. Quite frequently, however, only one parent will be able to attend. Mostly, this is the person who will be caring for the patient at home. Pediatric patients tend to take an interest in the nursing clinic the older they get. Usually, patients are 12 years or older when they decide to actively participate.
Conclusions: The instructional sessions allow parents and their children well-structured everyday living and in consequence a better quality of life at home. Moreover, heightened awareness of emergency signs assures fast intervention in situations that cannot be managed at home, e.g., severe febrile episodes in neutropenia and other situations that require direct communication with the treatment center.

P-209

"CHILDREN WITH CANCER: A GUIDE FOR EDUCATORS": THE CREATION OF A SCHOOL BASED RESOURCE BOOKLET

C. Murphy[1], S. Casey[1], D. Dekkers[1], T. Hamalainen[1]

[1]Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: There are approximately 1,000 children undergoing active cancer treatment in Ontario, Canada each year. Many of these children are school aged. A cancer diagnosis presents unique challenges for school administrators and educators to maintain and facilitate this vital aspect of a child's life. As part of their role, Pediatric Oncology Group of Ontario (POGO) Interlink Community Cancer Nurses work collaboratively with educators and families to support schools in the education of children with cancer. To supplement and enhance the sharing of information, a program specific resource booklet entitled 'Children with Cancer: A Guide for Educators' was created.
Methods: Literature regarding school reintegration was reviewed. The content of a well established program of educational support provided through POGO Interlink Nurses via telephone consultation, school meetings and classroom presentations were considered. Consultation with school administrators, educators, physicians and nurses contributed to the content of the booklet.
Results: The booklet is a school based resource that outlines general information about childhood cancer, treatments and practical strategies for supporting children and families

throughout the cancer experience. It guides educators by delineating the phases of treatment and outlining special academic and social considerations for when a child is diagnosed with cancer, when a child returns to school and in the event that a child's cancer recurs. Information and emotional support needs of the child, family, siblings, classmates and faculty are addressed. Colourful illustrations are used throughout the booklet to enhance content and clarity.
Conclusions: POGO Interlink Nurses began to distribute the resource booklets to enhance their support of Ontario schools in January 2014. Although formal evaluation is not planned until 2015, anecdotally the document has been well received by administrators and educators as a welcome resource in understanding and facilitating the educational needs of children undergoing cancer treatment.

P-210

COMBINATION MORPHINE AND KETAMINE IN HIGH RISK NEUROBLASTOMA PATIENTS RECEIVING CH14.18/CHO ANTIBODY/IL2 MAXIMISES ANALGESIA, MINIMISES SIDE EFFECTS AND OPTIMISES IMMUNOTHERAPY DELIVERY

G. Patton[1], C. Reilly[2], M. Canning[2], P. Cupples[2], T. Moores[2], G. Bell[2], M. Ronghe[1], J. Sastry[1], D. Murphy[1]

[1]Oncology, Royal Hospital for Sick ChildrenYorkhill, Glasgow, United Kingdom; [2]Pain Team, Royal Hospital for Sick ChildrenYorkhill, Glasgow, United Kingdom

Objectives: To obtain optimum pain control in patients receiving CH14.18/CHO antibody on the HR-NBL-1/SIOPEN protocol, with minimal side effects.
Methods: Neuroblastoma patients receive CH14.18/CHO antibody with or without aldesleukin. It is a monoclonal antibody that binds to GD2 receptors on the neuroblastoma cells and induces the killing of tumour cells by the patients own immune response. This treatment is significantly toxic. Patients experience sudden onset pain during the administration of the antibody, therefore concomitant PCA/NCA morphine treatment is a necessity. Pain assessment scoring identified that patients were not adequately analgised despite significant morphine dose escalations, and consequent side effects. Antibody infusions were interrupted to optimise pain management. This led to prolonged immunotherapy infusion times. Multidisciplinary team discussion led to the introduction of a low dose ketamine infusion as an adjunct to opioid analgesia. Ketamine provides good analgesia while preserving airway patency, ventilation and cardiovascular stability.
Results: The combination of morphine and ketamine was successful in controlling pain with far fewer side effects. Optimal pain management allowed immunotherapy delivery without any interruption. Ketamine and morphine co-analgesia is now standard for our patients receiving immunotherapy.
Conclusions: The combination of morphine and ketamine increased the patients' pain tolerance of CH14.18/CHO antibody without the side effects of high dose opiates. This permitted a substantial increase in the number of cycles delivered without delays or breaks and maximised the therapeutic impact of immunotherapy.

P-211

LITERATURE REVIEW OF NURSING FOR INFANTS WITH RETINOBLASTOMA AND THEIR FAMILIES

M. Nagayoshi[1], Y. Hirose[2]

[1]School of Medicine/Nursing Course, Yokohama City University, Yokohama, Japan; [2]Graduate School of Medicine Department of Nursing, Yokohama City University, Yokohama, Japan

Objectives: This study aimed to gain insight on nursing research in Japan by literature review of nursing care abroad for infants with retinoblastoma (rare eye cancer) and their mothers. Treatment for retinoblastoma was developed in recent years.
Methods: PubMed and CINAHL databases were explored, covering the last two decades, and 22 papers were selected for review. Based on a literature map developed, nursing care were assessed.
Results: The first paper was published in 1993, and zero to three papers were identified for each year thereafter. The nursing care provided was classified into three topics: nursing for treatment, nursing for visual impairment, and nursing for hereditary cancer. In nursing for treatment, brachytherapy, enucleation of the eye, and chemotherapy were covered. The studies also investigated nursing to prevent long-term psychological issues and long-term effects after treatment, and to coordinate community and school for the children coping with school, as the cure rate had increased. Particularly, in case of hereditary cancer, nursing care for counseling the family was important.
Conclusions: Because the long-term survival rate for infants with retinoblastoma continues to increase as hereditary cancer research advances, papers discussing support for post-treatment problems from a long-term perspective have now appeared. The results suggest the significance of further studies on continuing care for children with familial retinoblastoma and visual impairment, and their family in Japan to improve the quality of life after treatment.

P-212

APPETITE, SENSES AND JOY OF LIFE – A NUTRITION PROJECT

M.M. Nielsen[1], D. Kristensen[1], C. Thomsen[1]

[1]Pediatric Oncology Ward, Aalborg University Hospital, Aalborg, Denmark

Objectives: The project is towards children admitted to the paediatrics oncology ward at Aalborg University Hospital. The purpose of the project is to ad focus on nutrition to reduce the weight loss induced by chemotherapy. And also minimize the need for tube feeding formula and Parenteral Nutrition. Our intend is to change the hospitalised child's perception of food, to generate new knowledge and create the settings for, how the meal that favours the children's needs and wishes, can be implemented into the paediatrics ward.
Methods: The project is an interdisciplinary project in co- operation with the paediatric oncology ward, the hospital kitchen and the company Unisans. Both parents and children have been included in the project with interviews regarding wishes and needs concerning the children's diet. It has been studied, when the children's nutritional value is most threatened.A new kitchen has been build, where the families can cook and a new food concept has been developed with better content and more exciting food serving. In addition, a new pamphlet with inspiration has been developed. Food shops where parents and children have been cooking with a sense coach and chefs from Unisans were a part of the project. The "food shop" turned up every 14 days.
Results: All of the results have not yet been calculated, but we can conclude that a number of success criteria's have been fulfilled. Greater fellowship, joy in the eating situation, children who wanted to cook and participate in social gatherings including food. The children and teenagers have become more outgoing and eat more of the food served.
Conclusions: We expect that the project will help improve the children's psychosocial development. In the future, the experiences from this project can be used when designing new eating environments in paediatric wards.

P-213

DECISION-MAKING IN PARENTS OF CHILDREN WITH SICKLE CELL ANEMIA (SCA) CONTEMPLATING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

N. Noonan[1]

[1]BMT, Children's Hospital and Research Center Oakland, Oakland, USA

Objectives: Sickle cell disease is the most common inherited blood disorder in the United States, affecting an estimated 90,000-100,000 individuals. Despite improved supportive care in the past 20 years (hydroxyurea and chronic transfusions) the only known cure for SCA is HSCT. HSCT for SCA carries a 10-15% mortality risk. This risk, associated with potential morbidities and lack of studies directly comparing supportive therapy against HSCT, contributes to the controversy of supportive care versus HSCT for SCA. Our center is a comprehensive hematology/oncology/BMT program, including a pediatric hemoglobinopathy specialty-center. Since 2000, the BMT program has transplanted only 16 children with SCA: with 100% (16/16) OS and 94% (15/16) DFS, although we have consulted many more families.
Methods: A PubMed search of the past 20 years of research was performed to identify SCA parent/patient interest and decision-making process for families contemplating HSCT therapy. We aimed to identify key concepts related to HSCT for SCA interest; decision-making factors; educational material needs, and options for improving consultation services and informed consent.
Results: Only four studies surveyed HbSS and HbSβ^0 patients/families, although the focus varied. Surveys assessed: decision-making process regarding treatment choices or declination, patients' and parents' attitudes towards HSCT, factors associated with patient/parent interest in HSCT, and parents' attitudes towards risk acceptance of HSCT. Key themes identified were providing risk/benefit information and assessing both parental and patient interest when offering HSCT.
Conclusions: In conclusion, limited research and unanswered questions exist regarding interest and decision-making for SCA families regarding HSCT. Our next step is to implement either a survey or focus group to capture information specific to our center, then incorporate findings into HSCT/SCA educational materials and the HSCT consultation process. Specific interests also include the role of the referring/primary physician and outreach into the SCA community.

P-214

KNOWLEDGE AND ATTITUDES OF THE NURSING TEAM ON THE TREATMENT OF PEDIATRIC CANCER PATIENTS WITH MEDICAL CANNABIS

R. Ofir[1], S. Yontanov[1], M. Ben-Arush[1]

[1]Pediatric Hematology Oncology, Rambam Health Care Campus, Haifa, Israel

Objectives: Lately, there has been an increase in using medical cannabis on pediatric cancer patients. At Rambam Medical Center, we started using cannabis 3 years ago, as a request of parents of a 15 years old female at the end of life, in order to alleviate pain, improve her mood and increase her appetite. The use of cannabis raised some ethical issues among our team members. As a result of parents' requests and the need to improve supportive care, we

analyzed the knowledge and attitudes of the nursing staff (31 nurses) towards cannabis and in particular in relation to its use by pediatric cancer patients.
Methods: We composed a questionnaire that checked knowledge and attitude towards medical cannabis. The questionnaire consisted of demographic details and questions of knowledge and stance. Questionnaire I was given out without any prior exposure to the subject. As part of a staff meeting, the team heard a lecture and demonstration about medical cannabis and its benefits. About a month afterwards, questionnaire II was answered to check if there was any change in knowledge and attitude. 98% answered the 1st questionnaire and 80% on the 2nd.
Results: No significant changes between the averages of the staff's attitude in questionnaire I (2.55) and questionnaire II (2.71) were found. As to the question of attitude for use of cannabis, about 84% of subjects supported that idea. As for the issue of knowledge, there was a significant difference between questionnaire I (13.55) and II (22.22).
Conclusions: Results show that teaching the staff about the advantages of medical cannabis enriched their knowledge and changed their negative attitudes. The knowledge about cannabis increased significantly so it would help us to build a future medical training program about cannabis for children with cancer.

P-215

10 YEARS FOCUS ON CENTRAL LINE CARE

G. Petersen[1], M. Madsen[1], H. Hansson[1]

[1]Department of Pediatric Hematology/Oncology (5054), Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark

Objectives: To evaluate ten years focus on central line care
Due to an increased number of central line infections in 2004, a structured education program for nurses, patients and parents was developed. The program was evaluated in 2007 and showed a decrease in the number of Central Venous Catheters (CVC) removed due to infection from 20% to 15%, but still a need of focus on follow up on the training of patients and parents. All newly employed nurses are trained during the first two weeks and will receive their certification within the first 2 months after employment. The training of patients and parents is performed by certificated nurses and supported by written guidelines and photos. The education is documented on a checklist in the patient's medical record.
Methods: The certification of nurses in central line care is renewed every year by a practical and theoretical test. Training of patients and parents is evaluated by audit on the checklist in the medical record and by interview with patients and parents if a CVC related infection occurs.
Results: At almost every recertification of the nurses some habits needs to be changed to ensure that our guidelines are strictly followed. A recent audit on the education of the patients and parents unfortunately still showed lack of consistent follow up.
Conclusions: Education of nurses, patients and parents is important, it needs to be ongoing and constantly improved. Future plans on improvement for the education of patients and parents: A patient CVC booklet will be developed. Follow up on the patients and parents training will be scheduled during the whole treatment period. New ways of information: video, app and also new ways of education such as group sessions with special trained nurses will be developed and the individually training will be improved with shared responsibility.

P-216

ACUTE PEDIATRIC ONCOLOGY - SCENARIO TRAINING

P. Roland[1], L. L. Hjalgrim[1], T. Lindequist[1], S. U. Larsen[1]

[1]Pediatric haemathology oncology 5054, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark

Objectives: Children undergoing treatment for cancer are at continuous risk of developing life-threatening complications. Treatment-related complications may develop acutely, within *minutes* or hours. Early recognition, assessment and treatment of such complications are crucial to reduction in morbidity and mortality. In 2012 we conducted a questionnaire for doctors and nurses targeting their knowledge and skills in emergency situations with the child, specifically addressing ABC handling, teamwork and safe communication. The staff expressed great uncertainty and lack of knowledge in how to handle the critically ill child. The purpose was to test if the doctors and nurses experienced increased skills in handling the critically ill child with a special emphasis on ABC algorithm, safe communication and team work after scenario training in common oncological emergency situations such as sepsis and anaphylactic reactions.
Methods: Prior to scenario training staff were lectured in use of the ABC algorithm, team work and safe communication. Real time scenario training was conducted in the department in a patient room so the situation appeared as authentic and practice-oriented as possible involving one doctor and three nurses. After completing the scenario exercise debriefing was held.
Results: Overall, all 16 participants reported an increase from below average to above average in self-evaluated skills in relation to ABC algorithm, teamwork and safe combination, where the greatest improvement in skills were within the use of the ABC algorithm.
Conclusions: The emergency scenario training has significantly improved self-evaluated skills in care of the oncological child. Common standards, targeted training and education and the implementation of emergency carts and emergency tables, have improved work processes with clear roles and communication. Our aim in the future is to create an education- and scenario training program in early warning signs and treatment of oncological emergencies, and to test the staffs' skills prior and after completion of the program.

P-217

IMPACT OF STRUCTURED EDUCATION AND TRAINING FOR FAMILIES AND STAFF ON RATE OF INFECTION OF CVAD IN CHILDREN WITH CANCER

J. Sastry[1], D. Murphy[1], M. Ronghe[1], N. McGuire[2], B. Gibson[1], E. Chalmers[1], N. McIntosh[1]

[1]Department of Haemato-oncology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [2]Department of Haemato-oncology, Glasgow University School of Medicine, Glasgow, United Kingdom

Objectives: Introduction: Central venous access devises (CVADs) are central to the modern treatment/management of paediatric cancer patients. Infection is a serious, potentially life threatening complication of CVAD.1. To identify if the implementation of structured education and guidance for staff and families in the year 2000 has had an impact on infection rates. 2. To identify if CVAD care has been maintained when there was no longer a full time lead person responsible for the management of CVADs since January 2013.
Methods: A retrospective study was carried out for a period from January 2000 to November 2013 to identify the rate infection of CVADs. This period was then divided into two, one from Jan 2000 to December 2012 when a full time Advanced Nurse Practitioner (ANP) was in post and the second, Dec 2012- Nov 2013 when a full time ANP was no longer in post. Data was obtained from unit CVAD, microbiology and theatre data base. Evidence based educational methods, training programmes, policies, guidance and patient information booklets, were introduced in January 2000
Results: During the study period there has been a steady increase in the number of CVADs in situ from 50 to 70 patients per year. There has been a decrease in the rate of infection over this study period from 4% to 1.5%. The Decrease has continued into the second period where the full time ANP was no longer in post.
Conclusions: This audit demonstrates the implementation of structured education and training for families and staff has resulted in decrease in the rate of infection of CVADs despite the increase in the number of patients with CVADs. The decline in the infection rate has continued during the absence of full time ANP signifying that the education and training packages have now become a culture of the unit.

P-218

THE USE OF CHILDREN'S EMOTIONAL MANIFESTATION SCALE (CEMS) IN PEDIATRIC ONCOLOGY DAY- HOSPITAL PATIENTS

A. Schiavetti[1], E. Scardella[2], F. Patriarchi[1], P. Capelli[3], L. Vapore[3], A.M. Apollonio[4]

[1]MD Pediatrics, Sapienza University of Rome, Rome, Italy; [2]School of Nursing, Sapienza University of Rome, Rome, Italy; [3]Nursing Pediatric Oncology Day-Hospital, Sapienza University of Rome, Rome, Italy; [4]Nursing Coordinator Pediatric Oncology Day-Hospital, Sapienza University of Rome, Rome, Italy

Objectives: To identify the nursing interventions able to improve the compliance to treatment in children with cancer admitted to the day-hospital.
Methods: We used the Children's Emotional Manifestation Scale (CEMS), that considers 5 variables: facial expression, verbalization, activity, interaction and cooperation and assigns for each item a score from one to five, for a total score ranging from five to twenty-five. Over 8 months, 100 pts were evaluated by CEMS at: first admission (1) and/or subsequent admission (2). Pts were divided in < 5 years (40 pts) and > 5 years (60 pts).
Results: The study showed that the score is different at point 1 and 2. At first admission the most effective intervention was sound for pts < 5 years and play for pts > 5 years, with a score of 18 and 8, respectively. At second admission, the most effective intervention was distraction for pts < 5 years and explanation of the procedure with listening to the patient's request for pts > 5 years, with a score of 19 and 5, respectively.
Conclusions: This study could help the nursing staff to better manage the children with cancer admitted to the day-hospital.

P-219

ENGAGE, EDUCATE, STUDY AND EVALUATE: SUCCESSFULLY REDUCING CENTRAL VENOUS CATHETER-ASSOCIATED BLOODSTREAM INFECTIONS IN PEDIATRIC CANCER

R. Secola[1]

[1]Hematology Oncology, Children's Hospital Los Angeles, Los Angeles, USA

Objectives: Central Venous Catheters (CVCs) are indispensable for chronic or acutely ill patients requiring long-term and/or complex therapies. CVCs carry a high level of mortality

and morbidity directly related to the risk of infection. There have been substantial strides toward reducing CVC associated bloodstream infections (BSIs). These efforts have included implementation and adherence to CVC insertion and maintenance bundles along with ongoing education and monitoring. Treatment for most children and adolescents with cancer includes the use of a CVC. Despite the ubiquitous use of CVCs, few prospective studies have been conducted to address infection prevention strategies for pediatric oncology patients. The purpose of this presentation is to provide an overview of CVC types and selection, infection prevention strategies and interventions which include engagement and education of frontline staff from the Children's Hospital Los Angeles as well as other interventions for consideration.
Methods: Dedicated approaches to engage frontline staff utilizing multiple methodologies for education and accountability of CVC care; auditing and observations of care, root analyses for all CVC associated BSIs; implementation of reliability interventions and completion of a pilot study were accomplished.
Results: There remains sustained reduction in CVC associated BSI rates as a result of staff engagement, education, CVC care and BSI evaluation and implementation of reliability interventions. Furthermore, completion of a CVC infection prevention pilot study highlighted key risk factors for study to propose further valuable interventions.
Conclusions: Ongoing evaluation of education, monitoring and random observations of CVC care, critical analysis of each CVC associated BSI and interventions employed are necessary to sustain improvements. Additionally, rigorous study of key risk factors and critical mediators in pediatric oncology patients such as underlying malignancy, CVC type, patient acuity/clinical indicators are imperative for further strategic interventions such as a dedicated CVC team, chlorhexidine bathing regimens and oral care bundles.

P-220

EFFECT OF HEALTH EDUCATION: PARENTAL ASSESSMENT OF (KAP) KNOWLEDGE, ATTITUDE AND PRACTICE OF PEDIATRIC ONCOLOGY PATIENT

T. Thomas[1], A. Srivastava[1], B. Singh[1], A. Singh[1], R. Seth[1]

[1]Pediatrics, ALl India Institute of Medical Sciences, Delhi, India

Objectives: The aim of study was to find effect of health education on parent's attitude in care of pediatric oncology patient. Improved knowledge and quality care has effect on incidence of Febrile Neutropenia and hospital admission and long term event free survival.
Methods: Study samples consisted of 50 parents of pediatric oncology patient. The questionnaires were made in local language (Hindi) for the assessment of parental knowledge, attitude and practice about (4c's) clean food, clean water clean environment and clean hands.
Results: Diagnosis of cancer affected life of 90% of parents (N = 50) questioned, 10% parents had no prior knowledge of the disease before coming here, 96% of patient reported improved is understanding of disease after health education, 95% of patient were aware of importance of clean food, clean water and clean environment, 64% of parents reported that care of siblings of oncology patient was affected after their child was diagnosed with cancer.
Conclusions: Health education is important part of holistic care of oncology patient. Most of our patients were of low socio economic status with very little knowledge of hygiene and personal care. Health education improves care and quality of life of oncology patient by decreasing rate of infection and need for hospitalization.

P-221

THE INFLUENCES OF SCHOOL REENTRY SUPPORT ON RELATIONSHIPS THAT ADOLESCENTS WITH CANCER SHARE WITH PEERS AND TEACHERS

T. Soejima[1], I. Sato[1], J. Takita[2], K. Koh[3], M. Maeda[4], K. Ida[5], K. Kamibeppu[1]

[1]Department of Family Nursing, School of Health Science & Nursing Graduate school of Medicine The University of Tokyo, Bunkyo-Ku, Japan; [2]Department of Pediatrics, Graduate school of Medicine The University of Tokyo, Bunkyo-Ku, Japan; [3]Department of Hematology/Oncology, Saitama Children's Medical Center, Saitama-Shi, Japan; [4]Department of Pediatrics, Nippon Medical School, Bunkyo-Ku, Japan; [5]Department of Pediatrics, Teikyo University Mizonokuchi Hospital, Kawasaki-Shi, Japan

Objectives: Supportive relationships with peers and teachers, particularly the social support offered by these relationships, are especially important to adolescents with cancer. The purpose of this study was to clarify what forms of school reentry support for adolescents with cancer were related to the perceived social support. It was posited that adolescents with cancer would perceive supportive relationships with peers and teachers as high level of social support.
Methods: The questionnaire survey recruited 62 dyads of adolescents with cancer and their guardians. The questionnaire for adolescents had questions on perceived social support. The questionnaire for their guardians had questions on demographic information and school reentry support. Their guardians were interviewed to supplement the results of the questionnaire survey after completing their questionnaire.
Results: The questionnaire data from 37 dyads and the interview data from 3 guardians were analyzed. The questionnaire survey revealed that peers' visits, and their understanding of hospital experiences and how to interact with adolescents with cancer, were related to perceived social support from peers. Teachers' understanding about physical appearance, academic performance, and hospital experiences, as well as their status as a liaison between the hospital and school were related to perceived social support from peers and teachers. The interview survey found that adolescents with cancer could establish supportive relationships with peers and teachers when school reentry support led to 'adolescents' recognition that they are members of the local school,' 'peers' and teachers' understanding about the long-term recovery process of adolescents,' and 'adolescents' own awareness that they are struggling with the disease.'
Conclusions: Healthcare professionals should provide information to peers and teachers emphasizing adolescents' hospital experiences, and also encourage adolescents with cancer to regard their cancer experience as an opportunity to grow, which would help adolescents with cancer establish supportive relationships with peers and teachers.

P-222

CENTRALIZATION OF PAEDIATRIC ONCOLOGY NURSING EDUCATION IN THE NETHERLANDS: AN INCREASE OF THE SURVIVAL RATES?

C. van den Hoed-Heerschop[1]

[1]Bachelor of Nursing, University of Applied Sciences, Utrecht, Netherlands

Objectives: In the Netherlands approximately 550 children are annually diagnosed with cancer. These children are diagnosed and treated in 5 paediatric oncology centres (POC's) and 2 centres for allogenic stem cell transplantation. Treatment also takes place in secondary paediatric unites (Shared Care). About 75% of all children with cancer can be cured since 1990. The education and training of paediatric oncology nurses of the POC's and Shared Care is not according an existing and recognised competency framework. Training on the job is the method so far. Since 2009 there are major developments in the care for children and young people with cancer. Centralization of care is leading in this, not 7 hospitals but one National Paediatric Oncology Centre, the Princess Máxima Centre.
Methods: This study has a qualitative descriptive design.
Results: The current education of paediatric oncology nurses consists of: 4 years for the Bachelor Nursing degree (BN), 1 year Specialisation on Paediatric Nursing and training on the job in paediatric oncology nursing. To provide care at the highest level nurses should be highly qualified. Education and training is essential. In addition to centralization of care is centralization of education and training required for paediatric oncology nurses in the Princess Máxima Centre and the Shared Care.A start can be made with an outflow of students from the BN with a Paediatric Oncology Profile. Intensive cooperation is necessary between the study BN, internship's paediatric nursing and paediatric oncology nursing.
Conclusions: Only with one Paediatric Oncology Centre, the Princess Máxima Centre, in which specialised nursing care and nursing education and training are brought together at the highest level, the ambition of an increase in survival rates of more than 90% can be realised. Together with the highest possible quality of life during and after treatment.

P-223

A STUDY OF THE JAPANESE LITERATURE ON GRIEF CARE IN RELATION TO PEDIATRIC NURSING

K. Wada[1], A. Fuchita[2], A. Kato[3], T. Suyama[3]

[1]Nursing, Tokai University School of Health Science, Isehara, Japan; [2]Nursing, Tokai University Junior College of Nursing and Technology, Hiratsuka, Japan; [3]Nursing, Tokai University Hospital, Isehara, Japan

Objectives: To review Japanese studies on grief care in relation to pediatric nursing from the past 10 years and to ascertain the future direction of that research.
Methods: The keywords childhood cancer, grief care, and hospice were used to search for articles from 2004 to 2014 in a database of Japanese medical literature. Articles mentioning grief care were categorized and analyzed.
Results: The recipients of grief support were most often family members. The personnel providing grief care were most often nurses, followed by medical personnel. Grief care involved the need for grief care, difficulties of grief care, training in grief care, forms of grief care, and the grieving process.
Conclusions: Many studies have examined care for the bereaved, most of whom were family members, but few studies have examined care for other individuals such as nurses and children with cancer. The survival rate of children with cancer will improve in the future. A major issue that needs addressing is the mounting evidence of the need for grief care for children, and particularly those in the same ward as children who have died.

P-224

PAIN EXPERIENCED BY CHILDREN WITH CANCER: NURSE EXPERIENCE IN A RESOURCE LIMITED SETTING

J.W. Wekesa[1], A. Jebet[1]

[1]Hematoncology, AmpathOncology, Eldoret, Kenya

Objectives: To highlight pain experienced by children with cancer. To highlight challenges encountered.
Methods: An observation qualitative study was carried out. Through practice observing and interactions with children.
Results: Children with cancer felt pain during drawing of blood for investigations. Children also felt pain during fixing of branulars for administration of chemotherapy. When they have to receive injections for other treatments. During wound dressing. Pain from cancer itself especially during tumour progression.
Challenges:
- Lack of trained personnel to handle children with cancer.
- Lack of training opportunities and facilities to care for paediatric cancer. Lack of equipment and supplies such as POTTS, catheters for chemotherapy administrations.

Conclusions: Managing paediatric oncology pain reduces cancer suffering and improves quality of life.

P-225

EXPANDING PAEDIATRIC ONCOLOGY CARE INTO THE HOME: BUILDING NURSING COMPETENCE AND CONFIDENCE TO FACILITATE THE ADMINISTRATION OF SUBCUTANEOUS CYTARABINE AT HOME

C. Williams[1], J. Templeton[2], A. Shelly[1], J. Williamson[1]

[1]Paediatric Integrated Cancer Service, Royal Children's Hospital, Melbourne, Australia; [2]Childrens Cancer Centre, Monash Childrens Hospital, Melbourne, Australia

Objectives: A review of services provided by the "Monash Children's at Home " community nursing program indicated that many patients would benefit by expanding the nursing scope of practice to include the administration of subcutaneous cytarabine during treatment for acute lymphoblastic leukaemia (ALL). The general paediatric nurses indicated they lacked the confidence and competence to deliver this chemotherapy in the home. This project aimed to expand paediatric home-based outreach services to include the delivery of low complexity chemotherapy for paediatric ALL patients.
Methods: Staff attended the current foundations day offered for oncology nurses, as well as a 'fit for purpose' training module developed specifically to support this scope of practice This included training in chemotherapy safe handling, clinical trials and cell biology, and focused on the agent to be delivered. Nursing procedures for home administration of cytarabine were developed. Nurses were rostered to the oncology outpatient department for competency assessment.
Results: Fourteen paediatric community nurses have completed the competency program, providing a sustainable level of care. Nineteen children have so far been able to have their cytarabine delivered in the home. This has resulted in 133 hospital bed days saved, reduced 85 day oncology admissions and negated 48 inpatient weekend ward admissions. Travel distance saved across all families is estimated at 1,752 km.
Conclusions: This project illustrates the potential wide ranging benefits of implementing small, localised service improvement projects to families, staff and health services. By increasing the scope of practice and confidence of staff, the project has improved the care pathway for children and their families, with less hospital visits and more time at home. For the health services, it has freed up bed days and allowed the service to expand its level of care in the community. A fit for purpose model of training also encourages participation from services outside the oncology department.

P-226

PHYSICAL ACTIVITY SURVEY IN ADOLESCENTS WITH CANCER

J. Withycombe[1], M.C. Hooke[2], M. Wright[3], L. Gilchrist[4], K. Sachse[5], J. Danielson[6], K. Kelly[7]

[1]Children's Cancer and Blood Disorders Center, Palmetto Health, Columbia, USA; [2]School of Nursing, University of Minnesota, Minneapolis, USA; [3]Pediatric Oncology, McMaster's Children's Hospital, Hamilton, Canada; [4]Cancer and Blood Disorders Program, Children's Hospitals and Clinics of Minnesota, Minneapolis, USA; [5]Center for Cancer and Blood Disorders, Children's National Medical Center, Washington, USA; [6]Nursing Student, University of Minnesota, Minnesota, USA; [7]Division of Pediatric Hematology Oncology and Stem Cell Transplantation, Columbia University Medical Center, New York, USA

Objectives: Decreased physical activity has been well documented in childhood cancer patients, yet little is known about the adolescent's desire to engage in physical activity during treatment or the perceived barriers to these activities. Surveys were administered to 1) identify the exercise activities adolescents performed before diagnosis and what activities they are interested in during treatment as well as 2) to identify barriers for exercise during cancer treatment.
Methods: Participants (n = 43) were enrolled across six pediatric oncology centers in the United States and Canada. Participants were between 13-18 years, newly diagnosed with cancer, receiving chemotherapy with a planned treatment of at least 3 months, able to independently complete a written survey and able to provide assent/consent. Enrolled participants completed the Amherst Health and Activity survey describing their participation in physical activities before diagnosis and during month 2 of treatment, as well as physical activities that they would be interested in participating in during therapy.
Results: Adolescents' physical activity levels decreased during therapy, although interests remained high. Participation in calisthenics was 70% pre-diagnosis, 21% participation during therapy, with 51% expressing interest in this activity. Walking was reported as a 58% participation rate pre-diagnosis, 42% during therapy, with 51% expressing interest. Basketball was reported as the most commonly participated in team sport during therapy (16.3%). Interest was expressed for participation in basketball (42%), laser tag (37%), volleyball (32%), football (28%) and soccer (28%). Personal barriers to exercise were also reported.
Conclusions: Research has consistently shown that physical activity levels decrease during therapy. This study found that although activity levels declined, many adolescents still reported having an interest in being physically active during therapy. Awareness of the adolescents' interest in physical activity as well as the perceived barriers may assist healthcare professionals with engaging childhood cancer patients in maintaining more active lifestyles during therapy.

P-227

PERCEPTIONS OF CANCERFIGHTCLUB – AN INTERACTIVE INFORMATIONAL AND SOCIAL NETWORKING WEB-BASED PLATFORM FOR YOUNG ADULTS WITH CANCER

V. Wrzesien[1], A. Tsimicalis[1], C. Loiselle[1]

[1]Ingram School of Nursing, McGill University, Montreal, Canada

Objectives: Young adults with cancer are increasingly turning to online resources to meet their cancer-related needs; however, research is needed to explore their perceptions of these online resources. As a cancer survivorship platform, CancerFightClub (CFC) was created with the goals of providing young adults with cancer online access to support and resources. The study objectives were to: (a) explore the extent to which CFC addresses their practical, psychosocial and informational needs; and (b) explore how CFC could be enhanced.
Methods: A qualitative descriptive study was conducted with a purposive sample of young adults treated for cancer at a university-affiliated tertiary hospital in Montreal, Quebec, Canada. A one-time, face-to-face, semi-structured interview was completed for all participants. Data were audio-recorded, transcribed and thematically analyzed.
Results: Twelve participants of mixed age (range 19-39 years), gender (9 female), and first cancers (brain tumor, lymphoma, testicular, and breast) entered into the study. Participants expressed great interest in CFC; describing CFC as "important" and "definitely needed". They felt reassured in knowing they were not alone, as they were able to connect to a young adult cancer community — thus appeasing their feelings of isolation. CFC additionally provided a space where participants felt that they could find the information they needed without the information they wanted to avoid. Opportunities for enhancing CFC were recommended by facilitating direct peer connections, initiating diagnosis-specific discussions, providing support to family members, and raising awareness of CFC early-on.
Conclusions: CFC's regional online support community might contribute towards reducing young adults' feelings of isolation, and provide a resource that meets some of their needs. The positive reception to CFC helps to champion the continued development and use of such online support platforms for young adults. The cancer community should be made more aware of online-based support websites in order to refer their young adult patients to such helpful resources.

OTHERS

P-228

MAJOR ACHIEVEMENTS OF THE EUROPEAN NETWORK FOR CANCER RESEARCH IN CHILDREN AND ADOLESCENTS (ENCCA)

R. Ladenstein[1], M. Schrappe[2], K. Pritchard-Jones[3], A. Chiucchiuini[4], S. Essiaf[5], P. Kearns[6], A. Eggert[7], R. Haupt[8], G. Schreier[9], G. Vassal[10]

[1]Studies and Statistics on Integrated Research, Children's Cancer Research Institute, Vienna, Austria; [2]Department of General Pediatrics, University Medical Center Schleswig-Holstein Campus Kiel, Kiel, Germany; [3]Molecular Haematology and Cancer Biology Unit, UCL Institute of Child Health and Great Ormond Street Hospital NHS Trust, London, United Kingdom; [4]Grant Management & Research Support, Children's Cancer Research Institute, Vienna, Austria; [5]SIOPE Secretary General, SIOP EUROPE (the European Society for Paediatrc Oncology), Brussels, Belgium; [6]CRCTU, Birmingham Children's Hospital, Birmingham, United Kingdom; [7]Pädiatrie Onkologie und Hämatologie, Charité - Universitätsmedizin Berlin, Berlin, Germany; [8]U.O.S.D. Epidemiologia Biostatistica e Comitati, Istituto G. Gaslini, Genova, Italy; [9]Safety & Security Department, AIT Austrian Institute of Technology GmbH, Graz, Austria; [10]Research Clinical Division, Institut Gustave Roussy, Villejuif, France

Objectives: Building an effective European research arena by facilitating, fostering and coordinating regional, national and joint European pediatric and adolescent oncology programs and actions between European Member States to develop a virtual European Pediatric Oncology (PO) Institute
Methods: The European Network for Cancer Research in Children and Adolescents (ENCCA) project was funded by the European Union's FP7 program in 2011. ENCCA is driven by 34 leading organizations in 11 countries (18 structured work package activities) and

interacts with the SIOPE community, aiming to resolving fragmentation in translational research and biobanking, enhancing drug development, improving the clinical trial framework and population-based cancer registries and addressing special needs of patient groups with reference to age and given cancer diagnosis, including ethical aspects in clinical research.
Results: Having established the European Clinical Research Council as integrated platform for leukemia and tumor group chairs and presidents of national PO groups together with the European Parents& Patients Advisory Committee, ENCCA helped SIOPE to become the unique voice of European stakeholders resulting in a major impact on the new European Clinical Trials Regulation. ENCCA has designed an "Advanced Biomedical Collaboration Domain 4 ENCCA" (ABCD-4-E) which is a cloud-based solution for the "European Virtual Institute", and has created a roadmap towards the federation of pediatric cancer biobanking resources. Eight clinical trials are embedded in ENCCA, in addition to new methodological approaches and innovative trial designs. One of ENCCA's highlights is the development of the survivorship passport prototype for survivors. ENCCA triggered the establishment of new links of the PO community including patients/parents organizations to Industry and European regulators (EMA).
Conclusions: Actions undertaken so far are the basis for a sustainable EU Virtual Institute devoted to improve outcome and the quality of treatment of pediatric cancer and the quality of life of survivors.

RADIATION ONCOLOGY (PROS)

P-229

IMPROVING THE DELIVERY AND SAFETY OF PROTON BEAM THERAPY

J. Buchsbaum[1], B. Jyoti[1], V. Simoneaux[1], R. Reed[1], T. Conley[1]

[1]Radiation Oncology, Indiana Univeristy School of Medicine, Bloomington, USA

Objectives: In proton beam therapy production of secondary neutrons and its contribution to the risk of second malignancy is debatable. We hypothesized we could improve proton safety by decreasing neutron production. We simple methods to minimize neutron production.
Methods: The narrow proton beam produced by the accelerator needs to be laterally spread out to provide coverage of the target and use passive, active and pencil beam methods to achieve this. The amount of neutrons depends on the amount of high Z material intercepted in the path of the beam. Using a 12 cm snout and a 10 cm circular aperture at a 16 cm range and 10 spread out Bragg peak (SOBP) with 100 MU. Neutron readings were taken using a WENDI-II (Wide Energy Neutron Detection Instrument) neutron detector at a distance of 28 cm from the snout tip and 41 cm perpendicular to the snout tip on both the left and right sides. Five readings were collected per side. Various wobble (field) sizes and snouts were employed to compare neutron dose as wobble shape and size was compared to aperture size.
Results: Passive scanning averaged 71.05 mR. Active scanning averaged 52.68 mR. When the wobble was adjusted to mimic the aperture via only allowing a 1 cm overlap, the reading was 30.02 mR. Analysis of wobble shape showed decreasing neutron measurements as wobble sized decreased. When a real pediatric craniospinal field was treated via our 30 cm nozzle with an average wobble and an optimal wobble (30 x 16 versus 27 x 8 respectively) using a 7.5 cm deep 5 SOBP beam, the neutron reading fell from 47.0 mR to 28.87 mR.
Conclusions: Active scanning significantly decreased secondary neutron production relative to passive scanning. Wobble size directly impacted neutron production. It is possible to minimize neutrons via achievable methods using existing hardware.

P-230

IMPACT OF IMAGE-GUIDED RADIATION THERAPY (IGRT) ON PEDIATRIC RADIATION ACTIVITY

J. Francoise[1], V. Bogner[1], C. Reinaud[1], L. Padovani[1], X. Muracciole[1]

[1]Radiotherapy, Hopital de La Timone, Marseille, France

Objectives: To determine the impact of Image-Guided Radition Therapy (IGRT) on time and factors associated with magnitude of set-up displacement in pediatric population
Methods: The clinical data of 42 children treated between 2010 and 2013 in our institution were analyzed: 21 with IGRT (2DkV or CBCT) and 21 patients without IGRT (2DMV control). Time of session was calculated for the 2 groups. The setup errors were assessed by displacements in the superior-inferior (SI), anterior-posterior (AP), and medial-lateral (ML) directions and divided in minor (3 to 5 mm) and major (> 5 mm).
Results: 1069 sessions were delivered and 475 imaging were performed. In IGRT group, 321/583 (55%) sessions were realized with CBCT (72.6%) and 2DkV (27.4%) before irradiation versus 154 / 486 (27%) sessions with 2DMV. The mean time per session was 15 minutes for 2DMV group and 25 minutes for IGRT group. For children between 3 and 10, mean time of session with IGRT increased of 149% compared with session with 2D MV. In contrast, mean time of irradiation was similar whatever the irradiation modality. Minor displacements were found for 12.9% and 8.7% while major displacements for 4.1% and 0,3% respectively for group with CBCT and with 2DKV. Major displacement was found in 0.6% of cases if control was realized twice a week versus 4.6% for daily control. Major displacement concerned mainly the AP direction 8.1% vs 3.4% for SI and 0.85% for ML direction and children between 3 and 10 years old.
Conclusions: In pediatric population, IGRT control induced an increase of 40% for time of treatment. These results showed that using daily CBCT improved detection sensitivity and correction of residual errors exceeding 5 mm especially for children between 3 and 10 years old.

P-231

THE EMOTIONAL AND PSYCHOLOGICAL IMPACT ON RADIATION THERAPISTS OF TREATING CHILDREN IN A LARGE REGIONAL CANCER CENTRE, CANADA

L. Grimard[1], B. Smith[2], S. Hamilton[2]

[1]Radiation Oncology, The Ottawa Hospital, Ottawa, Canada; [2]Radiation Medicine, The Ottawa Hospital, Ottawa, Canada

Objectives: The aim of this study was to determine the psychological effects and difficulties that radiation therapists (RTs) experience while treating children. This study was intended to provide some information in order to assist RTs in their occupation, and complement the sparse literature on this topic
Methods: A survey was conducted in order to capture data on the emotional effects and opinions of RTs in one Cancer Centre. The questionnaire was inspired from the limited literature around this issue. The study converged on the reactions of RTs while children received radiation treatment and the impact on the RTs emotional state around this component of their practice. The questionnaire was distributed electronically via email. The answers were provided on a Likert scale for most questions.
Results: Sixty-two of the 104 RTs completed the survey of 20 questions. The questionnaire showed that gender and age played no major role in the RTs ability to cope mentally. Half of the RTs had children themselves; and of these, 66% indicated that having children made it somehow more difficult to cope emotionally with paediatric patients. Seventy-five-percent of all RTs indicated that the emotional state of parents or care givers of the affected children played a key role in the anxiety they felt during a child's treatment. Eighty-one percent of RTs stated that treating children caused higher anxiety levels than treating adults. Finally, our survey suggests that time constraints played a large part in the RTs stress level during treatments.
Conclusions: Overall, treating children did not cause much more distress than treating adults. Also, as a result of the survey, a new tool for RTs, describing the cognitive stages in children, was created in order to help RTs treat paediatric patients.

P-232

PROTON RADIATION FOR TREATMENT OF CHILDREN LESS THAN 18 MONTHS OF AGE

C. Hill-Kayser[1], Z. Tochner[1], M. Fisher[2], J. Minturn[2], J. Belasco[2], R. Bagatell[3], N. Balamuth[3], R. Womer[3], A. Reilly[3], P. Phillips[3], R.A. Lustig[1]

[1]Radiation Oncology, The University of Pennsylvania School of Medicine and The Children's Hospital of, Philadelphia, USA; [2]Pediatric NeuroOncology, The University of Pennsylvania School of Medicine and The Children's Hospital of, Philadelphia, USA; [3]Pediatric Oncology, The University of Pennsylvania School of Medicine and The Children's Hospital of, Philadelphia, USA

Objectives: Radiation therapy (RT) may be delayed, omitted, or reduced in dose for very young children in efforts to reduce toxicity. Proton therapy allows sparing of normal tissues, and may improve outcomes by allowing multidisciplinary treatment delivery to be delivered with maximal safety.
Methods: Ten patients requiring RT at age less than 18m were enrolled on a prospective registry. Radiation was delivered after induction chemotherapy and/or surgical resection where indicated based on diagnosis, but radiation was not delayed due to age. Radiation was planned after CT simulation and fusion of pre and post-operative imaging. The tumor bed, clinical target volume, and organs at risk were contoured with Eclipse planning software. Doses are reported in radiobiologic-equivalent-weighted absorbed dose (cGyRBE).
Results: The patient population at the time of RT ranged from 9-17m (median 13.5m), and 6 (60%) were female. Six patients had CNS tumors (medulloblastoma (1), ATRT (2), ependymoma (2), PNET (1)), with other diagnoses including neuroblastoma (2), undifferentiated sarcoma (1), and non-CNS rhabdoid tumor (1). Radiation treatment site included infratentorial brain (6), abdomen (2), and head/neck (2). Radiotherapy was delivered using passive scattered proton beams for 8 patients, and pencil beam scanning for 2. Dose ranged from 2160-5400. All patients received daily general anesthesia. No patient experienced greater than grade 1 (CTCAEv4) acute radiation-related toxicity. With a maximum follow-up of 22 months (range 1.4-22), all patients are alive, one with disease recurrence outside the radiation field. No patient has experienced serious (grade 3-4) long-term toxicity related to radiation.
Conclusions: Although radiotherapy for very young children must be undertaken with caution, proton therapy has potential to reduce normal tissue dose and maximize safety. Based on this series, proton radiation appears safe in the acute setting, even for extremely young children, and may improve outcomes compared to paradigms that eliminate RT. Long-term monitoring for late effects is paramount in this population.

P-233

FEASIBILITY OF BREAST SPARING DURING WHOLE LUNG IMRT IN CHILDREN WITH WILMS TUMOR LUNG METASTASIS: A DOSIMETRY STUDY

J. Kalapurakal[1], V. Sathiaseelan[1], Y. Gosiengfiao[2], J. Reichek[2], D. Walterhouse[2], M. Gopalakrishnan[1]

[1]Radiation Oncology, Northwestern Memorial Hospital, Chicago, USA; [2]Pediatric Oncology, Ann and Robert Lurie Children's Hospital, Chicago, USA

Objectives: We have demonstrated the feasibility and dosimetric advantages of whole lung IMRT in children. Several reports implicated whole lung irradiation (WLI) to be an important cause for the higher rate of secondary breast cancer in Wilms tumor (WT) survivors. We conducted a dosimetry study to estimate breast doses in females receiving WLI.
Methods: WLI plans using standard AP-PA (S-RT), IMRT and breast sparing IMRT (BS-IMRT) treatment plans were performed (ADAC system) using 6MV x-rays in 10 females (median age 4yrs). The doses to the breasts, breasts+5mm expansion, lung PTV, whole heart (WH), right ventricle (RV), left ventricle (LV) were compared. The PTV for IMRT included entire lung volume +1 cm margin, mediastinum and vertebrae. Heterogeneity corrections were applied. The RT dose was 12Gy/8fr. The organ-volumes (V) receiving specific RT doses (Gy): V_{12}, V_{10}, V_8 were estimated and compared.
Results: The mean breast dose with S-RT and IMRT was 9.2Gy (8.9-9.6Gy) and 10.6Gy (10.1-11.0Gy) respectively. The mean dose to the breasts+5mm expansion with S-RT and IMRT was 10.4Gy (10.2-10.7G) and 11Gy (10.8-11.2Gy) respectively. Following BS-IMRT the mean breast dose was 3.2Gy (2.8-3.4Gy) ($P < 0.0001$) and mean breast+5mm expansion dose was 4.9Gy (4- 5.5Gy) ($P < 0.0001$). The mean dose coverage to 95% of lung PTV was 95% of prescription dose with BS-IMRT and 98% with IMRT. The $V_{11.4}$, V_{10} and V_8 respectively for WH, LV and RV for S-RT was 96-100% and for IMRT and BS-IMRT was: WH 45% (<0.0001), 66% (<0.0001), 82% (<0.0001); LV 40% (<0.0001), 65% (0.0004), 84% (<0.0001); RV 21% (<0.0001), 54% (<0.0001), 77% (<0.0001).
Conclusions: This dosimetry study demonstrates that BS-IMRT can result in significant sparing of breast tissues in females with WT without compromising on improved lung volume coverage and cardiac protection compared to S-RT. BS-IMRT may be considered for young females with limited volume lung metastases.

P-234

RADIOTHERAPY OF CHILDHOOD RHABDOMYOSARCOMA: EXPERIENCE OF EGE UNIVERSITY HOSPITAL

S. Kamer[1], Y. Anacak[1], M. Kantar[2], S. Aksoylar[2], A. Celik[3], N. Cetingul[2], S. Kansoy[2]

[1]Radiation Oncology, Ege University School of Medicine, Izmir, Turkey; [2]Pediatric Oncology, Ege University School of Medicine, Izmir, Turkey; [3]Pediatric Surgery, Ege University School of Medicine, Izmir, Turkey

Objectives: Radiotherapy (RT) is frequently used in the treatment of RMS to contribute local-regional control. The planning and delivery of RT needs to be carefully organized in order to obtain maximum control with minimum late effects, regarding the small ages of the patients, tumor sites surrounded with critical organs, the need of high radiation doses to eradicate RMS. In this presentation we evaluated the results of RT in 38 children with RMS.
Methods: From January 2000 to October 2012, RT was used in 38 cases with RMS. Median age was 8 years (2-18) and M/F ratio was 2.4/1. Histological subtypes were embryonal in 17, alveolar in 16, botryoid in 1, mixt type in 4. Localization of tumors were pelvic in 16 cases (3 paratesticular, 7 vagina-bladder), head and neck in 10 (7 paramenengial), trunk in 7, extremities in 5 cases. From 2000 to 2006 patients were treated with SIOP/MMT-89 protocol (11 cases) and IRS III-IV was used after 2006 (27 cases). RT doses were 41-45 Gy for subclinical disease, 45-59 Gy for macroscopic tumors. External RT was used in 33 cases whereas brachytherapy alone was used in 3 cases and a combined external RT and brachytherapy was used in 2 cases.
Results: Median follow-up time was 30 months (5-100 months). Local-regional relapses were occurred in 11 while distant metastases were occurred in 10 patients. Unfortunately 14 patients were succumbed to progressive disease. Disease free survival rate at 3 years was 61% and overall survival rate 64%. Grade III/IV late effects of RT were detected in 8 patients (growth delay of bone and soft tissue in 6, renal atrophy in one and azospermia in one patient).
Conclusions: RT is effective treatment modality in the local–regional control of childhood RMS. Careful planning of RT is extremely important for maximum benefit. Long-term late effects need to be monitored in the pediatric age group.

P-235

FIFTEEN-YEAR EXPERIENCE IN CRANIOSPINAL IRRADIATION FOR THE MANAGEMENT OF PAEDIATRIC MEDULLOBLASTOMA PATIENTS

J.l. Lopez Guerra[1], P. Cabrera[1], R. Matute[2], J. Peinado[1], I. Marrone[2], G. Ramirez[3], A. Fernández-Teijeiro Álvarez[3], J.M. Praena-Fernandez[4], M.J. Ortiz[1], I. Azinovic[2]

[1]Radiation Oncology, Hospital Virgen del Rocio, Sevilla, Spain; [2]Radiation Oncology, Instituto Madrileño de Oncología/Grupo IMO, Madrid, Spain; [3]Pediatric oncology, Hospital Virgen del Rocio, Sevilla, Spain; [4]Methodology Unit- Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla, Hospital Virgen del Rocio, Sevilla, Spain

Objectives: Medulloblastoma (MB) is the most common malignant brain tumor of childhood. Craniospinal irradiation (CSI) is central to the management of these tumors. The purpose of this study is to assess the prognostic factors for survival in MB patients treated with postoperative CSI.
Methods: The study was conducted for patients with primary MB treated with CSI from August 1996 through May 2012 at 2 Institutions. Inclusion criteria included a minimum follow up of 6 months. Forty-eight patients (standard risk, N = 31; high risk, N = 17) met such criteria. Median CSI doses were 23.4Gy (13 fractions) and 36 Gy (20 fractions) for standard and high risk patients, respectively. The tumor bed received 50-60 Gy. Radiation therapy (RT) techniques used were two dimensional RT (N = 11), three dimensional RT (N = 15), volumetric modulated arc therapy (VMAT; N = 3), and tomotherapy (N = 19). Starting at the beginning of CSI, the intent was for standard-risk patients to receive eight weekly doses of vincristine. High risk patients underwent chemotherapy before RT. Adjuvant chemotherapy began approximately 6 weeks after patients completed RT.
Results: The median age at diagnosis was 8 years (range, 2-43) and the median follow-up 39 months (range, 7-198). Overall, 16 patients died. Two and three-year overall survival was 84% and 77%, respectively. There were 19 relapses. Two and three-year disease-free survival was 69% and 63%, respectively. The most common acute toxicity was hematological (87%), being grade ≥3 in 19 (39%) cases. In the univariate analysis, older patients (>8 years old) associated with higher risk of mortality (HR: 6.09; $P = 0.003$) and high risk patients associated with higher risk of relapse (HR: 2.67; $P = 0.047$).
Conclusions: Older patients associated with higher risk of mortality and high risk patients associated with higher risk of relapse. Further research is necessary to assess a better treatment approach in these patients in order to improve the outcome.

P-236

PREPARATION AND BEHAVIORAL TRAINING FOR PEDIATRIC PATIENTS TREATED BY PROTON BEAM THERAPY

M. Mizumoto[1], K. Ayuzawa[1], T. Miyamoto[1], Y. Oshiro[1], T. Okumura[1], T. Fukushima[2], H. Fukushima[2], H. Ishikawa[1], K.O.J.I. Tsuboi[1], H. Sakurai[1]

[1]Radiation Oncology, University of Tsukuba, Tsukuba, Japan; [2]Pediatrics, University of Tsukuba, Tsukuba, Japan

Objectives: Sedative care including anesthesia is often administrated for younger children during proton beam therapy (PBT). However, daily sedation contains something problem: manpower of specialist is required, anesthetic risk cannot be fully eliminated, and treatment time becomes prolonged. Besides, radiotherapy including PBT is associated with no pain, and daily treatment is doing same thing again for patients. Therefore, we consider PBT without anesthesia is possible even for pediatric patients who can communicate in some measure and have tried to administrate treatment training (preparation) for PBT not to use anesthesia.
Methods: From April 2010 to December 2012, 40 pediatric patients were treated by PBT in our institute. 24 of the 40 patients aged 2y 11m to 7y 4m were applied preparation and training for PBT as follows:At first, a patient look over the treatment room, and treatment fixator was made. Whole body fixation is made for pediatric patients, and treatment mask was prepared if necessary. During treatment planning and dosimetric measurement, patients come to treatment room every day, and simulated treatment with the fixator. The preparation was continued after the start of PBT.
Results: Fifteen of 24 patients could successfully receive PBT without sedation. The median age of 15 patients were 5y 8m (range: 3y 9m to 5y 8m). Sedative drugs were administrated to 9 patients at first, but became non-necessary for 5 of the 9 patients with daily training during PBT. The age of the 5 patients were ranged from 3y 9m to 5y 5m.
Conclusions: Preparation seems useful to perform PBT without sedation even for younger pediatric patients. Generally, PBT requires longer treatment time than photon radiotherapy. The preparation may be able to apply photon radiotherapy.

P-237

REVIEW ON 63 CHILDHOOD CANCER PATIENTS TREATED WITH ACCELERATED RADIATION THERAPY AT BACH MAI HOSPITAL, VIETNAM FROM JULY 2009 TO JULY 2013

K.H.O.A. Mai Trong[1], P. Pham Cam[1]

[1]Nuclear Medicine And Oncology Center, Bach Mai Hospital, Hanoi, Vietnam

Objectives: To review clinical and epidemiological characteristics of childhood cancers treated by accelerated radiation therapy at The Nuclear Medicine and Oncology Center, Bach Mai Hospital, Vietnam from July 2009 to July 2013.
Methods: Sixty-three childhood cancer cases underwent radiation therapy at The Nuclear Medicine and Oncology Center, Bach Mai Hospital, Vietnam from July 2009 to July 2013. This was a retrospective study

Results: Average age was 7.51 years old; youngest: 2, oldest: 15. The ratio male/female is 2,5/1. brain tumors (63,5%), wilms tumor (12.7%); bone tumor and soft tissue sarcoma (11.1%); leucemie with CNS infiltration (7.9%). Other kinds of tumors were less common. Clinical symptoms varied depending on cancer types: Intracranial tumors: 92.5% patients had headache and 85% had nausea or vomiting; other symptoms were hemiplegia (40%), cerebellar syndrome (25%). Wilms tumor: lumbar pain (75%), hematuria (50%), abdominal palpapble tumor (37.5%). Sarcoma: ischemia syndrome (85%), bone pain and limited movement (42.9%); infection syndrome (28%). Radiation doses changed depending on the natural of disease, stages and risk factors. Radiation side effects were reported mainly in the course of treatment such as headache (50.8%); nausea and vomiting (36.5%); fatigue (42.9%); anorexia (46%); hair loss (31%).
Conclusions: Accelerated radiotherapy in the combination of surgery and chemotherapy is an effective and safe method for the treatment of childhood cancers in pediatric patients (under 15 years old).

P-238

SHOULD PERCENTAGE NECROSIS INFLUENCE THE DECISION FOR ADJUVANT RADIOTHERAPY AFTER SURGICAL EXCISION IN EWING SARCOMA?

A. Puri[1], A. Gulia[1], N. Khanna[1], S. Laskar[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: To determine the indications of adjuvant radiotherapy after surgical excision in Ewing sarcoma.
Methods: Ninety-four consecutive patients of non metastatic Ewing sarcoma were analysed. Patients underwent appropriate surgical resection after receiving neoadjuvant chemotherapy. Excised specimen was analysed for chemotherapy induced percentage necrosis and divided as $< / > 90\%$ necrosis. Post operative adjuvant radiotherapy was decided on a case to case basis irrespective of percentage necrosis.
Results: One patient had involved margins. Necrosis was available in 80 patients. 25 had $< 90\%$ and 55 had $> 90\%$ necrosis. 23 of these patients received radiotherapy ($9 < 90\%$, $14 > 90\%$). All patients were available for follow up. The OS of all patients was 68% at 5 years. Currently 62 patients are alive (follow up range 33 to 90 months, median 61 months). There was no difference in OS in patients who received radiotherapy (57%) and those who did not (75%) $p = 0.133$. In the cases with $< 90\%$ necrosis the OS in patients who received radiotherapy was 56% as against 49% in those who did not $p = 0.760$. In the cases with $> 90\%$ necrosis, the OS in patients who received radiotherapy was 57% as against 85% in those who did not $p = 0.043$.
Conclusions: Our data suggest that the decision to offer adjuvant radiotherapy after surgical excision in Ewing sarcoma is multifactorial and independent of percentage necrosis after chemotherapy.

P-239

BEVACIZUMAB AS A TREATMENT FOR RADIATION-INDUCED NECROSIS (RIN): A PEDIATRIC CASE REPORT

M. Morici[1], C. Riccheri[1], D. Veron[1], S. Pampin[2], A. Muggeri[3], B. Diez[3]

[1]Pediatric, Hospital Nacional Prof A. Posadas, Buenos Aires, Argentina; [2]Neurosurgery, Hospital Nacional Prof A. Posadas, Buenos Aires, Argentina; [3]Neurooncogy, Fleni, Buenos Aires, Argentina

Background: RIN is a serious complication of radiation treatment for brain tumors. This damage results from local cytokine release, increase in capillary permeability and extracellular edema, and loss of the myelin covering of neurons. If allowed to progress, radiation necrosis can lead to small vessel occlusive disease and bleeding from friable small vessels. These changes combine to cause a definable worsening in patients' neurological signs and symptoms. Steroids are the standard of care treatment for brain RIN despite limited efficacy. Bevacizumab has been used in adults as a strategy to treat cerebral RIN
Purpose: We describe the use of Bevacizumab in a child with this complication.
Material and Methods: A ten- year- old male, who presented with a 4-week history of a progressively increasing headache, vomiting and left faciobrachiocrural paralysis. Magnetic resonance imaging (MRI) showed a supratentorial right temporoparietal lesion. Following complete resection of the tumor, histopathological examination revealed anaplastic ependymoma. He received conventional radiotherapy (5,940 cGy in 180 cGy fractions). After 12 months of radiation therapy, the patient reported severe neurocognitive impairment problems and urinary incontinence. The MRI revealed images suspected of RIN and confirmed by a stereotactic biopsy. After non effective steroid treatment, bevacizumab was administered for 2 cycles (7.5 mg/kg, at three-week interval)
Results: The child showed clinical neurological improvement and MRI revealed an important reduction in post-gadolinium and T2-weighted sequence analysis
Conclusions: Bevacizumab efficacy in the treatment of CNS RIN in adults justifies consideration of this treatment option for children who suffer RIN secondary to the treatment of brain tumors.

P-240

DAILY CBCT-IMAGING OF PEDIATRIC RADIOTHERAPY PATIENTS CAN REDUCE THE RISK OF SECONDARY CANCER

K. Seiersen[1], J. Hansen[1]

[1]Department of Medical Physics, Aarhus University Hospital, Aarhus C, Denmark

Objectives: Image-guided radiotherapy (IGRT) allows for accurate setup of patients for treatment, and in some cases daily IGRT makes reduction of PTV-margins possible. However, daily x-ray images also add to the integral dose delivered to the patient, and in pediatric cases many centers will limit IGRT due to the risk of secondary cancer. In this study we demonstrate that daily CBCT-imaging in combination with margin-reduction can reduce the total dose to the patient.
Methods: Thorough analysis of all uncertainties in our local radiotherapy process have shown that a PTV-margin as low as 2 mm can be used for small cerebral targets, when daily CBCT-imaging is applied. A 4-year old male ependymoma patient was planned and treated to 54 Gy over 30 fractions with a 3 mm PTV-margin. A second plan was prepared using a standard 5 mm PTV-margin. Care was taken to obtain similar target coverage and conformity index. The increase in integral dose from 3 to 5 mm margins was determined and compared to doses from CBCT-scans.
Results: Using tabulated data from vendor and published effective dose factors for children, we find that one CBCT-scan delivers an effective dose of 0.25 mSv. For 30 CBCT-scans this equals 7.5 mSv of added dose. Comparing the two dose plans, the plan with the 5 mm-margin gives an extra effective dose of about 31 mSv compared to the 3 mm-plan. The margin reduction thus reduces the effective dose 4 times more than the entire IGRT-procedure adds.
Conclusions: This case demonstrates that treating with standard radiotherapy margins without daily IGRT can result in a higher total effective dose, and thus risk of secondary cancer, than if reduced margins are used in combination with daily IGRT.

P-241

SHOULD FRACTIONATED FULL DOSE RADIOTHERAPY REMAIN THE STANDARD FOR TREATMENT OF METASTATIC SITES IN RHABDOMYOSARCOMA?

S. Skamene[1], D. Mitchell[2], S. Abish[2], C.R. Freeman[1]

[1]Radiation Oncology, McGill University Health Centre, Montreal, Canada; [2]Pediatric Hematology and Oncology, McGill University Health Centre, Montreal, Canada

Objectives: The current standard of care for patients with metastatic rhabdomyosarcoma includes full dose radiotherapy to each metastatic site. We wished to question this practice, which can cause side-effects and is often logistically challenging, by studying the pattern of failure in our pediatric and teenage patient population.
Methods: The McGill University Health Centre cancer registry was queried for patients diagnosed with rhabdomyosaroma aged 19 or less from January 1990 until January 2014. Twenty-nine patients were found and, of these, six had metastatic disease. Five of the six were treated with standard chemotherapy together with radiotherapy to the primary and metastatic sites with doses and fractionation according to site (36-50.4 Gy in 1.8 Gy fractions; 15 Gy in 1.5 Gy fractions for whole lung radiotherapy). Time to progression was calculated from the end of radiotherapy until radiological or pathological evidence of disease progression.
Results: Median age for the five patients was 13 years (range 12-18). Three were females (60%). All had alveolar histology and unfavorable primary sites (100%). Median number of metastatic sites treated was 2 (range 1-5). Three patients developed progressive disease outside the treated field (60%). One patient died from treatment-related complications without evidence of disease progression. Median time to progression was 14.3 months (range 1.9-88.6). One of the five patients remains progression-free at 88.6 months post radiotherapy.
Conclusions: Radiotherapy to metastatic disease sites prevented in-field progression in in all five patients with metastatic alveolar rhabdomyosarcoma. However, failure at sites outside of the radiotherapy volume occurred in 60% of patients and overall survival was very poor despite aggressive treatment to all sites of disease. Radiotherapy clearly has an important role in the management of patients with metastatic disease. Future studies should address radiotherapy dose and fractionation in the context of a need for better systemic control in this patient population.

P-242

REDUCING DOSE TO THE PANCREAS IN PEDIATRIC ABDOMINAL IRRADIATION WITH HELICAL TOMOTHERAPY START

E. Jouglar[1], G. Delpon[2], L. Campion[1], M.A. Mahé[1], S. Supiot[1]

[1]Radiation Oncology, Institut de Cancérologie de l'Ouest, Nantes-Saint Herblain, France; [2]Medical Physics, Institut de Cancérologie de l'Ouest, Nantes-Saint Herblain, France

Objectives: In children, irradiation of the pancreas and its tail was shown to increase the likelihood of secondary diabetes mellitus. We compare conformational radiotherapy (CRT) and helical tomotherapy (HT) for sparing the pancreas in children with abdominal irradiation.

Methods: We selected children with abdominal tumors treated in our institution who received ≥10Gy to the abdomen. Treatment plans were calculated using CRT (XiO, Elekta) or HT (TomoTherapy Treatment Planning System) in order to reduce the dose to the pancreas as low as possible while maintaining the same PTV coverage and the same dose-constraints to the other Organs At Risk (OAR). Dosimetric values were compared using Wilcoxon signed-rank test. The results were considered significant at the 0.05 level.
Results: The dose distribution of 20 clinical cases with a median age of 8 years (range 1-14) were calculated with different doses to the PTV: 5 medulloblastomas (36Gy), 3 left-sided and 2 right-sided nephroblastomas (14.4Gy to the tumor + 10.8Gy boost to para-aortic lymphnodes), 1 left-sided and 4 right-sided or midline neuroblastomas (21Gy) and 5 Hodgkin lymphomas (19.8Gy to the para-aortic lymphnodes and spleen). Using CRT or HT, similar target coverage was obtained. The doses to the other OAR were similar or better with HT. HT significantly reduced the mean dose to the Whole Pancreas (WP) and Pancreatic Tail (PT) in general (WP: 19.67Gy [SD 4.03] with CRT vs 12.56Gy [SD 5.05], p = 0.0001). The mean dose to PT was reduced in 17/20 patients with >10% difference and ranges -20% to -40% according to tumor location, reaching significance in midline and right-sided tumors, not in left (on 4 cases).
Conclusions: Using helical tomotherapy, it is possible to reduce the dose to the pancreas and its tail while maintaining a good PTV coverage and OAR sparing in children with abdominal irradiation.

P-243

A COMPARATIVE STUDY ON DOSE DISTRIBUTION OF PROTON BEAM THERAPY, AND CONFORMAL RADIOTHERAPY, AND INTENSITY-MODULATED RADIOTHERAPY FOR PEDIATRIC BRAIN TUMOR.

D. Takizawa[1], M. Mizumoto[1], T. Yamamoto[2], A. Muroi[2], T. Fukushima[3], H. Ishikawa[4], K. Tsuboi[4], T. Okumura[4], H. Sakurai[4]

[1]Radiation oncology, Faculty of Medicine University of Tsukuba, Tsukuba, Japan; [2]Neurosurgery, Faculty of Medicine University of Tsukuba, Tsukuba, Japan; [3]Child Health, Faculty of Medicine University of Tsukuba, Tsukuba, Japan; [4]Radiation oncology, Faculty of Medicine University of Tsukuba, Tsukuba, Japan

Objectives: The purpose of this study is to evaluate the effectiveness of proton beam therapy (PBT) for pediatric brain tumor compared to conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT).
Methods: From 2009 to 2012, 13 pediatric patients with brain tumor, who were treated by PBT in our institute, were evaluated. Seven patients of the 13 had ependymoma and 6 had germinoma. Localized irradiation and whole ventricle irradiation was performed for ependymoma and germinoma, respectively. The IMRT and 3D-CRT treatment plans were generated and optimized using the same practical treatment planning CT of PBT to compare dose distribution of PBT. The planning target volume (PTV) was identical among PBT, IMRT and 3D-CRT for each patient which was covered by 95% iso-dose line at all plans. The dose-volume histogram (DVH) for normal brain were calculated and compared
Results: At localized irradiation case, PBT could reduce 14 to 63% (median 38%) of normal brain dose compared to 3D-CRT, and 6 to 62% (median 38%) compared to IMRT. And whole ventricle radiation case, PBT could reduce 17 to 24% (median 22%) of normal brain dose compared to 3D-CRT, and 9 to 25% (median 21%) compared to IMRT.
Conclusions: PBT could reduce the dose of normal brain compared to 3D-CRT and IMRT.

P-244

PROTON BEAM IRRADIATION IN CHILDHOOD: FIRST EXPERIENCE AT THE WEST GERMAN PROTON THERAPY CENTRE ESSEN (WPE)

B. Timmermann[1], A. Steffen[2], S. Schulze-Schleithoff[2], D. Geismar[2]

[1]Clinic for Particle Therapy, West German Proton Therapy Centre Essen, University Hospital Essen, Essen, Germany; [2]West German Proton Therapy Centre Essen, University Hospital Essen, Essen, Germany

Objectives: Proton beam therapy (PT) is of increasing interest in pediatric oncology. The West German Proton Therapy Centre Essen (WPE) started treatments in May 2013. In September 2013, a registry was started to collect prospective data on children (<18 years) during and after PT.
Methods: Between June 2013 and March 2014, data on 26 children (sixteen males, 10 females, aged from 1.5-14.2 years (median 6 years)) were collected. Diagnoses were CNS (n = 20) and sarcomatous tumors (n = 6), respectively. Tumor sites were brain/head and neck (n = 22), spine (n = 2) and pelvis (n = 2). In 16 children, parallel chemotherapy was applied. Karnofsky performance status (KI) was below 80% in 13 patients at first presentation. Total PT doses ranged from 45 to 70 Gy (median 45 Gy). Side-effects were classified according to the Common Terminology Criteria for Adverse Events (CTCAE) grading system.
Results: Median follow-up (FU) was 4.3 months (range 1.8-8.4 months). In the majority of children, only grade 1 side-effects were observed as Erythema, Fatigue, Pain, Nausea, Fever and headache. In 2 patients, grade 2 pain and fever was observed. 1 patient presented with grade 3 oral Mucositis. At the end of PT, KI was scored 90-100% in 13, and below 80% in 13 children. Late side-effects were evaluable in 11 patients (FU> 90 days). One of them presented with a grade 3 keratitis. Otherwise, no or only mild late side-effects were documented: Fatigue, focal alopecia or skin reaction. At last FU, 7 patients presented with KI of 90-100% and 4 patients below 80%.
Conclusions: Current prospective and standardized data from WPE registry suggest excellent feasibility with only moderate early side-effects during and after intensive local PT in the majority of children. However, longer FU time and larger patient cohorts are needed to define the potential role of PT in pediatric oncology.

P-245

EARLY EXPERIENCES OF THE ADVISORY CENTRE FOR PARTICLE THERAPY IN PEDIATRIC ONCOLOGY IN GERMANY

B. Timmermann[1], S. Frisch[2], A. Steffen[2], S. Schulze-Schleithoff[2], D. Geismar[2]

[1]Clinic for Particle Therapy, West German Proton Therapy Centre Essen, University Hospital Essen, Essen, Germany; [2]West German Proton Therapy Centre Essen, University Hospital Essen, Essen, Germany

Objectives: Particle therapy (PT) is of increasing interest when modeling individualized oncological treatment concepts in childhood. The number of particle facilities is continuously increasing worldwide. Still, technical equipment and clinical indications treated with PT are diverging widely, and experts in this field are rare. Therefore, advising on PT is of increasing demand.
Methods: The advisory centre for PT in pediatric oncology offers support to referring centres, treating facilities and affected families. Support is provided in close collaboration with the respective radiation reference centre of the multidisciplinary trials of the German Society for pediatric oncology and hematology (GPOH) to ensure adequate treatment modality according to study protocols. Advising is given to define appropriate indications, to implement PT in new protocols or to push financial coverage by insurances. Until now, PT is considered in 9 interdisciplinary treatment protocols.
Results: Between January 1st, 2012 and December 31, 2013, 465 children and adolescents (<21 years, 57.8% males, 42.1% females) were presented to the advisory board. Age ranged from 0.1 to 19.9 years. Diagnoses were brain tumors (62.4%), sarcomas (22.8%) and miscellaneous (14.8%). In 44% advice was requested by radiation reference centres, in 39% by hospitals, in 13% by patients or family members, in 3% by PT centres and in 1% by other institutes. In the majority of inquiries, PT was recommended as first choice (59%). However, due to limited availability of PT-slots, external photon radiotherapy was proposed alternatively or exclusively in 50%. In 19% other treatment options were proposed.
Conclusions: The number of inquiries shows high demand in advisory services concerning PT. Efforts were made to establish PT in the multidisciplinary protocols to ensure evaluation and homogeneous approaches for PT. In future, advising activities will continue and data evaluation of the study groups accompanied by PT experts from the reference centre.
Supported by the German Children's Cancer foundation.

P-246

CLINICAL RESULTS OF PROTON THERAPY IN PEDIATRIC ONCOLOGY: SYSTEMATIC REVIEW OF LITERATURE

S. Vennarini[1], L. Vinante[1], B. Rombi[1], M. Amichetti[1]

[1]Department of Proton Therapy, APSS - Trento, Trento, Italy

Objectives: To systematically review the clinical results of proton therapy (PT) in pediatric oncology reported in the literature.
Methods: Two radiation oncologists searched independently in the Pubmed database the articles regarding PT in pediatric oncology, published between 01/01/1990 and 28/02/2014. The key words used, combined with Boolean operators AND/OR, were: "proton therapy", "pediatric cancer", "ependymoma", "medulloblastoma", "PNET", "craniopharingioma", "glioma", "rhabdomyosarcoma", "pediatric sarcoma", "Ewing sarcoma", "germ cells tumors", "osteosarcoma", "AT/RT", "retinoblastoma", "neuroblastoma", "Hodgkin lymphoma". Only articles reporting local control (LC), overall survival (OS) and late toxicity in series with ≥10 patients were selected. Reviews, editorials, congress abstracts and papers not in English language were excluded. The process was critically reviewed by other two researchers.
Results: Fourteen out of 104 selected articles were consistent with selection criteria. The median follow-up was limited (19-72 months). Four articles concerned chordoma (5-years (y) -LC = 60%-81%; 5y-OS = 60%-89%) and chondrosarcoma (5y-LC = 80%-100%; 5y-OS = 75%-100%), two soft tissues sarcomas (LC = 59%-75%; OS = 64-69%), one Ewing sarcoma (3y-LC = 86%; 3y-OS = 88%), one medulloblastoma/PNET (3y-LC = 92%, 3y-OS = 86%), one ependymoma (3y-LC = 83%; 3y-OS = 95%), one craniopharingioma (LC = 93%; OS = 80%), one low-grade glioma (LC = 78%; OS = 85%), one AT/RT (LC = 100%; OS = 90%), one germ cells tumors (LC = 100%; OS = 100%) and one neuroblastoma (3y-LC = 82%; 3y-OS = 75%). Late toxicity was usually of low-to-moderate grade. For intracranial or skull base malignancies the most reported toxicities were neuro-endocrinopathies (3%-50%), ototoxicity (3%-13%) and bone asymmetry (0-41%). Major events as brain necrosis or cerebrovascular problems were rare (≤7%). The cognitive function remained stable in comparison to the baseline. For peripheral tumors, dermatitis and vertebral asymmetry were the most frequent side effects observed.

Conclusions: The evidence of PT efficacy in pediatric oncology is limited. The clinical results reported confirm that PT can achieve similar LC rates as historic photon cohorts, while late toxicity appears to be reduced. These evidences are consistent with the results of dosimetric studies suggesting the potential clinical advantage of this technique.

RARE TUMOURS

P-247

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN CHILDREN: A TERTIARY CARE CENTER EXPERIENCE FROM INDIA

S. Agarwal[1], N. Radhakrishnan[1], D. Thakkar[1], V. Dinand[1], A. Gupta[1], V. Chinnabhandar[1], A. Sachdeva[1]

[1]Pediatric Hematooncology, Sir Ganga Ram Hospital, Delhi, India

Objectives: Hemophagocytic Lymphohistiocytosis (HLH), although rare, is being increasingly diagnosed nowadays. We discuss the clinical profile and treatment of patients diagnosed with HLH at our center over 2 years.
Methods: We retrospectively analyzed the patients diagnosed with HLH based on HLH 2004 criteria between January 2010 - December 2013. Search for secondary causes was performed in all patients. Patients who were <5years or with significant family history were evaluated for familial HLH.
Results: Out of total 31 cases diagnosed, Male: Female ratio was 3:1. Median age was 5 years. 5 children had parental consanguinity and 4 had previous sibling death. Presenting features included fever and hepatosplenomegaly (31), bleeding manifestations (6), lymphadenopathy (6), skin rash (4), shock (5), jaundice (11), CNS manifestations (8), renal failure (5), liver failure (1) and arthritis (1). All had pancytopenia. Other laboratory parameters include hemophagocytosis in bone marrow (23), hyperferritinemia (27), hypertriglyceridemia (26) and hypofibrinogenemia (26).
Secondary cause was identified in 12 patients. Infectious causes include EBV (2), typhoid (2), malaria (1), tuberculosis (1), juvenile rheumatoid arthritis (1), Pseudomonas (1), fungal (1) and CMV (1). Malignant causes include Hodgkin lymphoma (1) and anaplastic large cell lymphoma (1). Mutation analysis was positive in 6 out of 13 children evaluated. 2 children had FLH-3 (MUNK13-4), 1 each had FLH-4 (STX11), FLH-2 (Perforin) and Griscelli syndrome. A 8 weeks old child was heterozygous for MUNK 13-4; however sequencing for other mutations could not be done. Treatment given was according to HLH 2004 protocol. All received steroids, while only 17 received cyclosporine. 3 underwent stem cell transplant (2 Umbilical cord blood, 1 matched sibling bone marrow). 1 survived while 2 patients succumbed to secondary complications. Overall 17 patients expired (54%), 8 survived, 3 were lost to follow up and the rest are undergoing treatment.
Conclusions: Diagnosis of HLH should be considered in patients presenting with fever, hepatosplenomegaly and pancytopenia. Despite early and aggressive treatment we have encountered mortality in more than 50% of our patients.

P-248

LANGERHANS CELL HISTIOCYTOSIS: A SINGLE CENTER EXPERIENCE

K. Mutafoglu[1], D. Ince[2], E. Buke[2], D. Kizmazoglu[2], F. Yenigurbuz[2], E. Ozer[3], H. Guleryuz[4], A. Demiral[5], M. Olguner[6], N. Olgun[2]

[1]Dept. Pediatric Oncology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [2]Dept. of Pediatric Oncology, Dokuz Eylul University Insitute of Oncology, Izmir, Turkey; [3]Dept. of Pathology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [4]Dept. of Radiodiagnostics, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [5]Dept. of Radiation Oncology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [6]Dept. of Pediatric Surgery, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

Objectives: To evaluate patients with Langerhans cell histiocytosis (LCH) who were diagnosed and treated at our center.
Methods: The medical records of patients with LCH were rewieved. The clinical characteristics, treatment details and responses were analyzed retrospectively.
Results: There were 30 patients with LCH. The median age at diagnosis was 5.8yrs (3.4 month-15.8yrs), M/F ratio was 1.0. Complaints were: mass (47%), back/limb pain (47%), rash (20%), ataxic walking (13%), polyuria-polydipsia (3%), lymphadenopathy (3%). *Single system involved LCH (SSIG-LCH) (77%, n:23);* involvement sites were bone (87%), skin (4%), lymph node (4%), lung (4%). Surgery was performed in 52%, chemotherapy consisted vinblastin, prednisolone ± methotrexate, mercaptopurine was given in 48%, radiotherapy (RT) was given in 17% of cases. Out of primary relapse (n:1) occured, and treated by RT. Primary relapse (n:1) occured, and CR was achieved by cisplatin, interferon, vinblastin. The median follow-up time was 7.8yrs (1 week -18yrs), 15-years OS rate was 100% and 1-year and 15-years EFS rates were 95% and 88% respectively. *Multisystem involved LCH (MSIG-LCH) (23%, n:7);* involvement sites were bone (86%), skin (86%), lung (57%), pituitary gland (14%). In four patients had lung involvement as a risky organ (RO). Surgery was performed in two, chemotherapy consisted vinblastin, prednisolone ± methotrexate, mercaptopurine was given in all 7, and RT was given in two patients. Refractory disease (n:2) and out of primary relapse (n:1) occured in three patients. These three cases treated with cisplatin, interferon, vinblastin, prednisolone, CR achieved in two. The median follow-up time was 31month (8.5m-17y), the 2- and 5- years OS rates were%71 and EFS rates were 43%.
Conclusions: In MSI-LCH group age tends to be younger than SSI-LCH group, and these patients particularly had RO involvement. These patients need more intense therapy. Cisplatin containing chemotherapy is an effective treatment option for relapse/refractory LCH patients.

P-249

FOLLOW-UP OF CHILDREN WITH GENETIC MUTATION FOR ADRENOCORTICAL TUMORS IN WESTERN PARANÁ-BRASIL

C.M.C.M. Fiori[1], Rosa A.C.[1], L.F. Feracini[1]

[1]Hospital of Cancer, UOPECCAN Cascavel, State University of West Paraná, UNIOESTE, Cascavel, Paraná- Brazil

Introduction: The Adrenocortical tumors (ACT) is a relatively rare tumor accounting about 0.1% of malignancies. Despite its rarity, the South and Southeast regions of Brazil the incidence (ACT) is 15 times higher than the worldwide, about 3.4-4.2 casos/1.000.000 approximately. This incidence is considered an endemic problem in southern Brazil mainly in children under 5 years old. In a study conducted by Dr. Bonald Figueredo, through genomic screening of newborns, it was possible to identify the genetic mutation (R337H TP53 gene) in newborns of Paraná since 2005. The risk of developing the tumor in patients with mutation in Paraná is around 9.9%, as shown penetrance studies conducted by the same author in cases of ACT in Paraná.
Objective: Follow-up healthy children carry the germline TP53 mutation R337H for ACT, and refer early to a center for the Children's Oncology suspected cases.
Methods: Follow-up was performed in 29 children from the study by Pelé Pequeno Príncipe Research Institute, by collecting blood sample from the "heel prick " (DNA) specific to the ACT, with positive results for genetic mutation since 2006 until 2008. This monitoring was conducted at the outpatient clinic of Pediatrics of the University Hospital of the West of Paraná, Cascavel.
Results: Of the 29 children, 18 were female (62.0%) and 11 males (38%). And of these, three (10.3%) developed TCA, with clinical manifestations and initial hormonal level compatible with tumor development.
Conclusion: The clinical follow-up of healthy children with genetic mutation for ACT, in order to proceed with the investigation as early as possible in suspected tumor manifestation, will benefit those that eventually have tumor development and will increase the chance of cure.

P-250

FUNCTIONAL INHIBITION OF IGF1R IN ADRENOCORTICAL TUMORS CELLS PROMOTES CELLULAR DEATH AND CHANGES GENE EXPRESSION OF WNT/BETA-CATENIN PATHWAY COMPONENTS

C.A. Scrideli[1], R.C.P. Lira[1], L.F. Leal[1], P.F. Fedatto[1], C.E. Martinelli Jr[1], M. Castro[2], S. Tucci Jr[3], L. Neder[4], L.N.Z. Ramalho[4], M.L. Seidinger[5], I. Cardinalli[5], M.J. Mastellaro[5], J.A. Yunes[5], S.R. Brandalise[5], L.G. Tone[6], S.R.R. Antonini[6], C.A. Scrideli[6]

[1]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [2]Internal Medicine, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [3]Surgery, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [4]Pathology, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [5]Pediatrics, Centro Infantil Boldrini/State University of Campinas, Campinas, Brazil; [6]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil

Objectives: In preview analysis of 60 pediatric adrenocortical tumors (ACT), we observed a significant association of *IGF1R* high levels with tumor relapse and metastasis, especially in those with Weiss score ≥ 3. Interestingly, *IGF1R* expression presented correlation with some important genes from the Wnt/beta-catenin pathway, which could suggest some interaction between both pathways. The aim of the study was to evaluate IGF1R function in adrenocortical carcinoma cell line NCI-H295A.
Methods: The cells were treated with a specific IGF1R inhibitor (OSI-906) and performed cell proliferation and apoptosis assays. In addition, we investigated gene expression of components from IGF (*IGF1R*, *MAPK3*, *MAPK1PI3K*) and Wnt/beta-catenin (*CTNNB1*, *SFRP1*, *APC*, *AXIN1*) pathways after the treatment by quantitative RT-PCR.
Results: The OSI-906 treatment significantly decreased cell proliferation (concentrations between 125 and 3,000 nM) ($P < 0.0001$) after 48 and 72 hours, reaching 40% of reduction. The IC_{50} values were 2,636.7 nM ± 235.5 at 48 hours and 1,990.4 nM ± 777.3 at 72 hours. The apoptosis rate increased in a dose-dependent manner, reaching 70.8% of dead cells with 1000 nM ($P < 0.0001$; IC = 62.4 – 79.3). In addition, OSI-906 reduced gene expression of *CTNNB1*, *SFRP1* and *MAPK1* ($P = 0.034$; $P < 0.05$ and $P = 0.009$, respectively) and increased *IGF1R* ($P = 0.016$) after 6 hours. At 24 hours, it was observed significant low levels of *SFRP1* ($P < 0.05$) and *PI3K* ($P < 0.0001$).
Conclusions: The treatment with OSI-906 in adrenocortical carcinoma cells reduced cell proliferation and increased apoptosis rates in a dose-dependent manner, suggesting IGF1R as a potential therapeutic target. In accordance with the correlation observed in pediatric ACT, the inhibition of IGF1R function induced gene expression changes in Wnt/beta-catenin components, suggesting an association between both pathways.

P-251

MENINGEAL SARCOMA IN CHILDREN: A SURVEY FROM THE FRENCH SOCIETY OF PEDIATRIC ONCOLOGY (SFCE)

L. Mansuy[1], J.C. Gentet[2], D. Frappaz[3], C. Piguet[4], S. Gorde-Grosjean[5], J. Grill[6], E. Schmitt[7], S. Pall-Kondolff[1], P. Chastagner[1]

[1]*Pediatric Oncology, Children University Hospital, Vandoeuvre, France;* [2]*Pediatric Oncology, Children University Hospital, Marseille, France;* [3]*Pediatric Oncology, Institut Hop, Lyon, France;* [4]*children University Hospital, Children University Hospital, Clermont-ferrand, France;* [5]*pediatric Oncology, Children University Hospital, Reims, France;* [6]*pediatric Oncology, Institut G Roussy, Villejuif, France;* [7]*neuroradiology, Nancy University Hospital, Nancy, France*

Objectives: Describe the outcome of a population of meningeal sarcoma in children from the SFCE.
Methods: Retrospective study on patients harboring a meningeal sarcoma (MS) based on the French registry of pediatric tumor and pediatric oncologists questionnaires. Patient characteristics and treatments were collected. Pathology and imaging were centrally reviewed.
Results: Between 08/1989 and 05/2010 12 pts from 6 French centers, 3 months-14.5 years of age (mean: 3.3) were treated for a MS. Mean follow-up is 12 years (3 to 24 years). Tumor locations were: frontal (3), parieto-occipital (2), parietal (1), temporal (1), occipital (1), thalamic (1), pontocerebellar angle (1), cerebellar tentorium (1), cistern ambient (1). No metastase was observed. The first treatment was surgery in 10 cases, chemotherapy in 2. Resection was total in 6 cases, partial in 6. The pathological central review concluded to: high-grade undifferenciated sarcoma (8), chondrosarcoma (2), fibrosarcoma (1), myxoid desmoplastic tumor (1). 9 patients received 2 to 10 courses of chemotherapy (median 5). The number of patient alive is equal whatever the age (< or > 10 years) and tumor size (< or > 5 cm). 4 out of 6 pts who received radiotherapy are alive versus 1 out of 4 without radiotherapy. The 5-year EFS and OS are 50%. The median EFS in case of total resection is 39 months versus 16 in case of partial resection.
Conclusions: In this short series of very rare cancers, age and tumor size do not seem to be prognostic factors while total resection and radiotherapy seem to be essential. The role of chemotherapy is unclear.

P-252

INFLAMMATORY MYOFIBROBLASTIC TUMOURS IN CHILDREN-MASQUARDING PAEDIATRIC SOLID TUMOURS

M. Mir[1], M. Gull Bhat[1], A. Aejaz Shiekh[1], A. Rashid Lone[1]

[1]*Medical & Paediatric Oncology, Sheri-Kashmir Institute Of Medical Sciences (SKIMS) SrinagarJammu & Kashmirindia, Srinagar, India*

Objectives: Inflammatory myofibroblastic tumors (IMT) are rare, benign lesions most often seen in lung of young adults but can occur in children, in various sites. They mimic, clinically and radiologically, malignant tumors—especially sarcomas and lymphomas. The aim was to review the clinical, radiological and pathological data of children with diagnosis of IMT reffered to our department.
Methods: This retrospective study was carried out at the Department of Medical and Paediatric Oncology, Regional Cancer Centre, Sher-i-Kashmir Institute Of Medical Sciences (SKIMS), Srinagar, Jammu and Kashmir, India, from January 2012 to December 2013.
Results: Among 288 paediatric solid tumours registered during the study period, 5 (1.73%) had the diagnosis of inflammatory myofibroblastic tumours. There were 3 male and 2 female children (M:F ratio 1.5:1). The mean age was 5.32 years (range 2 to 9 years). The main symptoms were abdominal distension and pain in 60% (3 cases), breathlessness and cough in 20% (1 case) and right axillary area swelling in 20% (1 case). On Computed tomography of chest and abdomen,1 patient had mediastinal widening with impression of lymphoma, two patients were labelled as having retroperitoneal sarcoma, and 1 patient had an ileal growth with impression of burkitt lymphoma. In one patient with right axillary swelling, lymphoma was suspected. In 3 patients complete surgical excision was done (1 with axillary mass and 2 with abdominal disease). One patient with retropritonel mass had residual disease and received chemotherapy followed by complete second surgery. In case of mediastinal IMT, surgery was followed by local radiotherapy. Only 1 patients (20%) initial histopathology was diagnosed as IMT (retroperitoneal lesion), otherwise it was only after review with immunohistochemitry from an oncopathologist that diagnosis of Inflammatory myofibroblastic tumour was made. At present 4 patients are disease free and 1 patient with mediastinal IMT has residual progressive disease.
Conclusions: On presentation, IMT can constitute a formidable challenge, from diagnosis through to treatment.

P-253

MEDICAL TREATMENT OF CAPILLARY HEMANGIOMAS IN YOUNG CHILDREN

E. Unal Cabi[1], G. Yavuz[1], N. Tacyildiz[1], H. Dincaslan[1], Z. Gordu[1], G. Tanyildiz[1], S. Fitoz[1], K. Gundaz[1]

[1]*Pediatric Hematology-Oncology, Ankara üniversity Faculty of Medicine, Ankara, Turkey*

Objectives: Hemangiomas, common congenital lesions in infants and children are benign tumors that arise when islands of angioblastic tissue fail to connect with the developing vascular system. Capillary hemangiomas in young children are difficult to treat. The treatment of capillary hemangiomas is needed for both cosmetic and medical reasons including maceration and erosion of the epidermis, infection and risk of occlusive amblyopia when located in periocular site.
Methods: Between April 1996-February 2014, 270 patients, whose age ranged between 5 days to 7 years with capillary hemangiomas were followed. There were 196 females, 74 males. (F:M = 2.6:1)
Results: Among 270 patients 10 had multiple cutaneous lesions. Based on imaging studies of cranial and abdominal sites, there were no detected visceral hemangiomas. Most of the hemangiomas were located on head and neck in 148 (55%) cases and followed by 52 (19.6%) on the trunk, 44 (16.6%) on upper extremities, 20 (7.5%) on lower extremities, 8 (3%) on perineum, respectively. Medical management of hemangiomas included observation, corticosteroids, systemic beta blocker, local beta blocker, Interferon Alpha and sirolimus 49%, 6%, 12%, 13%, 20%, 1.3%, respectively.
Conclusions: Systemic steroids are tolerated well. Treatment with Interferon alpha 2-a is expensive, is used for vision threatening hemangiomas that are resistant to steroid treatment. Systemic propranolol has been effective and a reduction occurred in both radiographic and amblyogenic astigmastism. As the treatment does have potential complications, particularly cardiac, patients need to be monitored closely. Sirolimus have been effective in sizable hemangiomas resistant to steroids and systemic propranolol. It is highly recommended that patients should be monitored carefully.

P-254

GASTROINTESTINAL CANCER IN CHILDREN AND ADOLESCENTS - A SINGLE INSTITUTION EXPERIENCE

I. Daniluk[1], I. Filipek[1], D. Perek[1], B. Dembowska-Baginska[1], A. Brozyna[1], O. Rutynowska[1]

[1]*Pediatric Oncology Department, The Children's Memorial Helath Institute, Warsaw, Poland*

Objectives: To describe types and clinical course of gastrointestinal cancer in children and adolescents treated in our Institution.
Methods: Retrospective analysis of medical records of patients with gastrointestinal carcinomas treated between 1996 – 2013 was performed. Gender, age, tumor type, stage, treatment and it's results were analyzed.
Results: Out of 3,316 patients treated 14 (0.42%) were diagnosed with gastrointestinal tumors. There were 8 males and 6 females, aged 12 – 18 yrs, (median 15 yrs 10 m). Distribution of tumors was as follows: colorectal – 9 pts, pancreas – 4, stomach - 1. Two patients had FAP, 2 patients with ulcerative colitis developed colorectal carcinoma. Most patients presented with advanced disease at diagnosis (42% stage III and 35% stage IV). All patients underwent primary surgery, followed by adjuvant chemotherapy. Adult chemo-therapy regimens specific for disease type were used in first line treatment. At progression/ relapse chemotherapy was modified individually. Radiotherapy was implemented in 2 patients, targeted therapy - in 1 patient. There were 8/14 (57%) are alive, disease free from 3 to 120 months, median 14 months. Six patients died all from disease with time to death ranging from 3 to 32 months, median 5 months.
Conclusions: Insidious onset and advanced stage at presentation are hallmarks of digestive system carcinomas in childhood and adolescence. Early diagnosis has a crucial role. Individuals who are at risk based on carcinoma associated conditions should be closely monitored.

P-255

MANAGEMENT AND FOLLOW UP OF UROTHELIAL NEOPLASM OF THE BLADDER IN CHILDREN. A REPORT FROM THE TREP PROJECT

D. Di Carlo[1], A. Ferrari[2], G. Cecchetto[3], K. Perruccio[4], P. D'Angelo[5], A. Ruggiero[6], R. Alaggio[7], G. Bisogno[1]

[1]*Department of Paediatrics, University of Padua, Padova, Italy;* [2]*Paediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy;* [3]*Division of Paediatric Surgery, University of Padua, Padova, Italy;* [4]*Paediatric Oncology and Hematology Section, Santa Maria della Misericordia Hospital, Perugia, Italy;* [5]*Paediatric Hematology and Oncology, G. Di Cristina Children's Hospital, Palermo, Italy;* [6]*Paediatric Oncology Unit, A. Gemelli Hospital, Roma, Italy;* [7]*Institute of Pathology, University of Padua, Padova, Italy*

Objectives: Urothelial Neoplasms of the Bladder (UNB) are rarely found in paediatric patients. As part of the TREP (*Tumori Rari in Età Pediatrica*) project - an Italian network dedicated to very rare tumours - we present a nationwide series of patients with UNB with the aim to establish treatment and follow up guidelines.
Methods: From 2008 to 2013, 9 patients (age range 6-13 years) with UNB were registered. According to pTNM System, tumours were classified pTa: non-invasive, pT1: evidence of subepithelial invasion, pT2: muscle invasion, pT3: invasion of perivesical tissues, pT4:

invasion of extravescical organs. According to 2004 WHO Grading System we distinguished PUN-LMP, papillary urothelial neoplasm of low malignant potential (grade 1); LG-PUC, low grade-papillary urothelial carcinoma (grade 1 or 2); HG-PUC, high grade-papillary urothelial carcinoma, (grade 2 or 3).
Results: In all nine cases ultrasound showed a broad-based area or a polypoid lesion attached to the internal wall of the bladder (maximum diameter from 0.5 to 2.9 cm). All lesions were classified as pTa; 8 were considered G1-PUNLMP and 1 G2-HG-PUC. All lesions were completely resected by transurethral resection (TUR). In 3 children a single dose of intravesical chemotherapy was administered. One child had a recurrence one year after diagnosis and was treated by a new TUR and intravesical mytomicin. All patients are in complete remission (median FU 26 months). Follow up was performed differently in each patient and it was mostly based on ultrasound, cystoscopy at 2 months to 1 year interval and cytology.
Conclusions: We show that, in absence of defined guidelines, the management of children with UNB can be very heterogeneous and may include unnecessary and potentially toxic treatments. In consideration of the good prognosis, follow up should not be very intensive and the number of cystoscopies may be reduced.

P-256

PRIMARY PULMONARY TUMORS IN CHILDREN - 20 YEARS EXPERIENCE OF SINGLE CENTER

M. Cepelova[1], J. Malis[1], B. Frybova[2], M. Rygl[2], V. Mixa[3], D. Kodetova[4], M. Kyncl[5], J. Stary[1], J. Snajdauf[2]

[1]Dpt. of Paediatric Haematology and Oncology, 2nd Faculty of Medicine Charles University and University Hospital Motol, Prague, Czech Republic; [2]Dpt. of Paediatric Surgery, 2nd Faculty of Medicine Charles University and University Hospital Motol, Prague, Czech Republic; [3]Dpt. of Anaesthesiology and ICM, 2nd Faculty of Medicine Charles University and University Hospital Motol, Prague, Czech Republic; [4]Dpt. of Pathology and Molecular Medicine, 2nd Faculty of Medicine Charles University and University Hospital Motol, Prague, Czech Republic; [5]Dpt. of Radiology, 2nd Faculty of Medicine Charles University and University Hospital Motol, Prague, Czech Republic

Objectives: Primary pulmonary tumors in children are rare. Individual or single center experience is therefore limited. The aim of our study was to evaluate patients with primary pulmonary tumors at our institution during period of the years 1994 – 2013.
Methods: Between 1994 and 2013 we treated 27 children with primary pulmonary tumors. We retrospectively reviewed medical records and histological material of these patients.
Results: Twenty-seven patients (19 females, 8 males) were treated for primary pulmonary tumor. Median age at time of diagnosis was 8.7 years (range, 23 days to 19 years). The presenting symptoms were pneumonia (9x), cough (7x), fever (3x), wheezing (4x), dyspnea (2x), back pain due to bone metastasis (1x), failure to thrive (1x). CT scan was performed in all patients. Surgical procedure was pneumonectomy in three cases, lobectomy in 18 patients, segmental resection in four and biopsy in two patients. Nine histologic types of tumor were observed – twelve benign (seven inflammatory myofibroblastic tumors - IMT, two hamartomas, one invasive fibroblastic tracheobronchial tumor - IFTBT, one cystic histiocytoma, one fibro-histiocytic tumor), eight neuroendocrine tumors (typical carcinoid – NET) and seven malignant (four pleuropulmonary blastomas, one rhabdomyosarcoma and two mucoepidermoid carcinomas). All patients with malignant tumor received combined chemotherapy. At median follow-up of 12 years (range, 10 months to 20 years) 24 patients are alive without signs of disease, three patients died (11,1%) - one patient with pleuropulmonary blastoma and both patients with initially metastatic disease (mukoepidermoid carcinoma; carcinoid).
Conclusions: Primary pulmonary tumors are rare and their histopathology heterogenous. Estimated incidence in Czech Republic is 1.2:100 000 of live births. Prognosis of benign tumors after complete surgical resection is excellent, whereas malignant tumors are still associated with significant mortality.
University Hospital Motol participation is supported by Project for Conceptual Development of Research Organization No. 00064203

P-257

MUCOEPIDERMOID CARCINOMA IN CHILDREN: A SINGLE INSTITUITIONAL EXPERIENCE

P. Techavichit[1], J. Hicks[2], D. Lopez-Terrada[2], S. Sarabia[2], H. Sayeed[2], J. Nuchtern[3], J. Muscal[1], M.F. Okcu[1], M. Chintagumpala[1]

[1]Texas Children's Cancer and Hematology Centers, Texas Children's Hospital, Houston, USA; [2]Pathology, Texas Children's Hospital, Houston, USA; [3]Surgery, Texas Children's Hospital, Houston, USA

Objectives: To determine the clinicopathologic features and outcome of children with mucoepidermoid carcinoma.
Methods: Retrospective clinical, histopathologic and molecular findings were reviewed in patients with mucoepidermoid carcinoma at Texas Children's Cancer Center between 2000 and 2013.
Results: There were 9 females and 4 males. The mean age was 10.8 years (range 7-19 years). The tumors were located in the submandibular gland (4 cases), parotid gland (4 cases), soft or hard palate (2 cases) and tracheobronchial (3 cases). All patients with salivary gland and palate tumors presented with asymptomatic fluctuant mass while patients with tracheo-bronchial mass presented with persistent lower respiratory tract infection. The median duration of symptoms was four months. Among eleven patients with salivary gland and palate tumors, initial tumor biopsy was performed in six cases, while in five other patients gross total removal was attempted. Eight of eleven patients required additional surgical extirpation. Three patients required postoperative radiation therapy because of positive margin (2 cases) and mandible bone marrow involvement (1 case). Three patients with tracheobronchial tumors underwent bronchoscopy with tissue biopsy prior to total tumor removal by pulmonary lobectomy. Histological grades were low (1), intermediate (9) and high (3). Nine of ten informative cases were positive for *MECT1/MAML2* fusion transcripts by RT-PCR. There were no deaths, metastasis or recurrence in this series with a mean follow-up of 30 months. No patient was treated with chemotherapy.
Conclusions: In children and adolescents, MEC has a female predilection. Low to intermediate histological grades were more common as in adults. Complete excision is the treatment of choice with excellent outcome. The role of radiotherapy is unclear but maybe considered only in patients with positive surgical margin or incomplete resection.

P-258

THYMIC CARCINOMA IN CHILDREN: A REPORT FROM THE EUROPEAN COOPERATIVE STUDY GROUP FOR PEDIATRIC RARE TUMORS (EXPERT)

T. Stachowicz-Stencel[1], D. Orbach[2], G. Cecchetto[3], I. Brecht[4], D. Schneider[5], E. Bien[1], A. Synakiewicz[1], R. Julien[2], A. Ferrari[6], G. Bisogno[7]

[1]Department of Pediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [2]Department of Pediatrics, Insitut Curie, Paris, France; [3]Pediatric Surgery Unit Department of Woman's and Child's Health, Padova University Hospital, Padova, Italy; [4]Department of Pediatric Oncology, University Children's Hospital, Erlangen, Germany; [5]Clinic of Pediatrics, Municipal Hospital, Dortmund, Germany; [6]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [7]Division of Hematology-Oncology, Department of Pediatric University Hospital of Padova, Padova, Italy

Objectives: Thymic carcinomas belong to a group of rare thymic epithelial tumors arising from the anterior mediastinum and constitute 0.2 to 1.5% of all malignancies in adults. These tumors are extremely rare in children and no therapeutic guidelines has been established.
Methods: The clinical data and therapeutic characteristics of pediatric patients with malignant thymic tumors treated between 2000 and 2012 who were registered in the EXPeRT database of the cooperating national rare pediatric tumors working groups from France, Italy, Germany, United Kingdom and Poland.
Results: Twenty patients with thymic carcinoma, median age 14 years were enrolled into study. All patients were under 18 years old. Four children presented with autoimmune and paraneoplastic symptoms associated to tumor presence: myasthenia gravis, polymyositis, nephritic syndrome, and systemic lupus erythematosus associated to a hypertrophic pulmonary osteoarthropathy. Complete primary resection was performed in one patient, resection with microscopic residue was made in 3 cases and incomplete resection with macroscopic residue- in four patients. Chemotherapy with various regimens was administered to 17 children; 14 of them as neoadjuvant chemotherapy. Eight received additional radiotherapy. Fifteen children died. 5-year overall survival for the 20 patients with thymic carcinoma is $21.0 \pm 10{,}0\%$.
Conclusions: This study confirms very poor prognosis for pediatric patients with thymic carcinoma independent on the therapeutical management. Multidisciplinary and multicenter approach is necessary in order to make a common assessment.

P-259

BREAST MASSES IN CHILDREN AND ADOLESCENTS

S. Yesil[1], A. Karaman[2], C. Bozkurt[1], H.G. Tanyildiz[1], S. Tekgündüz[1], M.O. Candir[1], S. Toprak[1], I. Karaman[2], G. Sahin[1]

[1]Pediatric Oncology, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey; [2]Pediatric Surgery, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey

Objectives: The overwhelming majority of breast masses in children and adolescents are benign and self-limited. They have a variety of etiologies. Knowledge of the clinical and sonographic features allows the clinicians to guide appropriate management of these patients. In this paper we evaluated the breast masses in children and adolescents.
Methods: All children less than 18 years diagnosed with breast mass admitted to our center between March 2012 and March 2014 were analyzed for age, gender, complaint, history of malignancy, sonographic and pathological findings, diagnosis, retrospectively.
Results: Thirty-seven patients (29 females and 8 males) admitted with breast mass within last two years. The mean age was 14.6 years (range 5-18). Eleven patients had pain, 3 patients had nipple discharge, 2 patients had bloody nipple discharge. Two patients had family history of breast cancer. Ultrasonography was applied to all patients. According to BI-RADS (Breast Imaging Reporting and Data System) classification, 4 patients had category 3 and 2 patients

had category 4 masses. Four patients had operation of mass excision. Two of these patients were BI-RADS 4, and the remaining two patients were in BI-RADS 3 category. Furthermore three of operated patients' masses were more than 5 cm. Histopathologic diagnosis of these 3 patients were juvenile fibroadenoma. Pathologic diagnosis of fourth patient who had malignancy history was pseudoangiomatous stromal hyperplasia. The other patients diagnosis according to clinical and sonographic features were: Fibroadenoma 11 patients, gynecomastia 8 patients, breast abscess 6 patients, premature thelarche 3 patients, mammary duct ectasia 2 patients, accessory breast 1patient, fibrocystic change 1 patient and adenosis 1 patient. Patients followed up with ultrasound and none of them developed malignacy.
Conclusions: The prevalence of breast cancer in the pediatric age group is extremely low so a conservative approach of clinical and sonographic follow-up is more commonly adopted in children.

P-260

GENOME-WIDE APPROACH TO IDENTIFY GENE TARGETS OF PANCREATOBLASTOMA

T. Isobe[1], M. Seki[1], K. Yoshida[2], Y. Shiraishi[3], K. Chiba[3], H. Tanaka[3], Y. Sato[2], M. Kato[1], A. Hama[4], Y. Tanaka[5], S. Miyano[3], Y. Hayashi[6], S. Ogawa[3], A. Oka[1], J. Takita[1]

[1]Department of Pediatrics, The University of Tokyo, Bunkyo-ku, Japan; [2]Department of Pathology and Tumor Biology, Graduate School of Medicine Kyoto University, Kyoto, Japan; [3]Laboratory of DNA Information Analysis, Human Genome Center Institute of Medical Science The University of Tokyo, Bunkyo-ku, Japan; [4]Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Japan; [5]Division of Diagnostic Pathology, Kanagawa Children's Medical Center, Yokohama, Japan; [6]Hematology/Oncology, Gunma Children's Medical Center, Shibukawa, Japan

Objectives: Pancreatoblastomas (PBL) are unusual malignant neoplasms of the pediatric pancreas that may also rarely affect adults. Somatic alterations in the APC/beta-catenin pathway, including inactivating mutations in APC and activating mutations in CTNNB1, and loss of chromosome 11p have already been reported in the majority of PBLs. However, mainly due to its rarity, little is known about additional genetic changes that are responsible for the pathogenesis of PBL. To explore the genetic alterations underlying the pathogenesis of PBL, we performed whole transcriptome and exome analyses in 2 cases of PBL. Additional 6 cases of PBL were used as validation cohort.
Methods: Total RNA and DNA were extracted from fresh frozen tumors of the PBL patients. According to manufacture's protocol, mRNAs and exons were captured, and whole transcriptome/exome analyses using Illumina HiSeq 2000 were performed. DNA from matched germline samples were used as controls. All the candidate fusions and somatic mutations were validated by RT-PCR and Sanger sequencing.
Results: Across the coding regions of two cases, a number of candidate mutations and several novel fusion genes were identified. Similar to the other pediatric solid tumors, recurrent mutations were almost not detected in PBL, except for the CTNNB1 mutations (S33F and T41A). These CTNNB1 mutations were confirmed as somatic origin. Interestingly, we found a novel fusion transcript which associated with a beta-catenin related gene in one case.
Conclusions: As previously reported, our results revealed that alterations of CTNNB1-pathway could be responsible for the pathogenesis of PBL, and our result suggested that this pathway is a candidate for therapeutic target. To further elucidate pathogenesis of PBL, searching pathways enriched mutations, possibility of involvement of germline mutations, and epigenetic regulations should be assessed.

P-261

TREATMENT EXPERIENCE IN PEDIATRIC LANGERHANS CELL HISTIOCYTOSIS

D. Ince[1], B. Demirag[1], A. Erbay[2], R. Ortac[3], S. Kamer[4], Y. Oymak[1], G. Ozek[1], Y. Yaman[1], O. Carti[1], C. Vergin[1]

[1]Pediatric Hematology & Oncology Clinic, Dr Behcet Uz Children Hospital, Izmir, Turkey; [2]Dept. of Pediatric Oncology, Baskent University Faculty of Medicine, Adana, Turkey; [3]Pathology, Dr Behcet Uz Children Hospital, Izmir, Turkey; [4]Dept. of Radiation Oncology, Ege University Faculty of Medicine, Izmir, Turkey

Objectives: To summarize our treatment experience in patients with Langerhans cell histiocytosis (LCH).
Methods: Medical records of LCH patients were evaluated retrospectively for clinical features, treatment outcome.
Results: There were 20 patients with LCH with median-age-of-diagnosis 37mos (5mos-10yrs) and M/F-ratio 1.5. Nine had single system involved (SSI) LCH, 11 had multisystem involved (MSI) LCH.
SSI-LCH: Spontaneous complete remission (CR) without chemotherapy observed in both skin involved infants. Patient with Rosai Dorfman treated with LCH2 protocol. Surgery was performed in two patients with bone involvement, one of which also received RT. Remaining 4 patients with bone involvement received chemotherapy (LCH2 (n:3), LCH3 (n:1)), one of which was given additional RT. Out of primary relapse occured in three cases, CR achieved by RT in two patients. Median follow-up-time was 77mos (3mos–14.5yrs), 10-yr-OS 100%, 5- and 7-yr-EFS 60%.
MSI-LCH: Involvement sites were skin (n:8), lung (n:7), bone (n:7), liver (n:4), spleen (n:2), CNS (n:4), lymphadenopathy (n:1), gingiva (n:1); 8 patients had risky organ (RO) involvement. CR achieved in three without RO involvement. Five with RO involvement were treated with LCH2 treatment, (1) two died within one month due to progression, (2) one received additional RT and in CR, (3) PR achieved in one and liver transplantation was proposed, (4) one refused treatment at 4th month. Remaining 3 patients: (1) PR achieved with DAL HX90 protocol, then CR achieved with prednisolone, vinblastin, methotrexate, cyclophosphamide; (2) CR achieved with LCH3 and LCH4 protocols in remaining two patients. Primary and out of primary relapse occured in one of them, and treated with 2CdA containing chemo. Median follow-up-time was 49mos (1mo–10yrs), 5- and 10- yr-OS 82%, 5-yr-EFS 44%.
Conclusions: In addition to infants with spontaneous remission of skin involvement, there were infants with MSI-LCH who died early despite treatment. Pulmonary and liver involvements affected survival and outcome adversely. Multidisciplinary new treatment approaches are needed.

RENAL TUMOURS

P-262

TREATMENT OF RELAPSED WILMS TUMOUR (WT) PATIENTS: EXPERIENCE WITH TOPOTECAN

A.M.C. Mavinkurve-Groothuis[1], M.M. van den Heuvel-Eibrink[2], G.A. Tytgat[3], H. van Tinteren[4], G. Vujanic[5], K. Pritchard-Jones[6], L. Howell[7], N. Graf[8], C. Bergeron[9], T. Acha[10], F. Spreafico[11]

[1]Department of Pediatric Hematology and Oncology, Radboudumc, Nijmegen, Netherlands; [2]Department of Pediatric Hematology and Oncology, ErasmusMC-Sophia Children's Hospital, Rotterdam, Netherlands; [3]Department of Pediatric Oncology, Emma Children's Hospital, Amsterdam, Netherlands; [4]Department of Statistics, Dutch Cancer Institute (NKI-AvL), Amsterdam, Netherlands; [5]Department of Pathology, Cardiff University School of Medicine, Cardiff, United Kingdom; [6]Institute of Child Health, University College London, London, United Kingdom; [7]Department of pediatric oncology, Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom; [8]Pediatric Oncology & Hematology, Saarland University, Homburg, United Kingdom; [9]Pediatric Oncology & Hematology, Institut d'Hématologie et d'Oncologie Pédiatrie, Lyon, France; [10]Department of Pediatric Oncology, Hospital Materno-Infantil, Malaga, Spain; [11]Pediatric Oncology Unit Department of Hematology and Pediatric Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milaan, Italy

Objectives: Topotecan has been variably incorporated in the treatment of patients with relapsed WT who have previously been treated with the three or four drugs first line SIOP chemotherapy regimes. However, so far, no large series are available describing the efficacy of topotecan in this setting. Our objective was to describe outcome and to retrospectively investigate the potential role of topotecan in relapsed WT patients.
Methods: Children who were treated with topotecan as part of their chemotherapeutic regimens for relapsed/refractory WT were retrospectively identified and included in our study. Patient charts were reviewed for general patient characteristics, histology and stage at diagnosis, number and type of relapse, treatment schedules, toxicity, response to treatment and outcome.
Results: From 2000-2012, 27 children (median age at relapse 5.5 years, range 1.6-14.5) were treated with topotecan (refractory disease 10%, first relapse 43%, second relapse 30%, third relapse 7%, rest or partial response 10%). Topotecan was given as a single agent or in combination with other conventional drugs, e.g. cyclophosphamide, etoposide, carboplatin, ifosfamide. Sixteen patients had SIOP high-risk (HR) histology at diagnosis (including 11 diffuse anaplastic tumours). All died within 12 months because of progressive disease, except one, who had bilateral nephrectomy after a partial response to topotecan treatment. Eleven patients had intermediate-risk (IR) histology at diagnosis of which three patients displayed objective responses to topotecan. Overall, 5/11 IR patients survived (median follow up of 6 years), three of whom (stage V) had a bilateral nephrectomy after topotecan treatment.
Conclusions: Topotecan showed no effectiveness in the treatment of relapsed WT patients with high-risk histology. In patients with intermediate-risk histology, the role of topotecan might deserve further attention, to prove its efficacy.

P-263

SURGERY OF PATIENTS WITH LIVER METASTASES FROM WILMS TUMORS TREATED IN SIOP PROTOCOLS: SINGLE SURGICAL CENTER EXPERIENCE

A. Liné[1], C. Pasqualini[2], C. Patte[2], V. Fouquet[1], F. Guérin[1], G. De Lambert[1], S. Branchereau[1], D. Valteau-Couanet[2], H. Martelli[1], F. Gauthier[1]

[1]Pediatric Surgery, Bicetre hospital, Le Kremlin Bicêtre, France; [2]Pediatric Oncology, Institut Gustave Roussy, Villejuif, France

Objectives: Either synchronous or metachronous with renal tumor, liver metastases (LM) are less frequent than lung metastases in patients with Wilms tumors (WT). Persisting LM after

initial chemotherapy are proposed to excision. Our purpose is to report on a series of patients operated on for LM in a single pediatric liver surgical center.
Methods: All patients enrolled in SIOP studies 9, 93-01 and 2001, undergoing surgery for LM have been included in this retrospective study. Following points have been emphazised: synchronous (SLM) or metachronous (MLM) occurrence of LM, personal data, side, local stage and histology of renal tumor (s), vascular involvement and presence of lung metastases at diagnosis, number, location in liver of LM, surgical procedures and quality of resection of LM, follow-up and outcome of patients.
Results: Four patients with SML and 6 with MLM (diagnosed 1 to 123 months, average 23) after nephrectomy have been identified. Two had predisposing syndromes. Renal tumor was in right kidney in 6 patients, local stage III in 2, and high-risk histology in 1. At diagnosis 3 patients had caval involvement and 5 (4 SML + 1 MLM) lung metastases. At surgery all metastases, multiple in 6 cases, were in right liver, removed by means of wedge resection in 4 cases, "réglées" hepatectomies in 6 cases. Eight patients had complete (R0) and 2 incomlete (R1) microscopic resection. Three patients (one R1, two R0) had LM recurrence 4 to 12 months after LM surgery, and two of them died. The remaining 8 patients were alive and disease-free with a follow-up of 1 to 9 years.
Conclusions: These results point out the need for screening WT patients for LM after nephrectomy, and the major role of aggressive surgery aiming to microscopic complete excision of LM in their treatment.

P-264

PRELIMINARY TREATMENT OUTCOMES UTILIZING SIOP GUIDELINES IN A NOVEL ONCOLOGIC CARE MODEL FOR WILMS' TUMOR IN RWANDA

C. Shyirambere[1], S. Elmore[2], L. May[3], D. Umuhizi[4], N. Tapela[1], L. Lehmann[5], T. Mpunga[4]

[1]Non-Communicable Disease, Inshuti Mu Buzima/Partners in Health Rwanda, Butaro, Rwanda; [2]Medicine, Harvard Medical School, Boston, USA; [3]Global Health, Boston Children's Hospital, Boston, USA; [4]Butaro Cancer Center of Excellence, Ministry of Health, Butaro, Rwanda; [5]Clinical Pediatric Stem Cell Transplantation Center, Dana-Farber Cancer Institute, Boston, USA

Objectives: Wilms' Tumor (WT) is the most prevalent pediatric malignancy at the Butaro Cancer Center of Excellence (BCCOE), a Partners in Health-supported Ministry of Health facility in rural Rwanda. WT has been successfully treated in a few urban centers in Sub-Saharan Africa. There are currently no reports from rural centers on delivery of protocoled care via non-oncologist clinicians. This is the first report of preliminary outcomes using SIOP WT guidelines in this setting.
Methods: Patients treated for WT since program inauguration in July 2012 determined using electronic medical records and paper charts. Patients excluded if missing imaging or pathologic WT confirmation. Extraction performed using Excel with validation parameters. Descriptive analyses and non-parametric comparisons were performed with SPSSv20.
Results: 38 patients treated for WT, 61% female (n = 23), median age at intake 45 months (range:1-52). 68% (n = 26) presented with localized, unilateral mass, 24% (n = 9) metastatic, 5% (n = 2) localized bilateral, and 3% unknown (n = 1). Common metastatic sites were lung (89%; n = 8) and liver (67%; n = 6). 35 started pre-operative chemotherapy (Vinc/Act-D: 66%, n = 23; Dox/Vinc/Act-D: 34%, n = 12) and 71% (n = 27) had surgery. Post-surgically, SIOP staging: 37% (n = 10) I/II, 15% (n = 4) III, 11% (n = 3) IV, 4% (n = 1) V, 33% (n = 9) indeterminate/missing. 26 started post-operative chemotherapy (Dox/Vinc/Act-D: 92%, n = 24; Vinc/Act-D: 8%, n = 2). 21% (n = 8) died (median time intake-death: 11 days, range:1-45), 75% (n = 6). 17% of treated patients were lost to follow up (n = 5). 14 patients completed treatment, 57% (n = 8) had post-treatment evaluation. All evaluations showed clinical remission (median follow-up: 12 months, range:10-14).
Conclusions: WT can be successfully treated in a rural, resource-limited setting through a protocoled approach utilizing non-oncologist clinicians. Loss to follow-up remains low relative to comparable settings. Treatment vs. disease-related mortality is difficult to determine, though conservative analysis indicates treatment-related mortality estimates within reported ranges for SIOP PODC protocol. Further studies to determine mortality associated risk factors are needed.

P-265

PATIENTS WITH NEPHROBLASTOMA TREATED WITH SIOP 2001 PROTOCOL IN NATIONAL HOSPITAL OF PEDIATRICS, HANOI, VIETNAM – OUTCOME AND CHALLENGES

H. Tran[1]

[1]Oncology, National Hospital of Pediatrics, Hanoi, Vietnam

Objectives: Our aim is to replicate the result of SIOP 2001 protocol in our hospital and test its applicability in the Vietnam situation
Methods: All eligible patients with inclusion criteria of SIOP 2001 protocol will be enrolled to the study. For intermediate risk group, patients with stage II treated with AV2 regimen, patients with stage III treated with AVD + RT (no randomization). Patients enrolled on study from July 2008 to December 2012 and follow up to 30th June 2013.
Results: Eighty patients had enrolled to study: 7 died or abandoned during preoperative chemotherapy, 13 had other diagnosis after preoperative chemotherapy. 60 patients had diagnosis nephroblastoma and had full treatment, 2 were lost for follow-up after cease of treatment, and they were in EFS at last examination. After preoperative chemotherapy tumor's volume reduced in 86.5% cases and total volume of tumors reduced by 47.7%, 38.3% of tumors in stage I. 58 patients had been followed up to the end of study: 9 patients died, 13 relapsed. There are 75.9% of patients in event free survival and 84.5% in overall survival (follow up time 2-57 months, mean 27 months). Imaging diagnosis is corrected with pathological anatomy in 78.3% cases, much lower than SIOP data. The discrepancy may be due to less experience by our imaging specialists compared with SIOP institutions or a true higher incidence of rare tumors in our Vietnamese population. We experienced a higher incidence of 18% of clear cell sarcomas and rhabdoid tumors compared with 4-6% reported by SIOP. Pathological anatomy diagnosis is a difficult work because rapid central review is not available as in SIOP institutions
Conclusions: In National Hospital of Pediatrics, protocol SIOP 2001 had been applied successfully, our treatment outcome is much lower than SIOP data, imaging and pathological anatomy diagnoses are big challenges.

P-266

WILMS TUMOR: A RETROSPECTIVE STUDY OF 61 CASES IN THE CENTER OF TUNISIA

I. Chabchoub[1], M. Haj Mansour[1], F. Zairi[1], N. Kallala[1], H. Zaghouani[2], L. Ben Fatma[1], O. Gharbi[1], M. Hochlef[1], M. Nouri[3], S. Ben Ahmed[1]

[1]Medical Oncology, Farhat Hached, Sousse, Tunisia; [2]Radiological, Farhat Hached, Sousse, Tunisia; [3]Pediatric Surgical, Farhat Hached, Sousse, Tunisia

Objectives: To compare our results to SIOP 9 study.
Methods: We studied retrospectively 61 children with WT treated at the department of medical oncology of Farhat Hached Hospital, from January 1994 to December 2010. Kaplan Meier method with Log-Rank testing was employed for survival analysis.
Results: The mean age was 3.5 years old, with a sex ratio 0.48. Eighty percent of the children presented a painless abdominal tumor as a first sign. The tumor was mainly unilateral (93%), right for 56% of them. Ultrasounds, computed tomography showed an heterogeneous tumor in 52%, with a medium size of 16.5 cm, developed in 48% in the lower pole of the kidney. Venous thrombosis were diagnosed in 6.5%. WT were metastatic in 23%. Most of the patients received preoperative chemotherapy (98.3%) then enlarged nephrectomy was practiced (only 2 postoperative complications). Postoperative stage I, II, III were respectively 39%, 41%, 20% and according to SIOP 9 risk classification, there were 28%, 62%, 10% of low, intermediate and high histological risk. Postoperative chemotherapy was received in 84%. Adjuvant radiotherapy was practiced in 16%. The five-year overall survival was 68%, 80% in localized stages and 46% in metastatic stages. Thirty-four percent relapsed in an average of 9 months. No late sequelae was noticed.
Conclusions: This study shows less overall survival then the SIOP 9, due to a bigger rate of metastatic forms, late diagnosis and the difficulty to respect the time schedule of the protocol.

P-267

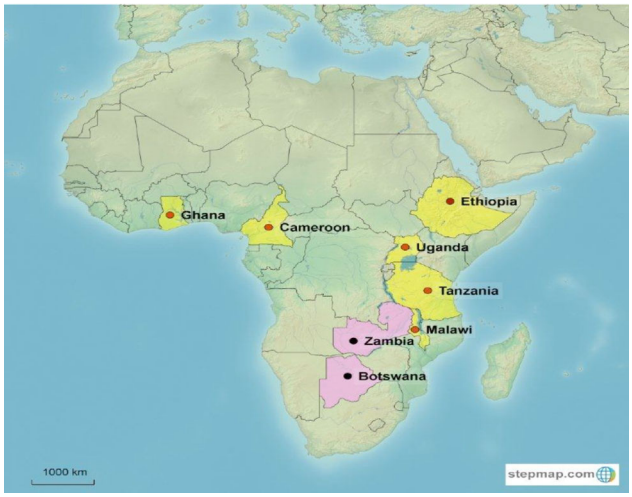
SIOP AFRICA/PODC COLLABORATIVE WILMS TUMOUR PROJECT – CHALLENGES AND PROGRESS

F. Kouya[1], E.M. Molyneux[2], P.B. Hesseling[3], J. Balagadde[4], V. Paintsill[5], T. Scanlan[6], L. Hadley[7], L. Burns[8], L.A. Renner[9], T. Israels[10]

[1]Department of Paediatrics, Mbingo Baptist Hospital, Mbingo, Cameroon; [2]Department of Paediatrics, College of Medicine, Blantyre, Malawi; [3]Department of Paediatrics and Child Health, University of Stellenbosch, Cape Town, South Africa; [4]Department of Paediatric Oncology, Uganda Cancer Institute, Kampala, Uganda; [5]Department of Paediatric Oncology, Komfo Anokye Teaching Hospital, Kumasi, Ghana; [6]Department of Paediatric Oncology, Muhimbili Hospital, Dar es Salaam, Tanzania; [7]Department of Paediatric Surgery, University of KwaZulu-Natal, Durban, South Africa; [8]Operational Manager, World Child Cancer, London, United Kingdom; [9]Department of Paediatrics, Korle Bu Teaching Hospital, Accra, Ghana; [10]Department of Paediatric Oncology - Outreach Program, VU University Medical Center, Amsterdam, Netherlands

Objectives: Reported survival of Wilms tumour (WT) patients in sub-Saharan Africa is 11 – 50%. Challenges include late presentation, malnutrition, less intense supportive care facilities and failure to complete treatment. We aim to improve care and survival in a feasible and sustainable fashion.
Methods: A regional collaborative group has been established with participation of eight institutes in five countries in sub-Saharan Africa. All institutes have had a dedicated childhood cancer unit, established Wilms tumour treatment and external (funding) support for several years. A SIOP PODC adapted treatment guideline for Wilms tumour and supportive care in low income countries was published. It includes an emphasis on the diagnostic role of ultrasonography, preoperative chemotherapy with a reduced dosage for malnourished children and social support to enable parents to complete treatment. This guideline is being implemented as a multi-centre prospective clinical trial, expecting about 200 new patients per year. Research questions include event free survival, reasons of treatment failure, efficacy and

toxicity of preoperative chemotherapy and the comparison of surgical staging, local pathology and central review pathology in stratifying postoperative chemotherapy.
Results: A comprehensive uniform treatment protocol, uniform data collection form and central data collection tool are in place. A collaborative agreement has been developed and signed by the different participating units. Local IRB approval has been sought in the different units. A baseline evaluation of outcome has been done for the years 2011 – 2013. World Child Cancer and SIOP have agreed to co-fund for 5 years. Enrolment started in January 2014. The project website is on paedonc.wix.com/wilmsafricaproject.
Conclusions: Prospective use of adapted treatment regimens for childhood cancers along with systematic data collection among regional partners is achievable in Sub-Saharan Africa. We hope to demonstrate in the future, that this leads to improvement in outcomes along with capacity building.



P-268

RESULTS OF THE SIOP-2001 TRIAL AND STUDY FOR THE TREATMENT OF NEPHROBLASTOMA AT A SINGLE INSTITUTION IN A DEVELOPING COUNTRY

C. Cafferata[1], W. Cacciavillano[1], A. Rose[1], L. Galluzzo[2], P. Flores[3], P. Zubizarreta[1]

[1]Hemato-Oncology, Hospital de Pediatría J.P. Garrahan, Ciudad Autónoma de Buenos Aire, Argentina; [2]Pathology, Hospital de Pediatría J.P. Garrahan, Ciudad Autónoma de Buenos Aire, Argentina; [3]Surgery, Hospital de Pediatría J.P. Garrahan, Ciudad Autónoma de Buenos Aire, Argentina

Objectives: Evaluate the outcome of patients with Wilms Tumor (WT), treated according to SIOP-2001 strategy.
Methods: A retrospective analysis of 141 consecutive patients with WT diagnosed at our institution between December 2001 and 2013 was performed. Kaplan-Meier survival estimates for overall survival (OS) and event free survival (EFS) were calculated.
Results: 115 patients, median age 38.8 months old (3-155) were assessable for analysis. Fine needle aspiration was initially performed on 88 patients (84.6%). Stage distribution was: stage I:33%; II:10.4%; III:27.8%; IV:13.9%; V:14.7%. Six patients (5.2%) were stage III because of tumor spill during surgery. Eleven patients (9.5%) underwent initial nephrectomy. The other patients received preoperative chemotherapy (POC). Adjuvant chemotherapy was given without randomization, using vincristine-actinomycin D for stage II and vincristine-doxorrubicin-actinomycin plus radiotherapy for stage III. With a median follow up of 52 months, 5-year OS and EFS were 91% and 84.5%. OS according to stage was: stage I:92%; II:99%; III:88%; IV:78%; V:99% ($p = 0.04$). There was no significant difference in EFS ($p = 0.4$). Seventy-eight patients (85.7%) were intermediate risk, and 11 patients (12%) high risk. Comparing blastemal subtype with intermediate-risk subtypes, the 5-year OS was 100% vs. 88% ($p = 0.47$), and EFS was 100% vs. 80% ($p = 0.92$). Five-year EFS according to tumor volume after POC was 95% for tumors $\leq$399ml and 60% for $\geq$400ml, respectively ($p = 0.0003$). There was no significant difference in OS ($p = 0.13$). Fifteen patients (13%) relapsed within 2 to 99 months (median 29,9). Eight patients (6.9%) died of progressive disease. There were no treatment-related deaths.
Conclusions: SIOP-2001 guidelines are feasible to be applied in our institution, with excellent results. The 5-year OS and EFS in our series are similar to those reported by the leading groups. Despite of small number of patients, blastemal subtype showed better outcome when treated with an intensified regimen.

P-269

OUTCOME OF WILMS TUMOR TREATED WITH SIOP WT 2001 (UK VERSION) GUIDELINES: A MULTICENTER EXPEREINCE IN PAKISTAN

S. Ashraf[1], S. Sultan[1], B. Ahmed[1], S. Aba Umar[1], S. Saulat[1], S.A.H. Rizvi[1]

[1]Paeds Urology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

Objectives: To study outcome of children with Wilms tumor treated with SIOP 2001 (UK version) guidelines
Methods: Retrospective chart review of all cases of Wilms Tumors registered at CCH and SIUT from July 2002 to October 2012. Children treated after immediate nephrectomy and those presenting with relapsed disease after chemotherapy were excluded. Only children received pre and post- operative chemotherapy as per SIOP WT 2001 (UK VERSION) guidelines were included. Outcome analysis was done with respect to disease stage at presentation (localized, metastatic and bilateral), post op- staging and risk group. Causes of death were recorded.
Results: There were 131 children diagnosed with Wilms tumor on pre-op biopsy during study period. The age range was 0.1 - 3 years (median 3 yrs). Male to female ratio was 1.46: 1. Abdominal mass (100%) and hematuria (15%) were most common presentation. At presentation localized, metastatic and bilateral diseases were seen in, 93 (71%), 25 (19%) and 13 (10%) respectively. The overall survival with median follow up of 5.5 years for whole cohort with and without abandonment is 64% and 76% respectively. Overall survival among localized disease with and without abandonment is 70% and 80%, for metastatic disease 48% and 55% and for bilateral disease it is 46 and 75%. Overall survival according to post-op stage for localized disease were stage 1 (95%), stage II (71%) and stage III (72%). Survival according to risk group among localized were low risk (100%), intermediate risk (84%) and high risk (76%). Major causes of death were relapses, inoperable tumor with poor response to chemotherapy and sepsis. Abandonment during treatment was a major adverse factor.
Conclusions: Treatment of Wilms tumor with SIOP approach in Karachi has shown good survival. This can be further improved with reduction in abandonment, toxicity deaths and better compliance with protocol.

P-270

WILMS TUMOUR IN MALAWI: SURGICAL STAGING TO STRATIFY POSTOPERATIVE CHEMOTHERAPY ?

E.S. Borgstein[1], S. Kamiza[2], G. Vujanic[3], D. Pidini[4], S. Bailey[5], T. Tomoka[2], G. Chagaluka[4], G.J.L. Kaspers[6], E.M. Molyneux[4], T. Israels[7]

[1]Department of Surgery, College of Medicine, Blantyre, Malawi; [2]Department of Histopathology, College of Medicine, Blantyre, Malawi; [3]Department of Histopathology, Cardiff University, Cardiff, United Kingdom; [4]Department of Paediatrics, College of Medicine, Blantyre, Malawi; [5]Department of Paediatric Oncology, Sir James Spence Institute of Child Health, Newcastle, United Kingdom; [6]Department of Paediatric Oncology, VU University Medical Center, Amsterdam, Netherlands; [7]Paediatric Oncology, VU University Medical Center, Amsterdam, Netherlands

Objectives: Wilms tumour postoperative chemotherapy is ideally stratified according to the pathologist's assessment of tumour stage and risk classification (tumour type). In sub-Saharan Africa results are often not available in time to influence therapy and in Malawi surgical staging has been used to stratify postoperative chemotherapy. Here we compare the results from surgical and both local pathology and central pathology review.
Methods: Children diagnosed with a Wilms tumour in Blantyre, Malawi between 2007 and 2011 were included if they had had a nephrectomy and the pathology slides were available. All tumour specimens were assessed in three different ways: the local surgeon documented the surgical stage of the tumour, and the risk classification and pathology stage were assessed both by the local pathologist and by a SIOP central review pathologist in Europe.
Results: Fifty patients had complete data available and were included in the analyses. Tumour risk classification differed between the local and central pathology review in two patients only (4%). Using central pathology review as the 'gold standard'; 60% of patients received the correct postoperative chemotherapy treatment based on surgical staging and 84% based on the local pathology stage and risk classification.
Conclusions: Local pathology capacity building is needed to enable timely assessment and reporting.

P-271

EPIDEMIOLOGY AND OUTCOME OF RARE RENAL TUMORS IN PEDIATRIC POPULATION IN A SINGLE TERTIARY CARE CENTRE IN INDIA

N. Pradhan[1], S. Punatar[1], S. Panda[1], A. Gupta[1], M. Prasad[1], G. Narula[1], T. Vora[1], G. Chinnaswamy[1], B. Arora[1], S. Banavali[1], P. Kurkure[1], S. Quereshi[2]

[1]Medical oncology, Tata Memorial Hospital, Mumbai, India; [2]Surgical oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Little data exists on the epidemiology and outcomes of renal tumors other than WIlm's in children. We aimed to study the epidemiological profile of rare renal tumors in pediatric population and their outcome.
Methods: This is a retrospective analysis of 10 years data from January 2004 to December 2013 from Tata Memorial Centre, Mumbai, India. Study included all children who presented to our hospital during this period with renal mass and post operative histopathology

or pre operative biopsy suggestive of tumor other than Wilm's tumor. Patients received standard treatment as per the diagnosis and their outcomes were analyzed
Results: We recorded total 38 cases of rare renal tumors in our study. There were 16 cases of clear cell sarcoma of kidney (CCSK), 5 primitive neuroectodermal tumor (PNET), 5 rhabdoid tumor of kidney, 4 renal cell carcinoma (RCC), 3 germ cell tumor (GCT), 2 translocation associated RCC, 2 congenital mesoblastic nephroma and 1 synovial sarcoma. Metastatic disease at presentation was found in total 10 cases (7 cases of CCSK, 1 case of PNET and 2 cases of rhabdoid tumor). Patients with metastatic disease received only palliative and supportive care. Four patients with localized disease had progression on treatment (1 RCC and 3 rhabdoid tumor) and 2 patients (both CCSK) relapsed after completion of therapy. Eleven patients (4 CCSK, 2 PNET, 2 RCC, 2 translocation associated RCC and 1 synovial sarcoma) are disease free at a median follow up of 2 years. Eleven patients were lost to follow up.
Conclusions: The most common renal tumor after Wilm's tumor in our patients is CCSK followed by PNET and rhabdoid tumor. Approximately one-fourth of patients present with metastatic disease. Patients with localized disease have reasonable long term survival when treated with standard treatment.

P-272

COMBINED-MODALITY NEOADJUVANT THERAPY FOR ADVANCED WILMS TUMOR: 10 YEARS EXPERIENCE

M. Li[1], S.H.A.N. Xu[2], D. Tang[2], Y.O.N.G. Huang[2], D. Wu[2], Q. Shu[1], J. Wang[1], C.A.N. Lai[3], H. Tang[4]

[1]Division of Pediatric Surgical Oncology Department of Pediatric Surgery, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [2]Division of Urology Department of Pediatric Surgery, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [3]Department of Radiology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [4]Department of Pathology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China

Objectives: Evaluate the effect of combined-modality neoadjuvant therapy using transcatheter arterial chemoembolization (TACE) and systemic chemotherapy for treatment of advanced Wilms tumor.
Methods: From January 2003 to December 2012, 46 patients (25 males and 21 females; median 2.9 years, range 0.5–11 years,) of unilateral advanced Wilms tumor were treated with TACE and systemic chemotherapy before surgery. Characteristics of the patients were maximal tumor diameter $\geq$ 10 cm, involvement of periaortic lymph nodes, inferior vena cava invasion, distal metastasis, or tumor with anaplastic histology. Patients subjected to TACE by Seldinger's method. A catheter was placed into the involved renal artery and chemoembolization emulsion consisted of cisplatin (80 mg/m2), pirarubicin (40 mg/m2), vindesine (3 mg/m2) and iodized oil (5 ml) was infused. Intravenous chemotherapy with vindesine (3 mg/m2 once a week) and actinomycin D (15 g/kg daily in a 3-day course) was administered one week after TACE. Surgical resection carried out 2 or 4 weeks after TACE. Postoperative therapy was according to NWTS IV protocol.
Results: No cardiotoxicity, renal insufficiency, or hepatic dysfunction were found in all patients. Grade I-II marrow suppression developed in 5 patients (10.9%). Tumor volumes were significantly reduced after neoadjuvant therapy. Complete surgical removal of the tumor achieved in 39 patients (84.8%). Surgical stages were stage II in 20 (42.6%), and stage III in 22 (46.8%) patients. Four patients had clinical stage IV disease at presentation. Histology results classified as FH in 43 and AH in 3 cases. Gross inspection revealed necrosis of tumor to variable extent in all cases. Total necrosis of tumor was observed in 11 cases (23.9%). Overall Survival and event-free survival were 100% and 97.8% respectively, with a median follow-up of 71.9 (range 15-109) months.
Conclusions: Combined-modality neoadjuvant therapy showed high clinical and pathological response rates for the treatment of advanced Wilms tumor.

P-273

BILATERAL WILMS' TUMOR; FREQUENCY, MANAGEMENT AND OUTCOME EXPERIENCE AT CHILDREN CANCER HOSPITAL - EGYPT

W. Zekri[1], E. Moussa[1], H. Monib[1], R. Soliman[2], A. Yones[3], M. El Shafie[3], M. Zaghloul[4], H. Taha[5], N. El Kinaai[5], A. Refaat[6]

[1]Pediatric Oncology, Children's Cancer Hospital - Egypt, Cairo, Egypt; [2]Research, Children's Cancer Hospital - Egypt, Cairo, Egypt; [3]Surgery, Children's Cancer Hospital - Egypt, Cairo, Egypt; [4]Radiation therapy, Children's Cancer Hospital - Egypt, Cairo, Egypt; [5]Surgical Pathology, Children's Cancer Hospital - Egypt, Cairo, Egypt; [6]Radiology, Children's Cancer Hospital - Egypt, Cairo, Egypt

Objectives: Successful treatment of Wilms' tumor requires meticulous attention to correct staging of the tumor and good communication between the pediatric oncologist, surgeon, radiodiagnosis specialist, pathologyist and radiotherapist. When combined with adjuvant therapy, nephron-sparing surgery for children with BWT is nearly always technically feasible, with few complications. In addition, it is believed that this operative intervention should be done early, by not more than 12 weeks after the initiation of chemotherapy, because little significant further change in tumor size is likely, and it is important to determine the exact tumor histology. We aim at evaluating patients' disease characteristics, assessing response and complications of different treatment modalities and survival analysis.
Methods: This is a retrospective study included all patients with bilateral Wilms' tumor (BWT) presented between July 2007 and March 2012 to the Children's cancer hospital- Egypt and they were followed up till March 2013.
Results: There was 25 patients during the selected time period, with age ranging between 4 months and 8.6 years (median = 2.7 years). The male to female ratio was 1:1.3. All cases had bilateral synchronous renal masses and no recorded cases of metachronous BWT. Using COG staging system, local stage distribution was: 20%, 12% and 68%, for stage I – III respectively, while initial metastatic BWT was diagnosed in 8 cases representing 32% of the cases studied. With a median follow up duration of 21 months, the 4 years OS was 78.2%, a RFS showed 73.9%. Presence or absence of metastatic disease was the only factor having statistically significant effect on OS and RFS.
Conclusions: The treatment of bilateral Wilms' tumors requires multimodality therapy with individualized decision to ensure cure while preserving as much renal parenchyma as possible. 3 months of preoperative chemotherapy allow to perform renal sparing surgery in most cases.

P-274

IS THREE DRUG CHEMOTHERAPY PROTOCOL FOR ALL STAGES OF WILMS TUMOR A PRACTICAL COMPROMISE FOR SUBOPTIMAL STAGING IN DEVELOPING COUNTRY? IS IT WORTH & SAFE?

S. Rastogi[1], S. Qureshi[1], T. Vora[1], G. Chinnaswamy[1], M.A.Y.A. Prasad[1], S. Laskar[1], N. Khanna[1], M. Ramadwar[1], S. Medhi[1], P. Kurkure[1]

[1]Paediatric Solid Tumor Management Group, Tata Memorial Hospital, Mumbai, India

Objectives: The obstacles in management of WT in tertiary cancer centres in developing country such as India are lack of awareness among caregivers in community regarding multidisciplinary management of WT leading to delays in referral for adjuvant treatment post surgery without adequate surgical and pathological details limiting appropriate stage assignment. To overcome these obstacles we started chemotherapy protocol using anthracyclines for all stages.
Methods: WT 10/90 protocol is the pulse intensive arm of NWTS-4 study comprising of vincristine, actinomycin D and doxorubicin. WT patients registered at Tata Memorial Hospital from Oct 1990 to Dec 2006 treated on WT 10/90 were analysed. Univariate analysis (UVA) for relapse free survival (RFS) and overall survival (OS) was performed using Kaplan-Meier method. Multivariate analysis (MVA) was performed using Cox Proportional Hazards model.
Results: There were 147 patients of WT treated on WT10/90 protocol from October 1990 to December 2006. Median age at presentation was 40 months with 59% males. Majority, 105 (71.4%) were operated outside and referred for adjuvant therapy. Of these, 101 patients were operated upfront, whereas only 4 received anterior chemotherapy followed by surgery. Favorable Histology (FH) was seen in 98.6%. Ten year RFS and OS were 84.7% and 89% respectively at median follow up of 88 months. Age group (40 months) ($p = 0.005$), histology ($p = 0.000$) were significant for RFS on UVA & MVA. Only histology ($p = 0.002$) was statistically significant on UVA and MVA for OAS. CHF occurred in 3 (2%) while 17 (11.5%) had asymptomatic echo-cardiographic changes. Chronic HBV in 12 (8.2%), skeletal abnormalities in 5 (3.4%), second malignancies in 3 (2.1%) and hypertension in 3 (2.1%) were other late effects.
Conclusions: Chemotherapy protocol comprising of three drugs for all stages of WT is a practical compromise to compensate for lacunae in staging and optimal therapeutic planning. Asymptomatic late anthracycline related cardiac toxicity needs to be monitored further for its impact on QOL

RETINOBLASTOMA

P-275

LIFE BEFORE EYE: IMPLICATIONS FOR THE WHOLE CHILD AND FAMILY OF ATTEMPTED EYE SALVAGE FOR UNILATERAL AND SEVERE BILATERAL RETINOBLASTOMA

A. White[1], B. Gallie[2]

[1]One Retinoblastoma World, Daisy's Eye Cancer Fund, Oxford, United Kingdom; [2]Ophthalmology, Hospital for Sick Children, Toronto, Canada

Objectives: Primary enucleation is standard care for unilateral retinoblastoma and International Intraocular Retinoblastoma Classification Group E eyes in children with bilateral disease, often curing and enabling careful pathology and genetic testing to evaluate further risks. Families and physicians are increasingly selecting innovative therapies in hope of saving the eye. In countries with limited access to advanced medical care, families seek international treatment. We evaluated physical, psychological and financial impact on the child and family of primary eye salvage for unilateral and severe bilateral retinoblastoma.
Methods: We reviewed treatment course, event free survival, psychological and financial impact, and primary reason for contact among families who approached Daisy's Eye Cancer Fund for assistance.

Results: Secondary enucleation rate was high, particularly among international patients and children with unilateral retinoblastoma. In two cases, parental request for enucleation of a unilateral blind eye was contested by the multidisciplinary team, leading to emotional trauma, extra treatment and delayed surgery. Mortality was most associated with poor follow up due financial limitations, resistance to secondary enucleation and, in developed countries, leptomeningeal metastasis following Intra Arterial Chemotherapy. Of 6 children who had bone marrow relapse following intensive therapy for unilateral retinoblastoma, 3 are alive with no evidence of disease at 2 years follow up. Reports consistent with Post Traumatic Stress Disorder are frequent in both children and parents, but only one child is diagnosed with PTSD. Diagnosis of Autism Spectrum Disorders is frequent. Financial distress is common, with many families unable to pay medical bills. Families seeking international treatment experience increased poverty on return home and lost-to-follow-up rates are high.
Conclusions: Primary enucleation for unilateral and advanced bilateral retinoblastoma saves lives. Significant financial and psychological burdens of eye salvage therapy must be weighed against perceived treatment benefits in the informed consent process, especially when consulting with families in resource-poor countries.

P-276

ONE RB WORLD ONLINE: A VIRTUAL RETINOBLASTOMA CLINIC

H. Dimaras[1], B.L. Gallie[1], C. Baik[2], M. Lee[2], K. Frasunkiewicz[2]

[1]Ophthalmology & Vision Sciences, University of Toronto, Toronto, Canada; [2]Human Biology, University of Toronto, Toronto, Canada

Objectives: Global research collaboration has been identified as key to improving outcomes for retinoblastoma. In 2009, the first retinoblastoma clinical practice guidelines were published in Canada. Optimal resources and expertise for retinoblastoma management were outlined, and serves as a guide to inform health policy, at national, regional and institutional levels. Subsequently these guidelines were adopted by the Kenyan National Retinoblastoma Strategy group. In both countries, a situational analysis of key treatment centers has informed systems of patient referral, educational capacity initiatives, and is predicted to result in enhanced patient care. We now apply this approach on a global scale, with an online virtual retinoblastoma clinic.
Methods: We conducted a survey of Global Retinoblastoma Treatment Centers to identify and document expertise and resources available for the care of children with retinoblastoma worldwide. An online platform was developed to disseminate this information in an interactive and data-rich format.
Results: The virtual clinic connects patient families to caregivers, and documents data on 90 centers in 50 countries. A survey functionality allows further data collection and updates. Knowledge of where and how retinoblastoma children are managed worldwide provides an efficient and rapid path for parents to access urgent care. The website indicates the closest expert center and all the contacts. Paths of referral and multicenter co-management aim to keep the children close to home while optimizing access to advanced therapies when needed. Estimated incidence vs location and capabilities of treatment centres reveals opportunities to increase capacity, collaboration and coverage in various regions.
Conclusions: The One Retinoblastoma World Virtual Clinic connects stakeholders and strengthens capacity to care for the global retinoblastoma population. This first-of its-kind collaboration promotes global standards of care, setting the stage for multicenter clinical trials and other research, thereby accelerating the translation of results from lab to clinic.

P-277

TRILATERAL RETINOBLASTOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. de Jong[1], W.A. Kors[2], P. de Graaf[1], J.A. Castelijns[1], A.C. Moll[3]

[1]Radiology, VU University Medical Center, Amsterdam, Netherlands; [2]Pediatric Oncology, VU University Medical Center, Amsterdam, Netherlands; [3]Ophthalmology, VU University Medical Center, Amsterdam, Netherlands

Objectives: Rarely, children with hereditary retinoblastoma (Rb) develop trilateral retinoblastoma (TRb): retinoblastoma combined with a histologically identical brain tumor, most commonly located in the pineal gland. Unfortunately many do not survive. The objective of this study was to provide an overview of published cases, and to analyze survival.
Methods: We searched Medline and Embase for TRb cases published from January 1966 through February 2014. This study was performed according to the PRISMA statement. Meta-analysis was performed on survival data.
Results: One hundred and sixty-two TRb patients from 87 studies qualified for meta-analysis. Patients diagnosed with TRb <1995 showed a 5-year cumulative survival rate (CSR) of 4% (95% confidence interval (95%CI): 1%–12%). In the period ≥1995 CSR rose to 45% (95%CI: 31%–59%), along with increased use of (high-dose) chemotherapy and decreased use of radiotherapy for the brain tumors. Pineal TRb showed CSRs of 6% (95%CI: 1%–15%) and 43% (95%CI: 24%–59%) for <1995 and ≥1995 respectively, whereas non-pineal TRb showed CSRs of 0% (95%CI: incalculable) and 53% (95%CI: 28%–73%) for <1995 and ≥1995 respectively. Restricted to actively treated patients, pineal TRb showed CSRs of 43% (95%CI: 27%–58%) and 5% (95%CI: 0%–18%) for asymptomatic and symptomatic disease respectively, whereas non-pineal TRb showed CSRs of 31% (95%CI: 10%–56%) and 35% (95%CI: 12%–59%) for asymptomatic and symptomatic disease respectively. Smaller tumor size showed statistically significant better survival in pineal TRb, but not in non-pineal TRb.
Conclusions: Survival has improved considerably over time. It is difficult to pinpoint the exact reason for this improvement as many factors have changed over the years, but the results of this meta-analysis suggest that early detection and proper treatment of subclinical tumors is the key to success, especially in pineoblastoma. However, patients with larger tumors and clinical symptoms also have a chance to survive, especially in non-pineal TRb.

P-278

BASELINE CENTRAL NERVOUS SYSTEM MAGNETIC RESONANCE IMAGING IN RETINOBLASTOMA: A SINGLE INSTITUTION EXPERIENCE IN EARLY DETECTION OF TRILATERAL RETINOBLASTOMA

M. De Ioris[1], P. Valente[2], F. Randisi[3], A. Carai[4], R. Cozza[1], F. Del Bufalo[1], A. Cacchione[1], A. Romanzo[2], B. Bernardi[3], A. Mastronuzzi[1]

[1]Hematology/Oncology, Pediatric Hospital Bambino Gesu', Roma, Italy; [2]Ophtalmology, Pediatric Hospital Bambino Gesu', Roma, Italy; [3]Neuroradiology, Pediatric Hospital Bambino Gesu', Roma, Italy; [4]Neurosurgery, Pediatric Hospital Bambino Gesu', Roma, Italy

Objectives: To report on frequency, as well as on clinical and imaging findings of trilateral retinoblastoma (TRB) from a single-institution retinobastoma (RB) series where a baseline MRI is adopted as routine investigation in all patients at the time of RB diagnosis
Methods: The RB database was checked in order to identify patients with TRB diagnosis from January 1999 to December 2012. All MRI were reviewed for this study.
Results: 107 RB patients were diagnosed over 14 years of regular use of baseline MRI screening. Sixty-two patients had unilateral RB and 45 bilateral RB. MRI revealed the presence of TRB in three patients (2.8%) aged 18, 16 and 10 months, respectively. In one patient the TRB was metachronous and in the other 2 patients was synchronous. TRB occurred in 3 out of 45 (6.7%) bilateral RBs and in one out 15 (6.7%) of familial RBs while no TRB was reported in the unilateral group. None of the patients had received prior chemotherapeutic treatment. Seven benign pineal cysts (6,5%) were diagnosed during the same period.
Conclusions: TRB represents a rare condition occurring, in our series, in 3 (2.8%) of all RB patients; its frequency appeared to be higher in bilateral/familial cases. A synchronous presentation seems most frequent when a baseline MRI is performed. Brain MRI is recommended to be performed in each patient with RB for a timely diagnosis. Further analysis on large series should address how to consider and treat small synchronous pineal lesion suggestive for a pineoblastoma.

P-279

ALTERATION OF MITOCHONDRIAL COMPLEX I PROTEIN IN HUMAN RETINOBLASTOMA

L. Singh[1], S. Kashyap[1], N. Pushker[2], T.C. Nag[3], S. Sen[1], A. Sharma[4], S. Bakhshi[5]

[1]Ocular Pathology, All India Institute of Medical Sciences, Delhi, India; [2]Ophthalmology, All India Institute of Medical Sciences, Delhi, India; [3]Anatomy, All India Institute of Medical Sciences, Delhi, India; [4]Ocular Microbiology, All India Institute of Medical Sciences, Delhi, India; [5]Medical Oncology, All India Institute of Medical Sciences, Delhi, India

Objectives: Mitochondria are critical for cellular function in cancer and play an important role in cell differentiation and survival. Deficiency of mitochondrial complex I is the most important factor in cancer cells. The purpose of this study was to determine the expression of mitochondrial complex I and the morphological changes of mitochondria in human primary retinoblastoma tissues.
Methods: Expression of mitochondrial complex I was performed in all the 38 cases by immunohistochemistry and then validated by western blotting on representative cases. Morphology of mitochondria was studied by transmission electron microscopy (TEM) in 5 cases.
Results: Deficiency of mitochondrial complex I was found in 29/38 (76.31%) cases by immunohistochemistry. Western blotting was performed to confirm the immunoreactivity results. Electron microscopy showed numerous degenerated and swollen mitochondria in tumor cells. On statistical analysis, the loss of mitochondrial complex I expression correlated significantly with poorly differentiated retinoblastoma and tumor invasion.
Conclusions: This is the first study to show the expression of mitochondrial complex I in retinoblastoma tumor. Electron microscopy revealed that numerous morphological changes in mitochondria which may be due to changes in mitochondrial protein expression. Correlation between mitochondrial D-loop variations and expression of complex I is being investigated. Investigating mtDNA alterations might be helpful for developing biomarkers in the management of retinoblastoma patients.

P-280

HISTOPATHOLOGICAL ANALYSIS OF CELL DIVISION CYCLE 25 (CDC25) PHOSPHATASE PROTEINS IN RETINOBLASTOMA

S. Kashyap[1], L. Singh[1], N. Pushker[2], S. Sen[1], A. Sharma[3], B. Chawla[2]

[1]Ocular Pathology, All India Institute of Medical Sciences, Delhi, India; [2]Ophthalmology, All India Institute of Medical Sciences, Delhi, India; [3]Ocular Microbiology, All India Institute of Medical Sciences, Delhi, India

Objectives: Retinoblastoma is the most common childhood intraocular malignant tumor of the developing retina. Cell Division Cycle 25 (CDC25) phosphatase is an essential regulator of the cell cycle machinery, functioning as a positive regulator by activating Cyclin-Dependent Kinases (CDK). CDC25A plays a pivotal role in controlling cell proliferation during development and tumorigenesis. Overexpression of CDC25A is detected in a number of tumors which implies dysregulation in malignant transformation. However, the role of CDC25A in patients with Retinoblastoma is still unknown.
Methods: Prospective analyses of 60 primary enucleated retinoblastoma cases over a period of one year (Jan 2011-Dec 2012). CDC25A protein expression was investigated by Immunohistochemistry in formalin fixed paraffin embedded sections and then validated by western blotting. Cytoplasmic staining was graded as weak/negative (1+), moderate (2+) and strong (3+). Semi-quantitative analysis for expression of CDC25A mRNA was performed by the Reverse-Transcriptase PCR (RT-PCR). Expression of CDC25A was correlated with tumor differentiation and various histopathological high risk factors.
Results: There were total of 45 poorly differentiated retinoblastomas and 15 well differentiated retinoblastomas. Necrosis and calcification was found in 37 (61.6%) and 17 (28.3%) respectively. Massive choroidal invasion, optic nerve invasion and scleral invasion was found in 20/60, 17/60 and 7/60 cases respectively. Immunohistochemistry showed CDC25A expression in total of 38/60 (63.3%) cases. Western blotting was performed to confirm immunoreactivity results on representative cases. mRNA expression was seen in 31/60 (51.6%) cases by RT-PCR. Expression of CDC25A showed statistically significant correlation with poor tumour differentiation and tumor invasion ($p < 0.05$).
Conclusions: Our results suggest that increased expression of CDC25A plays an important role in the pathogenesis of retinoblastoma. CDC25A was associated with invasion of ocular coats and poor differentiation. CDC25A expression might be a potential molecular target for novel drug development in tumor biology.

SOFT TISSUE SARCOMAS

P-281

A POSSIBLE ROLE FOR THE HEDGEHOG PATHWAY LIGANDS DESERT AND INDIAN IN RHABDOMYOSARCOMA

A. Almazán-Moga[1], J. Roma[1], C. Molist[1], P. Velasco[1], I. Vidal[1], M.F. Segura[1], A. Soriano[1], L. Jubierre[1], J. Sánchez de Toledo[2], S. Gallego[2]

[1]Translational Research in Paediatric Cancer Laboratory, Vall Hebron Research Institute, Barcelona, Spain; [2]Paediatric Oncology and Hematology Department, Hospital Vall Hebron, Barcelona, Spain

Objectives: To establish the mechanism of activation of Hedgehog (HH) pathway in Rhabdomyosarcoma (RMS). More concretely, to elucidate the role of HH ligands -Sonic HH (SHH), Indian HH (IHH) and Desert HH (DHH) - in the pathogenesis of this neoplasia.
Methods: Real-time PCR, Western blot and immunohistochemistry were used to determine HH ligands levels in RMS cell lines and tumor samples. Genetic inhibition of the ligands was performed by shRNAs in the lentiviral vector pGIPZ. Functional assays were performed in order to determine the effects of genetic inhibition of HH ligands in RMS cells.
Results: The mRNA analysis by real-time PCR showed medium or high IHH and DHH expression in all samples analyzed. Conversely, the expression of SHH was shown to be negligible in the majority of samples. However, approximately 30% of patients showed expression of SHH. Western blot and immunohistochemical analysis coincided with the results obtained by real-time PCR. SHH, IHH and DHH levels were correlated with GLI1 expression. SHH and DHH levels showed a significant direct correlations with GLI-1 expression. For IHH a tendency to correlate was observed but no significant correlation was obtained. Genetic inhibition of IHH significantly decreased cell proliferation.
Conclusions: Our results confirm the extremely low levels of SHH expression in the majority of RMS patients (approximately 70%). Interestingly, we found a prominent expression of IHH and DHH ligands in RMS. Together with the direct correlations observed between these two ligands and one of the targets of HH pathway (GLI1), our results support the possible existence of an autocrine ligand-dependent activation of the Hedgehog pathway in this neoplasia. These results suggest that the development of ligand-specific inhibitors may help to specifically inhibit the pathway in ligand-dependent tumors such as RMS, thereby providing a therapeutic alternative beyond cyclopamine derivatives or GLI-inhibitors.

P-282

INFLUENCE OF CYP2B6 POLYMORPHISM ON OUTCOME OF IRS-V TREATED RHABDOMYOSARCOMA PEDIATRIC EGYPTIAN PATIENTS

R. M Labib[1], D. Yassin[2], E. Elnadi[3], M. Emam[4]

[1]Research, Children's cancer Hospital-Egypt-57357, Cairo, Egypt; [2]Clinical Pathology, Children's cancer Hospital-Egypt-57357, Cairo, Egypt; [3]Pediatric Oncology, Children's cancer Hospital-Egypt-57357, Cairo, Egypt; [4]Clinical Pharmacy, Faculty of Pharmacy, Beni Swef, Egypt

Objectives: Cyclophosphamide is a conventional pro-drug used in rhabdomyosarcoma (RMS) and other malignancies. The highly polymorphic CYP2B6 is suggested as a major contributor in cyclophosphamide bioactivation. Polymorphisms of this enzyme may affect drug bioactivation and hence treatment outcome. The aim of this work was to investigate the impact of the CYP2B6 SNPs G516T, A785G and C1459T, on the outcome for cyclophosphamide treated RMS patients, in order to find biomarkers for personalized therapy.
Methods: Germ line DNA samples from 73 RMS patients presented at Children's Cancer Hospital-57357 from December 2010 till December 2012 were genotyped by RFLP for CYP2B6 SNPs G516T, A785G and C1459T. These patients were enrolled on IRS-V protocol based on cyclophosphamide and followed up till March 2014. Clinical data on survival, demographics, pathology, chemotherapy dose and clinical response were collected. We examined the association between these genotypes and overall survival, failure free survival and achievement of complete response.
Results: The CYP2B6-516 in this population was TT in 36 (49.3%), 29 cases (39.7%) were GT while it was GG in 8 patients (11%). CYP2B6 c.785G was GG in 33 (45.2%) of cases and AG in 32 (43.8%) while it was AA in 8 patient (11%) and CYP2B6 c.1459T which was TT in 24 (87.7%) of cases and CT in 8 (11%) while it was CC in 1 patient (14%). 3-years failure free survival was $59.7 \pm 10.4\%$ for those with CYP2B6 c.516TT genotype while it was $42.6 \pm 8.2\%$ for those with GT or GG genotypes (p-value $= 0.04$). 3years- failure free survival was higher in those with type CYP2B6 c. 785 GG and CYP2B6 c. 1459TT compared to those with a mutant genotype yet it was not statistically significant.
Conclusions: CYP2B6 c.516T can be used as a prognostic biomarker for rhabdomyosarcoma patients receiving cyclophosphamide.

P-283

EXPRESSION AND LOCALIZATION OF MHC CLASS-I RELATED CHAIN MOLECULES A AND B IN HUMAN RHABDOMYOSARCOMA CELLS

S. Uehara[1], M. Kawatsu[1], K. Nakahata[1], T. Oue[1], N. Usui[1]

[1]Pediatric Surgery, Osaka University Hospital, Osaka, Japan

Objectives: Natural killer (NK) cells are important effector cells for the first line of defense against tumors. The interaction of the MHC class I-related chain molecules A and B (MICA/MICB) with the corresponding natural killer group 2, member D (NKG2D) receptor triggers the cytotoxic effector activity of natural killer cells and certain T-cell subsets. Thus, the presence of MICA/MICB on the surface of tumor cells contributes to the tumor immunosurveillance. In this study, we investigated the expression and localization of MICA/MICB in human rhabdomyosarcoma (RMS) tumors and cell lines.
Methods: The immunohistochemical detection of MICA/MICB was performed using paraffin embedded samples obtained at surgery. The presence of MICA/MICB mRNA and protein in alveolar (RH30) and embryonal (RD, RMS-YM) RMS cells lines were evaluated by RT-PCR and a Western blot analysis. The surface expression levels of MICA/MICB were determined by flow cytometry.
Results: The immunohistochemical staining showed that 21 of 25 clinical tumor samples were positive for either MICA or MICB, while normal striated muscle cells were negative. In all RMS cells lines, MICA mRNA was detected by RT-PCR, whereas no MICB mRNA was detected in the RH30 cells. The Western blot analysis revealed that the MICA protein was presented in all RMS cells lines, as well as the mRNA, and the MICB protein was presented in the RD and RMS-YM cells. However, the surface expression of MICA and MICB was limited with only MICA being detected on RD cells.
Conclusions: Our results suggest that RMS cells have the ability to produce the MICA and MICB proteins, whereas only RD cells expressed MICA on their cell surface. Therefore, since the lack of MIC expression on the surface of RMS tumor cells may lead to the lack of the tumor recognition by NK cells, some modulators of MICA/MICB expression may be helpful to further activate NK cells.

P-284

ALDEHYDE DEHYDROGENASE 1 (ALDH1) IS A POTENTIAL MARKER FOR CANCER STEM-LIKE CELLS IN EMBRYONAL RHABDOMYOSARCOMA

K. Nakahata[1], S. Uehara[1], T. Oue[1], M. Zenitani[1], N. Usui[1]

[1]Department of Pediatric Surgery, Osaka University Graduate School of Medicine, Osaka, Japan

Objectives: Recent studies have demonstrated aldehyde dehydrogenase 1 (ALDH1) has been detected as the marker for cancer stem-like cells (CSCs) in adult cancers. In pediatric malignant tumors, however, there have been no studies regarding ALDH1 as a marker for CSCs. In this study, we hypothesized a subpopulation of cells with high ALDH1 activity ($ALDH1^{high}$ cells) would have characteristics of CSCs in rhabdomyosarcoma (RMS), and we examined the characteristics of $ALDH1^{high}$ cells in embryonal RMS.
Methods: We used the human embryonal RMS cell line, RD. Cultured cells were sorted into $ALDH1^{high}$ cells and a subpopulation with low ALDH1 activity ($ALDH1^{low}$ cells) using an ALDEFLUOR assay kit. To demonstrate $ALDH1^{high}$ cells had stronger CSCs characteristics than $ALDH1^{low}$ cells, we performed a colony-formation assay, a WST-8 assay *in vitro* and a tumor-initiating assay using immunodeficient mice *in vivo*.

Results: ALDH1^{high} cells comprised 5.8% of all cultured RD cells in ALDEFLUOR assay. In the colony-formation assay to document the self-renewability of the cells, the number of colonies of ALDH1^{high} cells was higher than that of ALDH1^{low} cells (36.3 vs. 21.3 colonies/well, respectively). With regard to chemoresistance, the survival rate of ALDH1^{high} cells was found to be one-and-a-half times as high as that of the ALDH1^{low} cells following treatment with vincristine. The survival rate of ALDH1^{high} cells was 1.9-fold and 1.8-fold compared to ALDH1^{low} cells when cultured with cyclophosphamide and etoposide, respectively. Tumor-formation was found in one of four mice injected with 1×10^3 ALDH1^{high} cells, and in two of three mice injected with 1×10^4 ALDH1^{high} cells, whereas no tumors were found in mice injected with ALDH1^{low} cells at either cell density.
Conclusions: We confirmed the ALDH1^{high} RD cells had characteristics of CSC, including colony-formation, chemoresistance
and tumor-initiation. These results suggest ALDH1 is a potentially useful marker of CSCs in embryonal RMS.

P-285

NOVEL SECONDARY SOMATIC MUTATIONS IN EWING'S SARCOMA AND DESMOPLASTIC SMALL ROUND CELL TUMORS IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS

V. Subbiah[1], Y. Jiang[1], F. Janku[1], J.A. Ludwig[2], A. Naing[3], R.S. Benjamin[2], R.E. Brown[4], P.M. Anderson[5], R. Kurzrock[6]

[1]Phase 1 program, UT MD Anderson Cancer Center, Houston, USA; [2]Sarcoma Medical Oncology, UT MD Anderson Cancer Center, Houston, USA; [3]Phase 1, UT MD Anderson Cancer Center, Houston, USA; [4]Pathology, UT Health UT Houston, Houston, USA; [5]Peds Hematology/Oncology/BMT/Cell Therapy, Levine Children's Hospital/Levine Cancer Institute, Charlotte, USA; [6]Division of Hematology & Oncology, UC San Diego - Moores Cancer Center, San Diego, USA

Objectives: Ewing sarcoma (ES) and desmoplastic small round cell tumors (DSRCT) are related small round blue cell tumors driven by an N-terminal containing EWS translocation. Very few somatic mutations have been reported in ES, and none have been identified in DSRCT. The aim of this study is to explore potential actionable mutations in ES and DSRCT.
Methods: Twenty eight patients with ES or DSRCT had tumor tissue available that could be analyzed by one of the following methods: 1) Next-generation exome sequencing platform; 2) Multiplex PCR/Mass Spectroscopy; 3) Polymerase chain reaction (PCR) -based single- gene mutation screening 4) Sanger sequencing
Results: Actionable somatic mutations were identified in four out of 18 patients with advanced ES and two of 10 patients with advanced DSRCT (six out of 28 (21.4%));*KRAS* (n = 1), *PTPRD* (n = 1), *GRB10* (n = 2), *c-MET* (n = 2) *and PIK3CA* (n = 1). One patient with both PTPRD and GRB10 mutations and one with a GRB10 mutation achieved a complete remission (CR) on an Insulin like growth factor 1 receptor (IGF1R) inhibitor based treatment. One patient who achieved a partial remission (PR) with IGF1R inhibitor treatment later developed resistance demonstrated a *KRAS* mutation in the post-treatment resistant tumor, but not in the pre-treatment tumor suggesting that the RAF/RAS/MEK pathway was activated with progression.
Conclusions: We have reported several different mutations in advanced ES and DSRCT that have direct implications for molecularly-directed targeted therapy. Our technology agnostic approach provides an initial mutational roadmap used in the path towards individualized combination therapy.

P-286

DOES ROUTINE IMAGING IN CHILDHOOD RHABDOMYOSARCOMA IMPROVE PATIENT SURVIVAL?

M. Okcu[1], J. Lin[2], P. Guillerman[3], P. Lupo[1], H. Russel[1]

[1]Pediatrics/Hematology Oncology, Texas Children's Cancer Center Baylor College of Medicine, Houston, USA; [2]Pediatrics, Baylor College of Medicine, Houston, USA; [3]Pediatrics/Radiology, Baylor College of Medicine, Houston, USA

Objectives: While routine imaging is often obtained for surveillance of disease relapse or response assessment in children with rhabdomyosarcoma, there is no evidence whether imaging improves patient outcomes. We compared survival in patients in whom relapse was detected on the basis of clinical symptoms versus routine imaging.
Methods: Forty-three children with relapsed rhabdomyosarcoma treated at Texas Children's Hospital from 1993-2012 were identified. Overall survival (OS) time after relapse was compared between two groups: (1) patients presenting with a symptom related to relapse; and (2) patients whose relapse was initially detected by imaging prior to symptoms. Differences in survival time were evaluated with Kaplan-Meier analysis with bivariate adjustment for age, stage, Clinical Group, and histology at diagnosis.
Results: Forty-three children with relapsed rhabdomyosarcoma treated at Texas Children's Hospital from 1993-2012 were identified. Overall survival (OS) time after relapse was compared between two groups: (1) patients presenting with a symptom related to relapse; and (2) patients whose relapse was initially detected by imaging prior to symptoms. Differences in survival time were evaluated with Kaplan-Meier analysis with bivariate adjustment for age, stage, Clinical Group, and histology at diagnosis.
Conclusions: Our results suggest that routine imaging surveillance for relapsed disease in children with rhabdomyosarcoma is not associated with longer patient survival. Validation of these results in a larger study and more limited use of surveillance imaging could reduce medical costs and radiation exposure without compromising patient outcome.

P-287

THE IMPACT OF RESPONSE TO INDUCTION CHEMOTHERAPY ON SURVIVAL AND LOCAL CONTROL IN EMBRYONAL PARAMENINGEAL RHABDOMYOSARCOMA

M. Ladra[1], H. Mandeville[2], A. Niemierko[1], S. MacDonald[1], A. Friedmann[3], N. Tarbell[1], T. Yock[1]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, USA; [2]Radiation Oncology, Royal Marsden Hospital, London, United Kingdom; [3]Pediatric Hematology and Oncology, Massachusetts General Hospital, Boston, USA

Objectives: Disease control remains a challenge in pediatric parameningeal rhabdomyosarcoma (PM-RMS). In this study we set out to identify predictors of failure in PM-RMS.
Methods: We identified 25 patients with localized, non-metastatic embryonal PM-RMS, age 2-18 years, without surgical resection. 24 of 25 patients had complete MRI imaging data. All patients were treated with chemotherapy followed by proton therapy, median dose 50.4 Gy_{RBE} (50.4-55.8 Gy_{RBE}). Tumor volumes were determined prior to initial chemotherapy and prior to proton therapy (after induction chemotherapy). The dimensions of each tumor were measured on MRI and ellipsoid tumor volumes were calculated using the formula $4/3\pi$ (r1 × r2 × r3).
Results: Median follow was 3.1 years. Actuarial 3-year FFS and OS were 52% (95% CI, 30% to 70%), and 64% (95% CI, 40% to 80%) respectively. Local failure (LF) predominated, seen in 9 of 12 failures with a 3-year cumulative incidence of LF of 41% (95% CI, 24% to 65%). Median time from initiation of CT to start of RT was 4.8 weeks. Patients with LF had a greater median pre-radiotherapy (pre-RT) volume compared to those with LC (40 cm^3 vs 7 cm^3) and a smaller relative percent reduction in tumor size after initial chemotherapy (6% vs 78%). Both pre-RT tumor volume and relative percent reduction in tumor volume were significantly associated with LF ($p = 0.03$ and $p = 0.003$, respectively, on univariate Cox regression) and FFS ($p = 0.05$ and $p = 0.01$, respectively). Other factors including age, sex, initial tumor volume, interval between CT and RT, and intracranial extension were not associated with LF or FFS
Conclusions: Poor response to induction chemotherapy appears to be associated with an increased risk of LF, FFS, and OS in pediatric embryonal PM-RMS.

P-288

RESULTS OF THE JAPAN RHABDOMYOSARCOMA STUDY GROUP JRS-I LRA0401 PROTOCOL, USING VINCRISTINE, DACTINOMYCIN AND CYCLOPHOSPHAMIDE AND RADIATION THERAPY, FOR LOW-RISK EMBRYONAL RHABDOMYOSARCOMA

H. Hosoi[1], H. Hojo[2], H. Okita[3], J. Hata[4], H. Masaki[5], M. Nozaki[6], T. Soejima[7], H. Ikeda[8], K. Horibe[9], S. Ohta[10], J. Hara[11], T. Takimoto[12], M. Miyachi[1], K. Tsuchiya[1], S. Teramukai[13], Y. Morikawa[14]

[1]Pediatrics, Kyoto Prefectural University of Medicine, Kyoto, Japan; [2]Clinical Medicine Diagnostic Pathology, Aizu Medical Center Fukushima Medical University, Aizu, Japan; [3]Pediatric Hematology and Oncology Research, National Center for Child Health and Development, Tokyo, Japan; [4]Central Institute for Experimental Animal, Kawasaki, Japan; [5]Radiotherapy, Kameda Medical Center, Kamogawa, Japan; [6]Radiology, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan; [7]Radiation Oncology, Hyogo Cancer Center, Akashi, Japan; [8]Pediatric Surgery, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan; [9]Innovative Clinical Research Center, National Hospital Organization Nagoya Medical Center, Nagoya, Japan; [10]Pediatrics, Shiga University of Medical Science, Seta, Japan; [11]Pediatric Hematology/Oncology, Children's Medical Center Osaka City General Hospital, Osaka, Japan; [12]Clinical and Epidemiological Research Center for Childhood Cancer, National Center for Child Health and Development, Tokyo, Japan; [13]Innovative Clinical Research Center, Kanazawa University Hospital, Kanazawa, Japan; [14]Pediatric Surgery, International University of Health and Welfare, Ohtawara, Japan

Objectives: Patients with localized, grossly resected, or gross residual (orbital only) embryonal rhabdomyosarcoma (ERMS) had 5-year failure-free survival (FFS) rates of 93% and overall survival (OS) rates of 98% using Intergroup Rhabdomyosarcoma Study Group protocol IV. However, the protocol prescribed 26.4 g/m^2 of cyclophosphamide, which causes infertility. JRS-I LRA0401 protocol objectives included reducing the cyclophosphamide dose to 9.6 g/m^2, which could keep fertility.
Methods: Subgroup A patients (lowest risk, with ERMS, stage 1 group I/IIA, stage 1 group III orbit, stage 2 group I) received 8 cycles (24 weeks) of vincristine, dactinomycin and 1.2 g/m^2/cycle cyclophosphamide (VAC1.2) therapy. Patients in group II/III received radiotherapy: 36 Gy for stage 1 group IIA patients and 45 Gy for group III orbit patients.
Results: Three-year PFS rates were 92% (95% CI, 76% to 100%) and 3-year OS rates were 100% for subgroup A patients (n = 12). Median follow-up was 5.6 years. Among five Group III patients, three patients achieved a best response of CR and two achieved a best response of PR. Adverse events included neutropenia (100%), anemia (67%), thrombocytopenia (58%),

nausea (50%), stomatitis (25%), peripheral neuropathy (17%) and constipation (25%). Administration of vincristine and dactinomycin was reduced in two cases who developed veno-occlusive disease. Late effects of orbital primary tumor included cataracts in three cases and ptosis and eye movement disorder in two cases. Bladder wall thickening, vesicoureteral reflux and hydronephrosis were observed in one case of paratesticular primary tumor. A cosmetic problem arose in the case of a head and neck primary tumor. No protocol-related mortality occurred.
Conclusions: No significant therapy-related toxicity occurred using 9.6 g/m^2 of cyclophosphamide. The survival rates were similar to those of the previous low-risk protocols of other study groups.

P-289

A DOSIMETRIC COMPARISON OF PROTON RADIOTHERAPY AND IMRT IN PEDIATRIC RMS PATIENTS ENROLLED ON A PHASE II PROTON STUDY

M. Ladra[1], S. Edgington[1], M. Moteabbed[1], A. Mahajan[2], D. Grosshans[2], S. MacDonald[1], N. Tarbell[1], T. Yock[1]

[1]Radiation Oncology, Massachusetts General Hospital, Boston, USA; [2]Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, USA

Objectives: With chemotherapy and radiation, pediatric rhabdomyosarcoma (RMS) is highly curable. However, cure may come with significant radiation related toxicities in exposed developing tissues. Proton therapy (PT) may spare excess dose to normal structures potentially reducing the incidence of adverse effects.
Methods: Between 2005 and 2012, 54 patients were enrolled on a prospective phase II trial of PT in pediatric RMS. Intensity modulated radiation therapy (IMRT) plans were generated for comparison to clinical PT plans. Clinical target and normal tissue volumes were held constant and IMRT plans optimized for target volume coverage and normal tissue sparing according to COG protocol guidelines.
Results: Target coverage was comparable between PT and IMRT plans with a mean CTV V_{95} of 100% for both modalities ($p = 0.82$). However, integral dose was 1.8 times higher for IMRT (range 1.0-4.9). By site; integral dose for IMRT was 1.8 times higher for H&N pts ($p < 0.01$), 2.0 times higher for GU ($p = 0.02$) and trunk/extremity pts ($p < 0.01$), and 3.5 times higher for orbital pts ($p < 0.01$). Significant sparing was seen with PT in 32 of 40 critical structures assessed. Mean temporal lobe V_{20} and V_{30} were 2.0 and 1.7 times higher and mean hypothalamic dose 1.8 times higher for IMRT plans in H&N and orbital sites ($p < 0.01$ for all cases). Lens dose of >6 Gy was seen in 16 (21%) of PT patients and 35 (45%) of IMRT patients ($p < 0.01$). Mean testicular dose was 0.5 Gy for PT and 5 Gy for IMRT ($p < 0.01$). Mean ovarian dose was 2 Gy for PT and 10 Gy for IMRT ($p = 0.05$). Pelvic growth plate V_{30} was 14% for PT and 68% for IMRT ($p = 0.02$).
Conclusions: Proton radiation lowers integral dose and improves normal tissue sparing when compared to IMRT for pediatric RMS. Correlation with clinical outcomes is necessary.

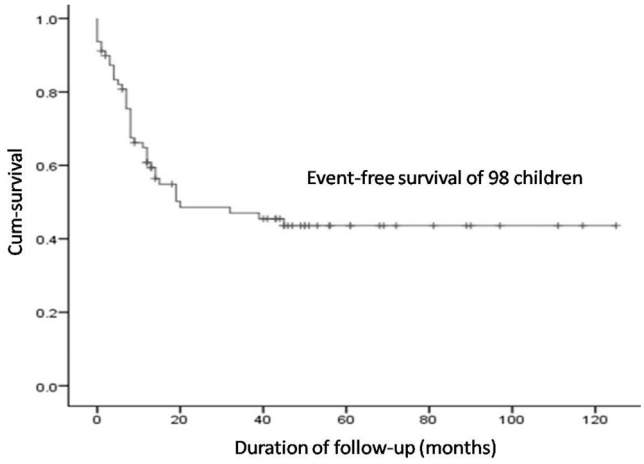
P-290

PROFILE AND OUTCOME OF CHILDREN WITH RHABDOMYOSARCOMA: 2 3-YEARS EXPERIENCE FROM PGIMER, CHANDIGARH, INDIA

D. Bansal[1], A. Das[1], A. Trehan[1], R. Kapoor[2], S.C. Sharma[2], K.L.N. Rao[3], N.K. Panda[4], R. Srinivasan[5], A. Rajwanshi[5], N. Kakkar[6], K.S. Sodhi[7], A.K. Saxena[7], R.K. Marwaha[1]

[1]Pediatric Hematology-Oncology unit Dept. of Pediatrics Advanced Pediatrics Centre, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [2]Radiotherapy, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [3]Pediatric Surgery, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [4]Otolaryngology, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [5]Cytology, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [6]Histopathology, Postgraduate Institute of Medical Education & Research, Chandigarh, India; [7]Radiodiagnosis, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Objectives: The aim was retrospective evaluation of the clinico-investigational profile and outcome of children with Rhabdomyosarcoma (RMS) from a single center.
Methods: The case records of children with RMS from 1990-2012 were analyzed.
Results: Case records of 159 children were examined. Median age at presentation was 4 years (interquartile range (IQR): 2-7). The M:F ratio was 2.3:1. The mean symptom-diagnosis interval was 2 months (IQR: 1-5). There were 20 (13%) infants; 5 (3%) had congenital RMS. Frequent sites of involvement included head/neck (44%) and genitourinary (18%); 67% were at an unfavorable site. A majority (43%) of tumors were >5 cms. The most-common pathology was embryonal (61%); pathology was not-specified in 30%. Risk-categorization: 33% low-risk, 56% intermediate-risk and 11% high-risk. Treatment included neo-adjuvant chemotherapy and surgical excision, if feasible, followed by radiotherapy for residual disease and inoperable tumors, as well as chemotherapy. Low risk patients were given vincristine and actinomycin-D for 26 weeks, while intermediate and high risk groups received vincristine, actinomycin-D, cyclophosphamide, doxorubicin and etoposide for 40 weeks. Treatment refusal (18%) and abandonment (33%) were major concerns. Among the 129 patients who opted for treatment, surgery was performed in 63 (49%); 54 (42%) received radiotherapy. Of the evaluable 77 patients, 5 (6.5%) died of febrile neutropenia, 7 (9%) had progressive disease, while 29 (38%) relapsed. The mean time to relapse was 11 months (IQR 7-15). There are 36 (47%) survivors, free of disease, on follow for a mean duration of 4.4 ± 2.6 years. The 5-year event free survival was $43.6 \pm 6\%$.



Conclusions: In a large study on pediatric RMS from India, the 5-year event free survival was $43.6 \pm 6\%$. Treatment abandonment was a major concern, particularly in the early years. The unit has strengthened the management strategy by initiating several remedial measures.

P-291

LONG TERM OUTCOME OF ORBITAL RHABDOMYOSARCOMA IN CHILDREN: EXPERIENCE OF THE INSTITUT CURIE

H. Boutroux[1], C. Cellier[2], V. Mosseri[3], S. Helfre[4], C. Levy[5], L. Desjardins[5], C. Plancher[3], P. Freneaux[6], J. Michon[1], D. Orbach[1]

[1]Pediatric Adolescent Young Adult Department, Institut Curie, Paris, France; [2]Department of Radiology, Institut Curie, Paris, France; [3]Department of Biostatistics, Institut Curie, Paris, France; [4]Radiotherapy Department, Institut Curie, Paris, France; [5]Ophthalmologic Department, Institut Curie, Paris, France; [6]Department of Pathology, Institut Curie, Paris, France

Objectives: Localized rhabdomyosarcoma is associated with a good survival rate, and considered as a favorable site when primary concerns orbit (ORMS). Treatment is based on a poly-chemotherapy associated to the best local therapy, sometime surgery but more often radiation therapy, regarding to initial tumor features and tumor response.
Methods: A retrospective monocentric analyze was set up to better define long-term outcome of patients with localized ORMS, parameningeal or not, treated in the Institut Curie between 1975 and 2010, in order to better define patients that can avoid aggressive local treatment at diagnosis.
Results: Ninety-five patients were analyzed. Median age at diagnosis was 6 years [Ranges: 8months -19 years], and median follow-up was 8.5 years [Ranges: 7 months -24 years]. Parameningeal extension was present for 25 patients. Irradiation therapy was part of primary therapy for 79 patients. At 5 years, event-free (EFS) and overall survivals (OS) were respectively $65.4 \pm 5.2\%$ and $85.6 \pm 3.9\%$. EFS was similar for parameningeal and non-parameningeal tumors ($60.3 \pm 10.4\%$ vs. $62.7 \pm 5.9\%$; $P = 0.07$) whereas OS was significantly better for non-parameningeal tumors ($90 \pm 3.9\%$ vs. $72.7 \pm 9.6\%$, $P = 0.0496$).). In multivariate analysis, initial tumor size remains statistically significant after adjustment on radiation therapy treatment ($P < 0.015$), whereas radiation therapy as first line was no longer a statistical prognosis factor for OS after adjustment on tumor and treatment characteristics ($P > 0.64$).
Conclusions: Localized ORMS remains a location with favorable outcome despite the actual tendency to reduce the agressivity and the indications of local therapy source of ophthalmologic and structural late effects. Patients with favorable pattern of strict ORMS can be treated without radiation therapy in first line treatment. ORMS with parameningeal extension should receive additional radiotherapy.

P-292

RETROSPECTIVE ANALYSIS OF OUTCOMES OF PATIENTS WITH RELAPSED, REFRACTORY AND METASTATIC SARCOMAS WHO HAVE RECEIVED METRONOMIC CHEMOTHERAPY

S. Kumar[1], A. Dongre[1], B. Arora[1], P. Kurkure[1], G. Chinnaswamy[1], B. Rekhi[2], S. Laskar[3], S. Kembhavi[4], A. Puri[5], S.D. Banavali[1]

[1]Medical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Pathology, Tata Memorial Hospital, Mumbai, India; [3]Radiation Oncology, Tata Memorial Hospital, Mumbai, India;

[4]Radiology, Tata Memorial Hospital, Mumbai, India; [5]Surgical Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: To study the efficacy and tolerability of metronomic therapy with tamoxifen, etoposide and cyclophosphamide in refractory, relapsed and metastatic soft tissue sarcoma (Ewing Sarcoma; Rhabdomyosarcoma; and other Soft Tissue Sarcomas).
Methods: This is retrospective, single institutional, observational study. We retrospectively reviewed data of patients with relapsed, refractory or metastatic soft tissue sarcoma (STS) [Ewing Sarcoma (ES);Rhabdomysarcoma (RMS) or STS] who were treated with the metronomic protocol of oral Tamoxifen, Etoposide and Cyclophosphamide (TEC) during the period April 1998 to September 2013. Approval was obtained from the Institutional Review Board and waiver of consent was granted. The patients included in the analysis were those who had relapsed after the primary protocols and then treated with metronomic TEC protocol; or those with primary refractory or metastatic disease (RMS, ES) and received metronomic TEC therapy.
Results: Forty-nine patients were enrolled. Among the 49 patients, 32 were diagnosed ES, 13 RMS and 4 other STS. For the whole cohort response rates (RR) were 59% and clinical benefit rate (CBR) was 79%. Patients in the study were grouped into the following subgroups. Systemic recurrent/relapsed disease (N = 24), metastatic disease at presentation (N = 15) and local disease (refractory/recurrent) (N = 10). None of the patients required blood or platelet support or admission for supportive care. The median PFS and OS was 12.35 months and 26.184 months for patients respectively with systemic recurrence v/s 16.8 months and 22.08 months for respectively for patients with primary metastatic disease and was best at 126.68 months and 138.87 months respectively for patients with locally recurrent/residual disease.
Conclusions: This study provides a preliminary evidence efficacy and tolerability of metronomic chemotherapy in poor risk ES and RMS. It also demonstrates that with this low cost low risk treatment few patients could go into long term remissions despite high disease burden. Also When given as maintenance therapy it shows excellent long term outcomes.

P-293

SYNOVIAL SARCOMA RELAPSES IN CHILDREN AND ADOLESCENTS: PROGNOSTIC FACTORS, TREATMENT AND OUTCOME

F. Soole[1], C. Maupain[2], A.S. Defachelles[3], S. Taque[4], V. Minard-Colin[5], C. Bergeron[6], Y. De Rycke[7], D. Orbach[1]

[1]Pediatric Adolescent Young Adult Department, Institut Curie, Paris, France; [2]Pathology Department, European Hospital Georges Pompidou, Paris, France; [3]Pediatric Oncology Department, Centre Oscar Lambret, Lille, France; [4]Pediatric Department, Hopital Sud Centre Hospitalier Universitaire, Rennes, France; [5]Pediatric Department, Institut Gustave Roussy, Villejuif, France; [6]Pediatric Department, Institut D'hematologie Et d'Oncologie Pediatrique, Lyon, France; [7]Biostatistical Department, Institut Curie, Paris, France

Objectives: Twenty-five to 32% of patients with synovial sarcoma (SS) relapse after appropriate treatment, and experience a poor outcome. Patients who can be salvaged by second-line therapy need to be more clearly identified.
Methods: Data of patients treated in SFCE (*Société Française des Cancers de l'Enfant*) centers with an initial diagnosis of localized SS before the age of 18 years and treated from 1/1988 to 12/2008, and who experienced at least one relapse were retrieved. After descriptive analysis, statistical analysis was performed to determine prognostic factors.
Results: Thirty-seven patients were identified. First relapse occurred after a median interval of 24 months and was localized in 73.0% of cases and metastatic in 24.3% of cases. Treatment of relapse consisted of new surgery in 75.7% of cases, second-line chemotherapy in 73.0% of cases and radiotherapy in 48.6% of cases. Response rate to ifosfamide-based regimens was 36.4%. Overall, 70.3% patients achieved a second complete remission. Median 5-year-event-free survival was 32.8% and 5-year overall survival was 42.1%. Factors significantly correlated with better survival were primary tumor involving the limbs, age less than 12 years at diagnosis, absence of chemotherapy or radiotherapy as initial treatment and local relapse.
Conclusions: Despite its poor overall outcome, relapse of synovial sarcoma sometimes remains curable. Aggressive surgery, when possible, in combination with chemotherapy and radiotherapy is the recommended treatment. Ifosfamide-based regimens may remain effective in patients with relapsed SS. However, alternative therapies should be proposed in patients with poor prognostic factors.

P-294

THE ROLE OF PROGNOSTIC FACTORS IN SOFT TISSUE SARCOMAS OF NEUROGENIC ORIGIN (MPNST) IN CHILDREN TREATED WITH CWS PROTOCOLS BETWEEN 1992 AND 2013

E. Bien[1], M. Krawczyk[1], B. Kazanowska[2], J. Godzinski[3], E. Adamkiewicz-Drozynska[1], E. Izycka-Swieszewska[4], P. Czauderna[5], W. Balwierz[6], A. Kurylak[7], M. Rychlowska–Pruszynska[8], G. Sobol[9], B.M., W. (. Zalewska-Szewczyk[10], M. Jazdon[12], J. Nurzynska-Flak[13], A. Reich[2], A. Urbanik[2]

[1]Pediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [2]Pediatric Hematology Oncology and Bone Marrow Transplantation, Medical University of Wroclaw, Wroclaw, Poland; [3]Pediatric Surgery, Marciniak Hospital, Wroclaw, Poland; [4]Laboratory of General Pathology and Neuropathology, Medical University of Gdansk, Gdansk, Poland; [5]Surgery and Urology for Children and Adolescents, Medical University of Gdansk, Gdansk, Poland; [6]Pediatric Oncology and Hematology, Jagiellonian University Collegium Medicum, Krakow, Poland; [7]Pediatrics Hematology and Oncology, Nicolaus Copernicus University Collegium Medicum, Bydgoszcz, Poland; [8]Oncological Surgery for Children and Youth, Mother and Child Institute, Warszawa, Poland; [9]Oncology Hematology and Chemotherapy, Medical University of Silesia, Katowice, Poland; [10]Pediatrics Oncology Hematology and Diabetology, Medical University of Lodz, Lodz, Poland; [11]Pediatric Surgery, Medical University of Silesia, Katowice, Poland; [12]Pediatric Oncology Hematology and Transplantology, Medical University of Poznan, Poznan, Poland; [13]Pediatric Hematology Oncology and Transplantology, Medical University of Lublin, Lublin, Poland

Objectives: The aim of the study was to assess the role of particular clinical prognostic factors in childhood soft tissue sarcomas of neurogenic origin (MPNST).
Methods: The study included 50 children with MPNST (M/F: 26/24, age 2-214 months; M: 142 months) treated with CWS protocols in Polish centers of pediatric oncology between 1992 and 2013.
Results: Neurofibromatosis type 1 (NF1) was found in 32% of patients. Over 70% of children presented with extensive invasive tumors (T2b). In 82%, only a diagnostic biopsy of primary tumor or R2 surgery was made. CR and PR response rate after CHT was 58%. Delayed surgery was done in 34% (R0 in most). Radiotherapy (RTX) in the Ist line therapy was used in 28% of patients. Recurrences occurred in 54%, including as many as 7/8 children initially qualified as IRS I and II. 42% of patients died of PD, 44% are alive in CR (FU 17 months-14 years). Negative prognostic factors for 5-y-OS included: tumor located retroperitoneally and in internal organs, tumor size> 10 cm and the coexistence of NF1. Failure to carry out complete resection of the tumor at any stage of the disease significantly worsened EFS and OS. Response to CHT depended only on the presence of NF1 and affected the 5-y-EFS significantly.
Conclusions: 1. High rate of local recurrences after R0 primary surgery suggests an underestimation of MPNST stages. 2. Patients after R1 primary resection require adjuvant local therapy (surgical and/or RTX).3. Complete resection of the tumor at any stage of the disease should be aimed, as it significantly improves the prognosis (77% of survivors had primary or secondary R0 resection).4. A sustained CR after CHT is unlikely, however, CHT may prevent the metastatic recurrence. 5. The coexistence of NF1 significantly worsens the prognosis in children with MPNST.

P-295

PHASE 2 STUDY OF SUNITINIB, AN ORAL MULTI-TARGETED TYROSINE KINASE INHIBITOR IN SUBJECTS WITH NF1 PLEXIFORM NEUROFIBROMAS: AN UPDATE

C. Shih[1], N. Swigonski[1], J. Case[1], K. Robertson[1], C. Dwight[1], C. Ho[1], M. Markel[1], F. Yang[1], D. Clapp[1]

[1]Pediatrics, Indiana University School of Medicine, Indianapolis, USA

Purpose
Sunitinib malate is an orally bioavailable, competitive inhibitor of vascular endothelial growth factor (VEGFR), platelet-derived growth factor (PDGFR), proto-oncogene c-KIT, and Fms-like tyrosine kinase 3 (FLT-3). This phase 2 efficacy trial is evaluating two cohorts of subjects, adult and pediatric, with NF1 and clinically significant plexiform neurofibromas. The primary response indicator is tumor response by 2D and 3D MRI imaging. Secondary response indicators include volumetric MRI imaging, quality of life measure, biomarker evaluation of cytokines and endothelial progenitor cells, and pain-related outcomes. The objective of the study was to assess a secondary response indicator i.e. pain in subjects with at least 6 months of follow-up.
Methods: Frequency, severity of pain, and medication usage was documented at initial enrollment visit and at 6 month follow-up for subjects on Sunitinib. Data from patients treated with Imatinib was obtained from retrospective chart review.
Results: To date 21/40 subjects have been enrolled, with 19 evaluable, consisting of 4 adult and 15 pediatric patients. Two subjects have completed the study, one with stable disease, and another with progressive disease. Two subjects withdrew from the study prior to being evaluated. Patients with at least 6 months of follow-up report 62.5% less pain, and 50% have decreased pain medication utilization, and no patients complained of either increased pain or pain medication usage. No subjects reported an increase in pain or in use of pain medication. When compared to patients treated with imatinib, patients treated with Sunitinib report statistically less pain ($p < 0.0001$) and less pain medication usage ($p = 0.0011$).
Conclusions: Limited patient follow-up data is currently available for other response indicators, but pain response as a secondary indicator and major contributor to quality of life and daily functioning for subjects on trial is encouraging.

P-296

KAPOSI'S SARCOMA IN CHILDREN: AN OPEN RANDOMISED TRIAL OF VINCRISTINE, ORAL ETOPOSIDE AND A COMBINATION OF VINCRISTINE AND BLEOMYCIN

G. Chagaluka[1], E. Molyneux[2], C. Stanley[3], S. Depani[4], I. Israels[5], S. Bailey[6], C. George[7]

[1]Paediatric and Child Health, Queen Elizabeth Central Hospital, Blantyre, Malawi; [2]Paediatric and Child Health, College of Medicine, Blantyre, Malawi; [3]University of Malawi, Chancellor College, Zomba, Malawi; [4]Oncology, Royal Marsden Hospital, London, United Kingdom; [5]Oncology, VU University Medical Centre, Amsterdam, Netherlands; [6]Oncology, The Great Northern Hospital, NewCastle, United Kingdom; [7]Oncology, Queen Elizabeth Central Hospital, Blantyre, Malawi

Objectives

Introduction: Kaposi's sarcoma (KS) is a common childhood cancer in places where HIV is endemic and access to antiretroviral therapy (ART) is delayed. Despite this there are no randomised trials to compare and assess chemotherapeutic regimens.

Methods: An open label, randomised trial comparing intravenous vincristine alone, vincristine and bleomycin, and oral etoposide, was carried out in children with Kaposi's sarcoma in the Queen Elizabeth Central Hospital, Blantyre, Malawi. HIV infected children were given ART after 2 to 3 courses of chemotherapy if they were not already on treatment. Neither HIV nor widespread KS are curable and treatment is aimed at disease reduction and improved quality of life. Tumour reduction was assessed by measuring the size of sentinel KS nodules and quality of life (QoL) by using the Lansky score. Follow up was until death or for one year.

Results: 92 children were enrolled of whom 46% were naïve to ART; 10 (11%) were HIV negative. Survival was not influenced by age or gender but was better in the oral etoposide and the vincristine and bleomycin groups. P = 0.0045. The group receiving oral etoposide had a better quality of life. Toxicity was not significant, and any drop in haemoglobin or white cell count could have been causally related to HIV infection rather than cytotoxic therapy.

Conclusions: Oral etoposide is a safe, effective treatment to contain KS and improve QoL which can be achieved without many visits to hospital and intravenous injections.

SUPPORTIVE CARE/PALLIATIVE CARE

P-297

HEALTH CARE UTILIZATION AND COSTS IN THE LAST YEAR OF LIFE FOR CHILDREN WITH MALIGNANCIES

P. Ananth[1], P. Melvin[2], J.G. Berry[3], J. Wolfe[4]

[1]Pediatric Hematology/Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Boston, USA; [2]Program for Patient Safety and Quality, Boston Children's Hospital, Boston, USA; [3]Division of General Pediatrics, Boston Children's Hospital, Boston, USA; [4]Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, USA

Objectives: Little is known about how children with malignancies utilize health care in the last year of life. Our objectives were: to describe the duration and costs of admissions in the last year of life for children with malignancies who died in one of 40 U.S. children's hospitals; and to examine hospital resource use in the terminal admission.

Methods: We studied 455 children with malignancies, ages 1-18 years, who died in 2012. Data were obtained from the Pediatric Health Information System database. Malignancies were identified using ICD-9 codes. We assessed hospital days (total and intensive care unit) and hospital costs, stratified by class of malignancy (solid vs. hematologic), in the last year of life. We also characterized hospital days and interventions received in the terminal admission.

Results: Median age at death was 9 years (IQR 4-15). 42% of children were non-Hispanic white; 68% had public insurance. In the last year of life, children with malignancies spent a median of 59 days in the hospital (IQR 22-113) and 6 days in the ICU (IQR 1-18). Compared to children with solid malignancies, children with hematologic malignancies (N = 204) had higher median hospital days and costs [median 85.5 hospital days (IQR 33.5-138); median cost $420,203 (IQR $170,531-$782,062). In the terminal admission, 322 children (71%) had unplanned hospitalizations. Children spent a median of 14 days (IQR 4-36) admitted, with 2 median ICU days (IQR 0-11). 55% of children were mechanically ventilated by this time; 36% visited the operating room in the terminal admission itself.

Conclusions: Children with malignancies experience lengthy, costly hospitalizations in the last year of life and undergo invasive procedures in the terminal admission. Children with hematologic malignancies appear to have the highest costs. Further investigation may reveal whether palliative care intervention for these children might improve hospital utilization and quality of life.

P-298

ASSESSMENT OF INVISIBLE FINANCIAL BURDEN FACED BY FAMILIES WITH CANCER CHILDREN IN A DEVELOPING COUNTRY

J. Pulivadula Venkatasai[1], J.X. Scott[1], R. Manipriya[1], M.S. Latha[1], A. Rajendran[1]

[1]Dept. of Pediatrics Division of Hemato-oncology, Sri Ramachandra Medical College And Research Institute, Chennai, India

Objectives: The diagnosis of cancer in a child is a family crisis. The costs of treatment are not only direct medical expenses but also non-medical expenses and loss of pay. Though, the existence of financial strain is well known, it is not studied systemically and under-researched in medical literature especially in developing countries like India. The principle objectives of this study are to systemically review the financial burden including invisible expenses incurred by the families of children with cancer from a social perspective.

Methods: 70 families with children undergoing treatment participated in the study. The parents/guardians were interviewed in a prepared questionnaire session. Study Period - Aug 2012 -Aug 2013.

Results: Of the 70 patients with hematological malignancies, with 69% males and 31% females, the mean age was 7.8 ± 2.2 years. 54% of the patients household annual income ranged between Rs.60,000-1,19,999. Non-medical expenses accounts for about 46% of their monthly household income of parents from rural areas and 22% of their household income from urban areas. Out-of-pocket expenses for food and travel have emerged as a major contributing factor for severe economic effect on the family. 63% of patients used public transport like trains or buses for travel for treatments and follow–up. Invisible expenses (loss of pay) are seen more often with working mothers than with fathers. Households with multiple children have restricted the need for other siblings to provide for the diseased child. 38% of families have borrowed money from money lenders with an average interest rate of about 12.5% which pushes them to a state of debt for the next few years.

Conclusions: By bringing the financial burden experienced by the families to limelight especially the invisible expenses, the issue can be taken into serious consideration during healthcare planning and policy making.

P-299

APREPITANT AS AN ADD-ON THERAPY IN CHILDREN RECEIVING HIGHLY EMETOGENIC CHEMOTHERAPY: A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

S. Bakhshi[1], A. Batra[1], B. Biswas[1], D. Dhawan[1], R. Paul[1], V. Sreenivas[2]

[1]Medical Oncology, Dr. BRA IRCH AIIMS, Delhi, India; [2]Biostatistics, Dr. BRA IRCH AIIMS, Delhi, India

Objectives: Aprepitant, a neurokinin-1 receptor antagonist, in combination with 5 HT-3 antagonist and dexamethasone is recommended in adults receiving moderately and highly emetogenic chemotherapy to reduce chemotherapy-induced nausea and vomiting (CINV). Data for use of aprepitant in children are limited and are not included in guidelines for prevention of CINV.

Methods: A randomized double-blind placebo-controlled trial was conducted at a single center in chemotherapy naïve children (5-18 years) receiving highly emetogenic chemotherapy. All patients received intravenous ondanseteron (0 · 15 mg/kg) and dexamethasone (0 · 15 mg/kg) prior to chemotherapy. Patients randomly assigned to aprepitant arm received oral aprepitant (15-40kg: days 1-3 80mg; 41-65kg: day1: 125mg and days 2-3 80mg) one hour before chemotherapy. Primary outcome measure was incidence of acute moderate and severe vomiting. Control group received placebo as add-on therapy.

Results: Of 96 randomized patients, three were excluded from analysis; 93 patients were analyzed (50 in aprepitant arm and 43 in placebo arm). Acute moderate and severe vomiting was reported in 72 · 09% patients receiving placebo and 38% patients receiving aprepitant (p = 0 · 001). During acute phase of assessment, oral intake including fluid and food was significantly decreased in control group when compared with aprepitant arm (72 · 09% vs 52%, p = 0 · 047; 62 · 47% vs 38%, p = 0 · 031 respectively). No major adverse effects were noted.

TABLE

	Placebo	Aprepitant	Difference (95%CI)	p
Acute		31 (62%)	34 (15-53) %	0·001
Nil-mild	12 (27·91%)			
Moderate-severe	31 (72·09%)	19 (38%)		
Delayed			14 (0-34) %	0·18
Nil-mild	19 (44·19%)	29 (58%)		
Moderate-severe	24 (55·81%)	20 (42%)		
Overall				
Nil-mild	7 (16·28%)	22 (44%)	28 (10-46) %	0·004
Moderate-severe	36 (83·72%)	28 (56%)		

Conclusions: This is the first double blinded, randomized placebo controlled trial which unequivocally shows that aprepitant significantly decreases incidence of acute moderate and severe vomiting when used as an add-on drug with ondanseteron and dexamethasone in children receiving highly emetogenic chemotherapy.
(ClinicalTrials.gov Identifier: NCT01402024)

P-301

ORAL VS INTRAVENOUS ANTIBIOTICS IN LOW RISK PAEDIATRIC FEBRILE NEUTROPENIA: A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

A. Vedi[1], R.J. Cohn[1]

[1]Kids Cancer Centre, Sydney Children's Hospital, Sydney, Australia

Objectives: Sepsis is a major cause of morbidity and mortality in paediatric oncology patients, particularly during periods of neutropenia, which is a well-recognised complication of immunosuppressive therapy. Stratification of patients into low and high-risk categories has facilitated a new tailored approach to empiric therapy. The availability of oral antimicrobial drugs with broad-spectrum activity against common pathogens may provide an attractive alternative. The aims were to determine whether, in low-risk febrile neutropenic paediatric populations, oral antibiotics are as effective as intravenous antibiotics in obtaining resolution of the febrile neutropenic episode.
Methods: A comprehensive literature search of MEDLINE, EMBASE and CENTRAL identified prospective, randomised controlled trials comparing oral antibiotics to intravenous antibiotics in the treatment of febrile neutropenic episodes in low-risk paediatric oncology patients. Outcomes assessed were mortality, rate of treatment failure, length of the febrile neutropenic episode and adverse events. The random effects model was used to calculate risk ratios (RR) for dichotomous data and mean difference with standard deviation for continuous data.
Results: Seven trials were included in the overall analysis, which included 934 episodes of febrile neutropenia in 676 patients aged between 9 months and 20 years. The overall treatment failure rates were not significantly different between oral and intravenous antibiotics (RR: 1.02, 95% CI 0.78 to 1.32, $p = 0.91$).
Conclusions: In carefully selected low-risk febrile neutropenic children, empiric treatment with oral antibiotics is a safe and effective alternative to intravenous antibiotics, as they lower the cost of treatment, and psychosocial burden on these children and their families.

P-302

BACTERIAL SPECTRUM AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF BLOOD STREAM INFECTIONS IN ACUTE LYMPHOBLASTIC LEUKEMIA CHILDREN WITH FEBRILE NEUTROPENIA AT CHILDREN CANCER HOSPITAL

A. Khatoon[1], F. Zameer[2], R. Punjwani[3], S. Narijo[4]

[1]Infection Control, Children Cancer Hospital, Karachi, Pakistan; [2]Microbiology, Children Cancer Hospital, Karachi, Pakistan; [3]Nursing Education, Children Cancer Hospital, Karachi, Pakistan; [4]Medical Record, Children Cancer Hospital, Karachi, Pakistan

Objectives: Bacterial infections are the major cause of morbidity and mortality in chemotherapy induced febrile neotropenic patients. Regular monitoring of bacterial epidemiology allows evaluation of antibacterial strategies. Purpose of this study is to identify the type of organisms and antibiotic resistance pattern. It is necessary to know the category of resistance organisms before starting the antibiotic.
Methods: Data were retrospectively collected from medical records at CCH. Patients who were diagnosed with ALL and had chemotherapy induced febrile neutropenia along with positive culture between January and December 2013 were analyzed.
Results: Thirty patients were studied over the period of one year, 20 males and 10 females with the median age of 7 years. 25 patients presented with febrile neutropenia during their induction phase, 3 patients while consolidation and the remaining 2 during re-intensification. The induction phase of treatment in acute leukemia is the major cause of FN in hematological malignancies at the children cancer hospital. According to preliminary analysis of the pathogens, 47% of the isolates were gram-negative organisms, 40% were gram-positive organisms, and 13% were fungi. The most populous gram-positive organism isolated was coagulase negative staphylococcus (30%), followed by vancomycin-resistant enterococcus (6.67%). For the gram negatives, Pseudomonas was isolated in majority (16.67%). Coagulase negative staphylococcus was resistant to oxacillin (32%), levofloxacin (37%) but not to vancomycin until now. Enteroccocus was resistant to vancomycin, levofloxacin and amikcin but only sensitive to linezolid (100%). Pseudomonas was mostly sensitive to most antimicrobials; Meronium, Tazocin, levofloxacin, Polymixin B and Amikcin.
Conclusions: Cougulase negative staph was mostly found in our study and that can be controlled with the help of effective infection control. Antibiotic cycling for neutropenic fever was implemented and followed over an extended time period. Gram-negative resistance remained stable. Further study is necessary to clarify the effect of cycling on antibiotic resistance, patient outcomes, and hospital cost.

P-303

PRESERVATION OF VARICELLA SEROLOGY TITERS IN PEDIATRIC ONCOLOGY PATIENTS FOLLOWING CHEMOTHERAPY

P. De Gouveia[1], A. Chiang[1], S. Um[1], C. Clarkstone[1], R. Ramphal[1]

[1]Hematology/Oncology, Children's Hospital of Eastern Ontario, Ottawa, Canada

Objectives: For pediatric oncology patients, current practice includes administering Varicella-Zoster Immunoglobulin (VZIG) as post-exposure prophylaxis (PEP) against Varicella-Zoster Virus (VZV) and isolating patients for 8 to 21 days. Pediatric oncology patients immune to VZV prior to their cancer diagnosis represent a population likely to preserve immunity against the disease. For these patients population the need for VZIG and isolation is poorly validated and may be an undue health care cost and inconvenience to patients. Therefore, we assessed VZV serology post-chemotherapy as a marker for persistence of immunity against VZV while on chemotherapy.
Methods: Approval from the research ethics board at the Children's Hospital of Eastern Ontario (CHEO) was obtained prior to this study. Varicella antibody titers were collected from 500 pediatric oncology patients treated at CHEO. Patients included in this study had positive titers at the time of their malignancy diagnosis and VZV antibody titers were re-tested at 6-months or 1-year post-chemotherapy treatment.
Results: Of the eligible 190 patients with positive antibody titers to VZV at time of malignancy diagnosis, 139 (73%), 16 (8%), and 5 (2.3%) patients had positive, negative or equivocal post chemotherapy VZV antibody titers, respectively. Moreover, 19 (10%) had varicella breakthrough disease and 11 (5.7%) developed zoster during chemotherapy or post-chemotherapy but prior to re-testing for VZV antibody titers. There was no correlation between age or tumour type with preservation of VZV antibody titers.
Conclusions: The majority of pediatric oncology patients with prior VZV antibody titers preserve their VZV immunity post chemotherapy. Consequently for this population, VZIG PEP and isolation in hospital may not be necessary. In Japan and the United Kingdom, acyclovir is used as a cost-effective alternative. For patients VZV seropositive prior to malignancy, further studies to determine the risk factors predisposing these patients to breakthrough disease may identify a subgroup for whom VZIG PEP is necessary.

P-304

ROLE OF PARVO VIRUS B19 INFECTION IN CAUSING UNEXPLAINED COMPLICATIONS DURING CANCER CHEMOTHERAPY IN CHILDREN – A COMMONLY UNRECOGNISED PROBLEM

A. Kumar[1], N. Roy Moulik[1], N. Verma[1], A. Jain[2], P. Jain[2]

[1]Pediatrics, King George Medical University, Lucknow, India; [2]Virology, King George Medical University, Lucknow, India

Objectives: In children with cancer, cytopenias and transaminitis inappropriate to the intensity of chemotherapy cause treatment delays and may raise the concern for relapse. The causes for these often remain undetected. We examined the role of parvo virus B19 (B19V) in causation of such unexplained complications.
Methods: Children on cancer chemotherapy with unexplained cytopenias and/or transamnitis were screened for Parvovirus B19 infection (by anti IgM and/or DNA PCR) from January to December 2013. The clinical course, laboratory parameters and response to IVIg (intravenous immunoglobulin) of those who tested positive is described.
Results: B19V infection was detected in 52 of 163 (31.9%) children screened (30 of 84 leukemias, 4 of 24 lymphomas and 15 of 55 solid tumors). Of the 52 positive patients, isolated anemia, neutropenia and thrombocytopenia were seen in 18,11and 5 patients respectively. The remaining 18 patients had anemia along with neutropenia and/or thrombocytopenia and/or transaminitis.B19V positive children with haematological malignancies had significantly lower haemoglobin when compared to those with solid tumors (5.15 ± 1.76 vs 9.07 ± 1.99 gm/dl; $p < 0.001$). Chemotherapy interruption (>7 days) was seen in a higher proportion of children with haematological malignancies (36%) as compared to solid tumors (18%). Of the B19V positive children IVIg was given to 19/20 with severe illness. Only one child, who had not been given IVIg, expired (B19V report was available post-mortem). The median duration of recovery of counts in children who received IVIg was 11.0 (range: 4-14) days, thus allowing an early resumption of chemotherapy.
Conclusions: B19V accounted for nearly one-third of the cases with unexplained complications during chemotherapy in our series. Illness was more severe in children with haematological malignancies. Clinical suspicion and early treatment with IVIg reduces disease severity and duration of chemotherapy interruption.

P-305

FEASIBILITY OF A NEW SCREENING TOOL TO OPTIMISE THE MANAGEMENT OF PATIENTS WITH CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY (CIPN)

P. Loughnane[1], F. Clinton[2], M. Capra[2]
[1]Department of Physiotherapy, Our Lady's Children's Hospital, Dublin, Ireland;
[2]Department of Haematology Oncology, Our Lady's Children's Hospital, Dublin, Ireland

Objectives: The Dublin CIPN screening tool was developed to enhance the quality of pre chemotherapy examinations in patients receiving Vincristine, thereby improving detection rates of CIPN, and facilitating appropriate onward referral.
Methods: A retrospective review, undertaken in 2010, highlighted limitations in the pre chemotherapy assessment of patients receiving Vincristine at a tertiary children's cancer centre. The Dublin CIPN screening tool was consequently developed. It was piloted throughout 2013, as part of pre chemotherapy assessment in patients receiving Vincristine. A prospective review evaluated quality of pre chemotherapy assessment, CIPN detection rates, and subsequent management of CIPN. Compliance with the screening tool and user satisfaction rates were also evaluated.
Results: Introduction of the Dublin CIPN screening tool at a tertiary children's cancer centre resulted in increased recognition of potential signs and symptoms of CIPN (65.96% versus 33.3%). It prompted more frequent modification of Vincristine doses (19.15% versus 8.33%). Close monitoring of CIPN changes allowed administration of higher cumulative doses of Vincristine before dose modification was necessary (10.33 mg/m^2 versus 7.26 mg/m^2). Staff compliance with utilisation of the Dublin CIPN screening tool was 83.03%. Satisfaction rates

were very high, although difficulties in examination of children less than 5 years of age were highlighted.
Conclusions: Introduction of the Dublin CIPN screening tool resulted in increased detection rates of CIPN, more timely recognition of severe CIPN, and more frequent modification of Vincristine doses at a tertiary children's cancer centre. We recommend that the Dublin CIPN screening tool, with minor amendments, be adopted as routine standard of care at this centre.

P-306

HEALTH-RELATED QUALITY OF LIFE (HRQL), FATIGUE AND SLEEP AMONG CHILDREN WITH CANCER

D. Wakefield[1], T. Ruiz[2], A. Orsey[3]

[1]Center for Public Health and Health Policy, University of Connecticut Health Center, Farmington, USA; [2]Clinical Trials Unit, Connecticut Children's Medical Center, Hartford, USA; [3]Hematology/Oncology, Connecticut Children's Medical Center, Hartford, USA

Objectives: To investigate the relationship between health-related quality of life (HRQL), fatigue and sleep in pediatric patients receiving chemotherapy and/or radiation therapy (RT) for cancer.
Methods: Between 11/12/09 and 03/19/14, 59 pediatric oncology patients 8-18 years of age completed the study. Participants were receiving chemotherapy and/or RT for cancer and were evaluated over 7 days without hospitalizations. HRQL of the study participants was assessed using the PedsQL 4.0 and PedsQL 3.0 Cancer Module administered to the children with cancer and their parents. Sleep was assessed objectively by actigraphy as sleep time, wake after sleep onset (WASO), number of wake bouts and sleep efficiency. Sleep was assessed subjectively by sleep diaries completed by participants and their parents to determine sleep time, sleep quality and morning mood. Fatigue was assessed using the Fatigue Scale (Child, Adolescent and Parent).
Results: The study participants consisted of 59 pediatric patients receiving chemotherapy and/or RT for cancer (36 males, 23 females, mean age 12.2 years). The HRQL scores were significantly correlated to sleep quality ($p = 0.03$) and fatigue scores ($p < 0.0001$). Participants who reported significant fatigue also reported lower HRQL scores ($p = 0.001$). Although the parent-reported fatigue correlated with parent-reported HRQL scores ($p < 0.0001$), the HRQL reported by the patients was higher than their parent's assessment of their HRQL for every HRQL domain ($p < 0.01$). Parents of teens rated their children's procedure and treatment anxiety higher than parents of younger children ($p < 0.01$).
Conclusions: HRQL was significantly associated with sleep and fatigue. Although the proxy report by parents demonstrated correlations between HRQL and fatigue, the discrepancy between participant and parent reports warrant further investigation. Fatigue and sleep may be modifiable factors which may offer a mechanism to improve HRQL among children with cancer.

P-307

FULFILLING THE VISION OF YOUTH-FRIENDLY CANCER CARE: HOW WELL ARE WE MEETING THE SUPPORTIVE CARE NEEDS OF ADOLESCENT AND YOUNG ADULT (AYA) PATIENTS?

S. Drew[1], R. McNeil[2], M. McCarthy[3], D. Dunt[4], L. Orme[5], T. Hotchkin[6], S. Sawyer[1]

[1]Centre for Adolescent Health and Department of Paediatrics, Royal Children's Hospital and University of Melbourne and Murdoch Childrens Research Institute, Melbourne, Australia; [2]Centre for Adolescent Health, Murdoch Childrens Research Institute, Melbourne, Australia; [3]Children's Cancer Centre, Royal Children's Hospital and Murdoch Childrens Research Institute, Melbourne, Australia; [4]Centre for Health Policy Programs & Economics, University of Melbourne, Melbourne, Australia; [5]OnTrac@PeterMac Victorian Adolescent and Young Adult Cancer Service and Children's Cancer Centre, Peter MacCallum Cancer Centre and Royal Children's Hospital, Melbourne, Australia; [6]Department of Paediatrics, University of Melbourne, Melbourne, Australia

Objectives: Despite global interest in cancer service reform, evidence for best practice adolescent and young adult (AYA) care is scare. This study investigated on-treatment experiences of AYAs/parents to inform a program logic model of best-practice psychosocial supportive care.
Methods: Stage 1 involved qualitative telephone interviews with AYA ($n = 60$) and parent/partner carers ($n = 60$). Stage 2 involved surveys with a nationally representative sample of AYA ($n = 200$) and parents ($n = 200$). Surveys were a combination of pre-established questions from other needs surveys and psychometric measures, as well as new questions prompted by analysis of the interviews. Topics included psychological health, information needs, social support and practical needs. 17 treatment centres disseminated surveys (5 paediatric, 12 adult).
Results: There is little information on-treatment experiences of AYA, even less the experiences of their carers. For both, this project describes social, emotional and financial impacts of cancer and treatment, perceptions about quality of interactions with healthcare staff, types of supportive care services accessed (and barriers). This presentation focuses on unmet supportive care and information needs during treatment and soon after treatment ends. These include areas such as mental health support, exercise therapy, educational and vocational support, genetic counseling, peer support, and access to cancer-related information specifically designed for this age group. We also illustrate the way these issues differ across different treatment settings.
Conclusions: Data indicate considerable room for improvement in many areas of AYA supportive care, with several themes not previously described in the literature. Results show the value of conceptualizing an ecological model of supportive care needs, which attends to AYA and carers as individuals, but also as part of an inter-related system. This data has informed articulation of a best practice model of AYA care. Implications of these findings for health care delivery and the importance of attending to both patient and carer supportive care needs will be addressed.

P-308

PAIN EXPERIENCE OF ADOLESCENTS WITH CANCER: REPORT FROM A LONGITUDINAL ELECTRONIC MOMENTARY ASSESSMENT STUDY

L. Jibb[1], J.N. Stinson[2], C. Nguyen[2], P.C. Nathan[1], A.M. Maloney[1], L.L. Dupuis[1], J.T. Gerstle[3], S. Hopyan[4], B. Alman[5], C. Strahlendorf[6], C. Portwine[7], D. Johnston[8]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada; [3]General and Thoracic Surgery, The Hospital for Sick Children, Toronto, Canada; [4]Orthopaedic Surgery, The Hospital for Sick Children, Toronto, Canada; [5]Orthopaedic Surgery, Duke University School of Medicine, Durham, USA; [6]Hematology/Oncology, British Columbia Children's Hospital, Vancouver, Canada; [7]Hematology/Oncology, McMaster Children's Hospital, Hamilton, Canada; [8]Hematology/Oncology, Children's Hospital of Eastern Ontario, Ottawa, Canada

Objectives: Adolescents with cancer report pain as a distressing element of the disease and its treatment, which negatively impacts health-related quality of life. Regardless, little is known about the daily pain experience of these adolescents, especially in everyday settings (e.g., home, school). This study used a multidimensional smartphone pain assessment application to understand the within- and between-day self-reported pain experience of adolescents with cancer.
Methods: A longitudinal, descriptive study was used to collect momentary pain data twice daily for 14-days from 70 adolescents recruited at 4 pediatric tertiary care centers. Adolescents were aged 8-18 years with various cancer diagnoses and were undergoing outpatient cancer care. Each adolescent completed a 22-question multidimensional pain assessment on a smartphone each morning and evening. Intensity scores were rated on a 5- cm visual analogue scale (0-10 point ranking), pain location was captured using a body map and categorical data related to pain duration, pain management and affective pain descriptors were recorded.
Results: Pain was reported by 93% ($n = 65$) of adolescents during the 2-week period. Eleven adolescents (16%) reported currently experiencing pain on every assessment. Current pain was rated as 3.7/10 ($SD = 2.1$) and worst pain was rated as 5.5/10 ($SD = 2.4$). Mean pain interference with daily activities was 3.7/10 ($SD = 2.4$). Adolescents reported pain as occurring in the abdomen (57%), head (42%), and low back (33%). Most adolescents (91%) did not use a pharmacological intervention when in pain, but often used non-opioids if a pain medication was used. Adolescents also used rest (70%), distraction (44%), and deep breathing (40%) to manage pain. Pain was described as tiring (31%), sickening (29%) and cruel (23%).
Conclusions: Adolescents with cancer reported pain as a common symptom that interferes with daily living. Despite its occurrence, adolescents frequently do not manage pain in the home setting and may benefit from interventions that provide in-the-moment pain management support.

P-309

POLYSOMNOGRAPHY AND MULTIPLE SLEEP LATENCY TEST FINDINGS IN CHILDREN WITH CRANIOPHARYNGIOMA PRIOR TO PROTON THERAPY

B. Mandrell[1], V. Crabtree[2], M. Smith[2], M. Wise[3], N. West[1], D. Indelicato[4], T. Merchant[5]

[1]Division of Nursing Research, St. Jude Children's Research Hospital, Memphis, USA; [2]Department of Psychology, St. Jude Children's Research Hospital, Memphis, USA; [3]Sleep Center, Methodist University Hospital, Memphis, USA; [4]Proton Center, University of Florida, Gainesville, USA; [5]Department of Radiation Oncology, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Sleep related problems, such as excessive daytime sleepiness (EDS) are common in pediatric brain tumor patients. Craniopharyngioma patients are especially at risk due to the hypothalamic-pituitary-adrenal axis tumor location and an aggressive therapy regimen. Hypothalamic obesity is a common result of tumor and treatment and may contribute to sleep disordered breathing. Daytime sleepiness and slepp-related breathing patterns have yet to be explored in this population at time of diagnosis.
Methods: Pediatric craniopharyngioma patients ($n = 37$) underwent an overnight poly-somnography and multiple sleep latency test (MSLT) prior to proton therapy to assess for sleep disorders and daytime sleepiness. Age ranged from 3 to 19 years ($M = 9.59$), and the sample was primarily female (56.8%).
Results: On average, participants spent 514.62 ± 77.45 minutes in bed while only sleeping an average of 453.34 ± 83.01 minutes. Sleep efficiency scores ranged from 55.4 to 99.6 ($M = 89.04 \pm 9.48$). Mean AHI $= 1.03 \pm 1.18$ with PLM $= 6.78 \pm 10.60$. Results from the

MSLT indicate the sample to be in the troublesome range for EDS (M SOL = 9.68 ± 5.43) with n = 9 (24%) having 2 or more SOREM. 17 (46%) were diagnosed with clinically significant EDS. 3 (8%) were found to have sleep disordered breathing.
Conclusions: Craniopharyngioma survivors have high rates of clinically significant EDS. This work demonstrates that nearly half of the children with this tumor present with clinically significant EDS and provides evidence for tumor and surgery-related impairment of alertness. Longitudinal assessment is planned for this cohort to describe the trajectory of sleepiness after proton therapy and interventions in this population.

P-310

NUTRITIONAL STATUS OF PAEDIATRIC CANCER PATIENTS IN THE UK: A PROSPECTIVE COHORT STUDY

R. Revuelta Iniesta[1], D.C. Wilson[2], I. Paciarotti[3], J.M. McKenzie[3], M.F.H. Brougham[4]

[1]Haematology and oncology, Royal Hospital for Sick Children, Edinburgh, United Kingdom; [2]Medicine and Veterinary Medicine, Child Life and Health University of Edinburgh, Edinburgh, United Kingdom; [3]Dietetics Nutrition and Biological Science, Queen Margaret University, Edinburgh, United Kingdom; [4]Haematology and Oncology, Royal Hospital for Sick Children, Edinburgh, United Kingdom

Objectives: To investigate the prevalence of malnutrition (undernutrition and overnutrition), patterns of change in nutritional status (NS) and, potential factors that may contribute to the development of malnutrition in paediatric oncology patients.
Methods: A multicentre prospective cohort-study was performed. NS was assessed between Aug 2010-Oct 2013 using anthropometry, body composition and dietary assessment. Childhood cancer was categorised into four groups: solid tumours, haematological malignancies, brain tumours and other associated cancers. The primary outcome was malnutrition defined as body mass index (BMI) according to UK growth chart centiles; underweight (<2.3rd), overweight (85-95th) and obese (>95th). NS was also assessed by arm anthropometry; mid-upper arm circumference (MUAC) and triceps skinfold (TSF), and body composition; muscle (FFM) and fat mass (FM). Frisancho's (1981) percentiles were used to establish NS by arm anthropometry. Correlations, independent t-test and multilevel analysis were performed.
Results: Seventy-four patients were studied. At diagnosis, the prevalence of undernutrition was 9.5%, overweight 5% and obesity 11%. TSF identified the highest prevalence of undernutrition 13.5% and the lowest of obesity 1%. BMI [$p = 0.03$; 95% CI (−17 to -12)] and FM [$p < 0.05$; 95% CI (677-1122)] significantly increased after 3 months and remained steady thereafter, whilst FFM [$p < 0.001$; 95% CI (2992-3550)] significantly decreased during the first year. Only energy intake showed minor correlation with BMI ($r = 0.1$; $p = 0.04$) and TSF ($r = 0.2$; $p = 0.03$) at diagnosis. No significant differences were observed between diagnostic categories during the first year. However, haematological malignancies showed higher BMI at 12 [$p < 0.05$; 95% CI (−34.9 to -0.2)], 18 [$p = 0.02$; CI (−45.6 to –3.7)] and 24 months [$p = 0.03$; 95% CI (−60.6 to -1.6)] post-diagnosis in comparison to solid tumours.
Conclusions: Undernutrition was particularly prevalent at diagnosis, yet overnutrition increased significantly during treatment, especially in children diagnosed with haematological malignancies. The body composition changes observed emphasises the need to implement targeted strategies to improve the NS of paediatric cancer patients.

P-311

OLANZAPINE FOR TREATMENT AND PREVENTION OF ACUTE CHEMOTHERAPY-INDUCED VOMITING IN CHILDREN: A RETROSPECTIVE, MULTI-CENTRE REVIEW

J. Flank[1], J. Thackray[2], D. Nielson[3], A. August[4], T. Schechter[5], S. Alexander[5], L. Sung[5], L.L. Dupuis[6]

[1]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada; [2]Department of Pharmacy, Memorial Sloan Kettering Cancer Center, New York, USA; [3]Department of Nursing, Children's Medical Center, Dallas, USA; [4]Department of Pharmacy, Children's Mercy Hospitals and Clinics, Kansas City, USA; [5]Division of Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [6]Department of Pharmacy, The Hospital for Sick Children, Toronto, Canada

Objectives: The addition of olanzapine to standard antiemetic prophylaxis improves chemotherapy-induced nausea and vomiting (CINV) control in adults. Published experience in children with cancer is lacking. The purpose of this review was to describe the safety and efficacy of olanzapine use for chemotherapy-induced vomiting (CIV) control in children.
Methods: Children <18 years old who received olanzapine for acute CINV control from December 2010 to August 2013 at 4 institutions were identified. Patient characteristics, chemotherapy, antiemetic prophylaxis, olanzapine dosing, CIV control, liver function test results and adverse events were abstracted from the health record. Complete CIV control was defined as the absence of vomiting or retching throughout the acute phase. Toxicity was graded using CTCAEv4.03 and the likelihood that toxicity was attributable to olanzapine was assessed using the Naranjo Scale.
Results: Sixty children (median age 13.2 years; range: 3.10-17.96) received olanzapine during 158 chemotherapy blocks. Olanzapine was most often (59%) initiated due to a history of poorly controlled CINV. The mean initial olanzapine dose was 0.1mg/kg/dose (range: 0.026-0.256). Most children who received olanzapine beginning on the first day of the chemotherapy block experienced complete CIV control (83/128; 65%). There was no association between the olanzapine dose/kg and complete CIV control (OR 1.01; 95% CI: 0.999 to 1.020; $p = 0.091$). Sedation was reported in 7% of chemotherapy blocks and was significantly associated with increasing olanzapine dose (OR: 1.17; 95% CI: 1.08 to 1.27; $p = 0.0001$). Of the 25 chemotherapy blocks where ALT and/or AST were reported more than once, grade 1-3 elevations were observed in 5. The mean weight change in 31 children who received olanzapine during more than one chemotherapy block was 0% (range: -22 to +18).
Conclusions: Olanzapine may be an important option to improve CIV control in children. Prospective controlled evaluation of olanzapine for CINV prophylaxis in children is warranted.

P-312

CENTRAL LINE PLACEMENT AT TIME OF DIAGNOSIS IN CHILDREN WITH ACUTE LEUKEMIA: DOES THE NEUTROPHIL COUNT MATTER?

P. Vallance[1], V. Lewis[1], M. Brindle[2], P. Beaudry[2], U. Amendy[3], D. Strother[1], L. Lafay-Cousin[1]

[1]Pediatric Hematology Oncology and Bone Marrow Transplantation, Alberta Children's Hospital, Calgary, Canada; [2]Pediatric Surgery, Alberta Children's Hospital, Calgary, Canada; [3]Pediatric Diagnostic Imaging, Alberta Children's Hospital, Calgary, Canada

Objectives: There are conflicting data on the risk of infections associated with early insertion of central venous cathethers (CVL) in neutropenic patients. We reviewed our institutional practice of CVL placement in children with newly diagnosed leukemia for quality assurance purposes and to provide further evidence to the ongoing controversy.
Methods: We retrospectively reviewed consecutive children at our institution diagnosed with leukemia and requiring CVL placement. Neutrophil counts, febrile episodes, documented infections, mechanical complications, thrombosis and CVL removal within the first 60 days of treatment were recorded.
Results: Between 2008-2013, 80 patients (49M/31F; median age 4.46 years) diagnosed with leukemia (61 ALL, 18 AML and 1 CML) underwent CVL placement at a median time of 1 day after diagnosis. The type of CVLs placed were port-a-caths (46), Broviacs (23) and PICCs (11). At time of CVL insertion, 39 (49%) patients had a neutrophil count < 500 (median ANC = 200). In the group of patient neutropenic at CVL placement 25 episodes of febrile neutropenia were described in 20 patients. Among these, 5 had documented infections (3 bacteremia, 2 tunnel infections). Two port-a-caths were removed for documented infection both at 22 days post-insertion. In the group of patients non-neutropenic at line placement, 38 episodes of febrile neutropenia were described in 20 patients. Among them, 3 had documented infections (bacteremia). One PICC was removed for thrombosis at 10 days post-diagnosis. There was no significant difference between the 2 groups in terms of number of lines removed ($p = 0.53$), documented infections ($p = 0.42$), or febrile neutropenic episodes ($p = 0.42$).
Conclusions: Our data indicate that there was no difference in febrile neutropenic episodes or line complications between neutropenic and non-neutropenic patients who had CVL placed at the time of diagnosis. Therefore, delaying Broviac or port-a-cath insertion to avoid infections or other line complications may not appear indicated for this population. The number of infections (tunnel infections), indicate vigilance is required after CVL placement.

P-313

SIGNIFICANT IMPACT OF TREATMENT SUBSIDY AND INTENSIFIED COUNSELLING STRATEGY ON THERAPY ABANDONMENT IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA – A PROSPECTIVE INTERVENTIONAL STUDY

N. Roy Moulik[1], K. Kulkarni[2], A. Kumar[1]

[1]Pediatrics, King George Medical University, Lucknow, India; [2]Pediatrics, IWK Health Centre, Halifax, Canada

Objectives: Treatment abandonment is a significant impediment to improvement in survival outcome of childhood ALL in developing nations with paucity of studies assessing impact of interventions to reduce abandonment. The present study was designed to assess the impact of treatment subsidy and counselling on the previously high abandonment rates in ALL at our centre.
Methods: Case records of ALL patients from 2007-2013 were assessed. The interventions evaluated were (i) intensified counselling and (ii) treatment subsidy. Treatment subsidy included (a) free supportive care drugs/antimicrobials from 2010, (b) free chemotherapy/radiotherapy from 2011 and (c) free investigations from 2012. Since 2010, support of a social worker and data manager obtained through a research scheme, allowed improved post-abandonment tracking and counselling. Intensified structured multi-stage pre-therapy counselling by multidisciplinary team of physicians and allied health workers (for disclosure of diagnosis, introduction of supportive services and therapy plan) with participatory and supportive family centred approach and periodic group counselling sessions (including physicians, social workers, survivors and families with children undergoing treatment) were introduced from 2010. Early and late abandonment were defined as abandonment before and after completion of induction respectively.

Results: There were 77/418 (18.2%) patients who abandoned therapy. The rate of abandonment after 2010 (post intervention) (9.1%,24/263) declined significantly ($p < 0.0001$) as compared to earlier (34.2%,53/155). Patients presenting before and after 2010 were comparable in their socio-economic and demographic characteristics. Most parents (72%) attending the group counselling sessions rated them as "very useful/a moral boost" to fight the disease. The post 2010 decline was significant in early (from 17.5% to 2.3%; $p < 0.0001$) as well as the late abandonment (from 16.7% to 6.8%, $p = 0.009$).
Conclusions: The present study is one of the first to prospectively demonstrate significant impact of subsidised treatment, intensified pre-therapy counselling as well as group counselling in reducing both early and late abandonment in ALL patients.

P-315

FUNCTIONAL INTERLEUKIN-6 AND CANCER-RELATED FATIGUE IN CHILDREN AND ADOLESCENTS WITH CANCER: EARLY FINDINGS

E.O. Bomfim[1], E. Anatriello[1], M.D.R. Nunes[1], L.C. Lopes Junior[1], R.A.G. Lima[1], L.C. Nascimento[1], M. Flória-Santos[1]

[1]Department of Maternal-Infant and Public Health Nursing, University of Sao Paulo, Ribeirão Preto, Brazil

Objectives: Persistent cancer-related fatigue (CRF) is one of the most troubling and prevalent side-effects of cancer and its tratement. Evidence suggests that cytokines might play a role in the etiology and mechanisms of cancer-associated symptoms, including fatigue. The objective of this study was to evaluate the associations among chemotherapy, proinflammatory cytokines (IL-6, TNF-α) and fatigue in children and adolescents with cancer.
Methods: A questionnaire was used to provide social-demographc information and clinical information (phase of treatment, week of treatment, medications in use, levels of hematocrit and hemoglobin lately performed). The 18-item PedsQL Multidimensional Fatigue Scale was used to measure fatigue in pediatric patients and a blood sample were collected. Flow cytometry was used to evaluate interleukin IL-6 and TNF-(levels using BD™ *Cytometric* Bead Array (*CBA*) flex kits from BD Bioscience. The entire procedure was performed following the instructions indicated by the manufacturer.
Results: A total of 39 blood collections were performed and the results showed heterogeneity among the different cancer types presented by our population, their chemotherapy protocols, subject's clinical characteristics and fatigue endpoints. The mean levels of IL-6 was 238, $2 \pm 375{,}1$ (MD ± SD), and regarding TNF-(levels were $215{,}2 \pm 368{,}6$ (MD ± SD). Weak to moderate correlations were observed among IL-6, TNF-(levels, and different degrees of fatigue. Diverse types of chemotherapy treatments might lead to varying presentations and severities of cytokine-induced fatigue. A number of confounding factors was identified to interfere with the expression levels of cytokines: subjects' cancer types, age, gender and psycho cognitive characteristics such as sleep patterns.
Conclusions: Our results suggest a role for proinflammatory cytokines in cancer-related fatigue. However, due our sample size our conclusions are limited. Methodological recommendations are proposed to improve future studies of this issue.

P-316

BRINGING CHEMOTHERAPY ADMINISTRATION IN TO THE DAYTIME TO IMPROVE EFFICIENCY AND PATIENT SAFETY: A QUALITY IMPROVEMENT INITIATIVE

K. Magee[1], J. Bates[1], M. Nanji[1], B. Gandhi[1], J. McLean[1], A. Clarke[1], Z. Swysten[1], S. Alexander[1]

[1]Oncology, The Hospital for Sick Children, Toronto, Canada

Objectives: The safety and efficiency of chemotherapy delivery is paramount to the of care of pediatric oncology patients. In 2011, in our large tertiary pediatric oncology center, 97% of all planned chemotherapy was initiated after 6pm on the day admission. Concerns were identified related to late in the day initiation of chemotherapy, including less availability healthcare professionals to address chemotherapy administration related questions and to respond to reactions as well as additional nursing handoffs. Two improvement processes were initiated to move the time of initiating chemotherapy to prior to 6pm.
Methods: The first initiative, a standardized pre-chemotherapy rapid hydration protocol, was implemented after a literature review and consensus building. The second initiative was developed following a value stream mapping process used to identify barriers to efficient admission and initiation of chemotherapy. A streamlined patient admission process was generated and then evaluated in five Plan-Study-Do-Act (PDSA) cycles.
Results: The pediatric oncology program at the Hospital for Sick Children has approximately 550 planned chemotherapy admissions/year. Baseline data found that 3% of children had their planned inpatient chemotherapy initiated before 6pm on the day of admission. The implementation of a rapid hydration protocol improved this to 26%. The five sequential PDSA cycles designed to evaluate and improve the admission and start of chemotherapy process demonstrated continuous improvement. With the 5th PDSA cycle, which included 109 admissions over 9 weeks, 79% of all patients had chemotherapy initiated before 6pm. An analysis of length of stay for similar chemotherapy pre and post implementation of rapid hydration and early admission strategies demonstrated an average a one day decrease per cycle.
Conclusions: Two QI initiatives were successful in improving the percentage of patients initiating their chemotherapy prior to 6pm from 3% to 79%. The success of the initiatives was dependent on engagement of front line staff in design and implementation of changes.

P-317

PROSPECTIVE TRACKING OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA WHO ABANDONED THERAPY: PARENTAL PERSPECTIVES, CAUSES AND IMPLICATIONS OF THERAPY ABANDONMENT FROM A TERTIARY CANCER CARE CENTRE

A. Kumar[1], N. Roy Moulik[1], K. Kulkarni[2], N. Verma[1]

[1]Pediatrics, King George Medical University, Lucknow, India; [2]Pediatrics, IWK Health Centre, Halifax, Canada

Objectives: Therapy abandonment is being increasingly recognised as a major contributor to inferior survival outcome in developing nations. Limited information is available on the reasons and outcome of treatment abandonment. The current study provides insights obtained by tracking families of patients with acute lymphoblastic leukemia (ALL) who abandoned therapy at a large tertiary care cancer center in India.
Methods: Case records of all children with ALL managed at King George's Medical University who abandoned therapy were retrieved after ethics approval. Families who abandoned therapy were subsequently tracked using predesigned and prestructured telephonic interviews.
Results: There were 77/418 (18.4%) children who registered from January 2007 to July 2013 abandoned treatment.17/77 (22.1%) refused treatment upfront. The rest abandoned during various phases of chemotherapy [induction 16 (20.7%), consolidation 10 (12.9%), interim-maintenance 11 (14.2%), delayed-intensification 8 (10.5%), or maintenance 15 (19.4%)]. Rate of illiteracy was significantly higher in mothers ($p = 0.008$) and fathers ($p < 0.0001$) of children who abandoned therapy. There were 39/77 (50.6%) families that could be tracked telephonically. Of these, 18 had expired, 13 were reported to be well at home (50% had abandoned after maintenance, and all after consolidation) and 8 came back for retreatment (4 with relapse). Parents cited financial constraint as the most common reason for abandonment. Perception of incurability was more common in families abandoning before completion of induction. Those abandoning later thought their children to be already cured of ALL. Survival outcome was better in 11/18 who completed induction therapy (median 180 days) before abandonment as compared to 7/18 who did not (70 days); $p = 0.000$ (Log-rank test).
Conclusions: Abandonment rates were highest before completion of induction (42.8%) followed by maintenance therapy (19.4%). Survival was worse in children who abandoned therapy before completion of induction. Illiteracy, financial constraints and false perceptions about cure contributed to abandonment in majority.

P-318

SHORT TERM EFFECTS ON PHYSICAL FITNESS OF A 12-WEEK EXERCISE AND PSYCHOSOCIAL TRAINING PROGRAM IN CHILDHOOD CANCER PATIENTS

K. Braam[1], E.M. Van Dijk-Lokkart[2], T. Takken[3], M.A. Veening[1], J. Huisman[4], M. Bierings[5], J.H.M. Merks[6], M.M. Van den Heuvel- Eibrink[7], G.J.L. Kaspers[1], E. Van Dulmen- den Broeder[1]

[1]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Medical Psychology, VU University Medical Center, Amsterdam, Netherlands; [3]Child Development and Exercise Center, Wilhelmina Children's Hospital UMC Utrecht, Utrecht, Netherlands; [4]Medical Psychology, Wilhelmina Children's Hospital UMC Utrecht, Utrecht, Netherlands; [5]Pediatric Oncology/Hematology, Wilhelmina Children's Hospital UMC Utrecht, Utrecht, Netherlands; [6]Pediatric Oncology, Emma Children's Hospital Academic medical Center, Amsterdam, Netherlands; [7]Pediatric Oncology/Hematology, Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands

Objectives: Evidence for exercise training interventions in childhood cancer patients (CCP) is limited. This study investigated the short-term physical fitness effects of a 12-week combined physical exercise and psychosocial training program, compared to usual care, in CCP.
Methods: In a multicentre randomized controlled trial CCP, 8-18 years old, on or within the first year after treatment, were invited to participate. Stratification included age, sex, solid tumour/haematological cancer and during/after treatment. Physical fitness was determined by cardiopulmonary exercise testing (peak oxygen uptake) at baseline (T0) and shortly after the intervention period (T1).
Results: Fifty-five CCP, aged 12.8 ± 3.1SD years (54% male) were included in the analyses; $N = 34$ were treated for a haematological malignancy. The median change scores in both treatment groups, corrected for baseline scores, on peak oxygen uptake (ml/kg/min) were not significantly different ($P = 0.78$); intervention group (INT): 0.04 (IQR: -0.09 – 0.10); control group (CTRL) 0.06 (IQR: -0.01 – 0.21). At T0 66% ($N = 16$) of the INT scored below -2 standard deviation (SD) of Dutch paediatric norm values peak oxygen uptake, and 33% within the low normal range (− 2 SD to 0); and for the CTRL this was 64% ($N = 20$) below the normal range, and 32% in the low normal range, plus one (3%) with above mean scores. At T1 three children of the INT and nine of the CTRL progressed from below the normal range to the

low normal range (INT change within groups: P = 0.08; CTRL change within groups: P = 0.001; change between groups: P = 0.15).
Conclusions: Both treatment groups showed little increase on maximal cardiopulmonary capacity. In contrast to the expected, the Intervention did not lead to short-term improvements. Factor analyses will be performed to further assess the study results.

P-319

PLASMA 25-HYDROXYCHOLECALCIFEROL BEFORE AND AFTER SUPPLEMENTATION IN PAEDIATRIC ONCOLOGY PATIENTS IN THE UK: A TIME-SERIES CROSS SECTIONAL STUDY

M.F.H. Brougham[1], D.C. Wilson[2], I. Paciarotti[3], R.F.H. Chin[2], C. Brand[4], J.M. McKenzie[3], R. Revuelta Iniesta[3]

[1]Haematology and Oncology, Royal Hospital for Sick Children, Edinburgh, United Kingdom; [2]Medicine and Veterinary Medicine, Child Life and Health University of Edinburgh, Edinburgh, United Kingdom; [3]Dietetics Nutrition and Biological Science, Queen Margaret University, Edinburgh, United Kingdom; [4]Accident and Emergency, Royal Hospital for Sick Children, Edinburgh, United Kingdom

Objectives: To assess the impact of micronutrient and macronutrient supplementation on plasma 25-hydroxycholecalciferol [25 (OH) D] in Scottish paediatric oncology patients
Methods: A time series case-control cross-sectional study was performed. Plasma 25 (OH) D was measured in healthy children (controls) and in paediatric oncology patients (cases). Children aged <18 years diagnosed and treated for cancer in SE Scotland were included. Childhood cancer was categorised into four groups: solid tumours, haematological malignancies, brain tumours and other associated-diagnoses. Macronutrient (enteral+/- parenteral nutrition) and micronutrient (vitamin D, multivitamins +/-macronutrient) supplementation was prescribed according to Subjective Global Assessment by the multidisciplinary team. 25 (OH) D deficiency was classified according to Endocrine Society Clinical Practice Guidelines-2011; suboptimal (50-75nmol/L), insufficient (25-50nmol/L) and deficient (<25nmol/L). Plasma 25 (OH) D was measured using the Automated Vitamin D Immunoassay in Glasgow Royal Infirmary Laboratory. Descriptive statistics and Wilcoxon test were performed.
Results: Plasma 25 (OH) D levels did not statistically differ between the 35 healthy-controls (median (IQR) 31 (15-56) nmol/L) and the 67 patients (median (IQR) 38 (20-61) nmol/L) at diagnosis. Children diagnosed with solid tumours had the highest prevalence of 25 (OH) D deficiency and insufficiency (26.4%) followed by haematological malignancies (19.4%). 40/67 patients had plasma 25 (OH) D measured before and after supplementation. Median (IQR) time between diagnosis and supplementation was 2.9 (0.9-6.3) months and between supplementation and the repeated 25 (OH) D measurement was 2.7 (1.6-6.7) months. At baseline, plasma 25 (OH) D was suboptimal in 23% of patients and insufficient or deficient in 62.5%. 17.5% received macronutrient supplementation alone; of these 43% remained below suboptimal and median (IQR) 25 (OH) D decreased from 77 (42-81) to 54 (19-89) nmol/L. Conversely, those additionally supplemented with micronutrients (82.5%) had a significant improvement in 25 (OH) D with median (IQR) increasing from 26.5 (15-37) to 65.5 (44-87) nmol/L ($p < 0.001$; r-0.7); however, 20% remained below suboptimal levels.
Conclusions: 25 (OH) D deficiency was highly prevalent, only improving following micronutrient supplementation. To optimise the 25 (OH) D status of this population, regular monitoring alongside appropriate supplementation should be incorporated into clinical practice.

P-320

VINCRISTINE INDUCED CRANIAL NEUROPATHY DURING THERAPY FOR PEDIATRIC MALIGNANCIES

R. Brennan[1], C. Nickols[2], A. Eftink[3], K. Strachota[3], K. Ness[4], I. Qaddoumi[1], M.W. Wilson[5], J. Thompson[6]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]School of Medicine, University of Missouri-Kansas City, Kansas City, USA; [3]Rehabilitation Services, St. Jude Children's Research Hospital, Memphis, USA; [4]Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [5]Ophthalmology, University of Tennessee Health Science Center, Memphis, USA; [6]Otolaryngology-Head and Neck Surgery, University of Tennessee Health Science Center, Memphis, USA

Objectives: Vincristine is widely used to treat pediatric cancer. However, the incidence and severity of vincristine-induced cranial neuropathies (jaw pain, facial weakness, vocal cord dysfunction, dysphagia, dysphonia, optic neuropathy) have not been well described.
Methods: Retrospective chart review of patients with hematologic and solid malignancies exposed to vincristine protocol-based therapy from 2000-2010 for evidence of symptomatic cranial neuropathies (CT-CAE grade 3 or 4 toxicity). Patients with cranial neuropathy at diagnosis or those receiving cranial radiation were excluded.
Results: Twenty-six of 1706 eligible subjects (1.5%) experienced cranial neuropathy. Toxicity was more common among solid malignancies (15/214, 7%). Fifteen were male and 24 were Caucasian with a median age of 4.9 years (range 0.2-20.8y). Diagnoses included acute lymphoblastic leukemia (n = 10), Ewing sarcoma (n = 5), rhabdomyosarcoma (n = 3), retinoblastoma (n = 3), Wilms tumor (n = 2), primitive neuroectodermal tumor (n = 2) and T-cell lymphoblastic lymphoma (n = 1). Dysphagia and jaw pain were most prevalent (9 each). Vocal cord (VC) dysfunction was noted in seven patients, and one of these required monitoring in the intensive care unit. Three of seven patients with swallowing dysfunction required intervention: dose reduction (n = 3), naso-gastric tube (n = 1), honey-thickened liquids (n = 1), and speech therapy (n = 3). Ten patients experienced multiple episodes of toxicity with re-exposure to vincristine therapy. Doses of vincristine were reduced, delayed or omitted in 14 of 18 patients with cranial neuropathy other than jaw pain. All patients recovered from toxicity within a median of 13 days (range 1-112).
Conclusions: This review, limited to protocol documentation, summarizes the reported incidence and morbidity of vincristine induced cranial neuropathy in children with cancer. Identification of patients at risk and early assessment of symptomatic patients is essential for therapy modifications and/or clinical intervention to ameliorate ongoing toxicity.

P-321

PREVENTION AND CONTROL STRATEGIES IMPLEMENTED AFTER A HEPATITIS B VIRUS OUTBREAK IN A PAEDIATRIC HAEMATOLOGY AND ONCOLOGY UNIT IN SOUTH AFRICA

A. Buchner[1], N.M. Du Plessis[2], T. Avenant[2], F.E. Omar[1], J. Vermeulen[1], S. Mayaphi[3], A.F. Haeri Mazanderani[3], D.T. Reynders[1]

[1]Paediatric Oncology Unit, University of Pretoria, Pretoria, South Africa; [2]Paediatric Infectious Diseases Unit, University of Pretoria, Pretoria, South Africa; [3]Department of Medical Virology, University of Pretoria, Pretoria, South Africa

Objectives: Hepatitis B remains an important public health concern in South Africa, despite the introduction of hepatitis B vaccination in 1995. Horizontal transmission of hepatitis B plays an important role in developing countries, and occurs mainly through body fluids like saliva. A recent nosocomial hepatitis B virus (HBV) outbreak involving 38 patients occurred in the paediatric haematology and oncology unit of a large tertiary hospital in South Africa. Possible breaches in standard infection control precautions, contaminated multiple-dose vials and transmission through body fluids were implicated. We describe subsequent infection prevention and control strategies that were implemented.
Methods: A series of strategies to minimise nosocomial transmission of HBV was implemented. Universal infection control precautions were emphasized, including strict hand washing and use of gloves. Further policies included eliminating use of multi-dose vials, cleaning and disinfecting reusable equipment, and preventing sharing of personal utensils. Testing for HBV infection and immunity on first admission and vaccinating patients with low levels of anti-HBs antibodies were put into practise. A full vaccination schedule is initiated in patients with anti-HBs titres <10 mIU/ml, and a booster HBV vaccine given to those patients with anti-HBs titres <100 mIU/ml. All patients attending the unit are routinely monitored every 3 months for declining levels of anti-HBs antibodies, and vaccinated if titres fall below 100 mIU/ml.
Results: Preventive measures that were introduced reduced the incidence of HBV infection significantly. Only one new case of HBV infection, suspected to be unrelated to the outbreak, has occurred in 13 months following implementation of these measures.
Conclusions: This outbreak highlights the importance of adequate infection prevention and control strategies in the prevention of nosocomial transmission of HBV. Paediatric haematology and oncology units should implement policies of active on-going surveillance for HBV infections and formulate clear guidelines for prevention and control thereof.

P-322

THE LAPAROSCOPIC ONCOLOGIC SURGICAL PATHOLOGY AND POSTOPERATIVE PAIN MANAGEMENT THROUGH INTRAPERITONEALLY LOCAL ANESTHETIC IN PEDIATRIC PATIENTS

D. Galante[1]

[1]University Department of Anesthesia and Intensive Care, University Hospital Ospedali Riuniti, Foggia, Italy

Objectives: Although pain after laparoscopic surgery is less intense than after open surgery, some patients still experience considerable discomfort in PICU. Postoperative pain after laparoscopic oncologic surgical pathology is an important limiting factor for a rapid return to normal activity. In our study we demonstrate the efficacy and safety of intraperitoneally administration of low doses of local anesthetics.
Methods: After IRB approval 46 patients ASA I-II, 9-14 years old, received in double-blinded fashion 40 ml of 0.9 normal saline solution (group S), ropivacaine 0.2% (group R), levobupivacaine 0.25% (group L). A standard general anesthesia was performed with propofol, cisatracurium, mixture of air/O_2/sevoflurane and remifentanil in continuous infusion. The anesthetic solutions were intraperitoneally administered at the end of laparoscopic procedure and repeated in PICU through an intraperitoneally catheter. Postoperative pain was assessed during the first 24h (T_0 end of surgery, T_1 2h, T_2 4h, T_3 8h, T_4 12h, T_5 24h) using visual analogic scale (VAS 0-10). Further anesthetic drug in postoperative time, if administered, were also recorded.
Results: Pain was less intense in the group L, particularly in T_0-T_4-T_5 and rescue analgesic drugs consumption was lower in this group respect ropivacaine and normal saline groups.

Postoperative pain at deep inspiration was higher in ropivacaine group respect levobupivacaine and normal saline groups.
Conclusions: The efficacy and safety of of intraperitoneally administration of local anesthetics has been well demonstrated in many studies but there is a lack of consensus regarding dose and concentration in laparoscopic oncologic surgical procedures. In our study we showed that the use of lower concentrations of local anesthetics led to significantly lower pain scores particularly for what concerns levobupivacaine.
References
1. Ioannidis O et al. Intraperitoneal administration of local anesthetics in laparoscopic surgery: pharmacological, anatomical, physiological and pathophysiological considerations. Minerva Chir 2013; 68:599-612

P-323

VARICELLA ZOSTER VIRUS INFECTIONS AFTER HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN CHILDREN WITH MALIGNANCY

L. Guerrini-Rousseau[1], F. Roquet[2], C. Dufour[3], C. Pasqualini[3], G. Goma[2], D. Valteau Couanet[3]

[1]Pédiatrie, Institute Gustave Roussy, villejuif, France; [2]Statistic, Institute Gustave Roussy, villejuif, France; [3]Pediatrie, Institute Gustave Roussy, villejuif, France

Objectives: Varicella zoster virus (VZV) infection is a frequent complication of High-Dose Chemotherapy (HDC) followed by Autologous Stem Cell Transplantation (ASCT) in children but few and conflicting data are published. The aim was to determine frequency, consequences and risk factors of VZV infection after ASCT in a large cohort and to adapt our therapeutic management.
Methods: We analyzed prospectively collected data of children treated with HDC and ASCT in the Pediatric Oncology Department of Institut Gustave Roussy and compared patients who developed or not VZV infection after intensive treatment.
Results: Between January 1985 and July 2009, 1056 children received HDC and ASCT without any VZV prophylactic treatment. Two hundred and thirty-six patients (22.3%) developed 244 VZV events (23.1%) consisted of 29 varicella (11.9%) and 215 herpes zoster (88.1%) including 8 double events. The median time of the VZV infection onset was 119.5 days post ASCT. Most (90.2%) of cases occurred within the first year. Evolution was simple with aciclovir treatment in 88% of the patients. Complications all resolved with treatment and consisted mainly in post VZV neuralgia. Age at date of the first ASCT ($p = 0.000003$), underlying disease ($p = 0.056$) and administration of a sequential HDC ($p = 0.0001$), were significant factors associated with VZV infection's occurrence in the whole population, defined by Fisher test. Logistic regression models after single course of HDC and ASCT showed both in univariate and multivariate analysis that age under 3 years at date of the first graft and Hodgkin lymphoma was associated with the occurrence of VZV infection.
Conclusions: This incidence of VZV infections compared to these found in literature and the favourable outcome with a curative treatment with aciclovir, confirm the absence of benefits of a prophylactic strategy in management of children who received HDC followed by ASCT.

P-324

RISK FACTORS TO DEVELOP A SEVERE INFECTION IN PEDIATRIC ONCOLOGY PATIENTS WITH FEBRILE NEUTROPENIA

C. Mata Fernández[1], B. santiago garcia[2], B. hernandez ruperez[2], R. herraiz[1], I. casas fleca[3], U. sautu[3], C. Garrido Colino[1], J. Huerta Aragonés[1], J. Saavedra Lozano[2]

[1]Sección Oncohematología Pediátrica, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Sección Enfermedades Infecciosas Pediátricas, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [3]Lab. Gripe y Virus Respiratorios, Instituto Salud Carlos III, Madrid, Spain

Objectives: To evaluate risk factors of suffering a "life-threatening " infection in myelosuppressed patients with a febrile neutropenia (FN) episode. Episodes were classified as high-risk febrile neutropenia (HRFN) or as low-risk febrile neutropenia (LRFN) and different approach was taken accordingly.
Methods: A study including all children prospectively enrolled with FN admitted to the hospital from October 2010 to December 2013 was performed. Patients were classified into two groups on admission:LRFN and HRFN, according to a previously implemented protocol based on physical examination, laboratory tests, medical and social background, bacterial or fungal cultures and a nasopharyngeal wash for 16 respiratory viruses (RV) using a multiple-PCR test.
Results: One hundred and thirty FN episodes were evaluated from 45 patients (56.2% female, median age 5.6 years[3.1-13.8]). Among them, 108 (83.1%) were classified and treated as HRFN and 22 (16.9%) as LRFN. LRFN episodes were associated to a higher number of RV infections (40.9% vs 25.7% in HRFN), and fewer episodes of Gram negative bacterial infections (0% vs 12%) ($p = 0.086$). Among all episodes evaluated, 44 (33,8%) were finally diagnosed as moderate or severe infection and 86/130 (66,2%) as mild ones. Trimethoprim-Sulfamethoxazole prophylaxis was associated to a lower incidence of moderate or severe infections (31.1% vs 63.6% in patients not receiving prophylaxis) ($p = 0,029$). Moderate to severe infectionswere related to a higher value of PCR (PCR$\geq$9 mg/dl at diagnosis or 48 h later; 54.5% vs 33.7% in mild infections) ($p = 0,022$), higher incidence of arterial hypotension (15.9% vs 2.3%;$p = 0.004$), higher value of procalcitonin (PCT$\geq$2 mg/dl:83.3% moderate to severe infection vs 16,7% mild infection ($p < 0,0001$). There was a higher incidence of moderate to severe infection in non-remission leukaemia and non-hodgkin lymphoma compared to other malignancies ($p = 0.003$)
Conclusions: Respiratory viral infections are associated to LRFN episodes. A higher CRP ($\geq$9mg/dl) and PCT ($\geq$2mg/dl), hypotension and chills and the absence of TMP-SMX prophylaxis may predict a moderate to severe infection and, therefore, the need for a HRFN management.

P-325

SEEKING FOR A SECOND OPINION IN PEDIATRIC ONCOLOGY

O. Mordechai[1], S. Tamir[1], M. Weyl-Ben-Arush[1]

[1]Pediatric Oncoloy, Rambam Health Care Campus, Haifa, Israel

Objectives: The number of second opinions consultations in pediatric oncology is increasing, yet the grounds on which families decide to seek a second opinion have been little studied. The goal of the study was to identify patients and families factors that appeared to contribute to a second opinion being sought.
Methods: 150 parents (75 from jewish origin, 75 from arab origin) of children with cancer recently treated in the Hematology Oncology Pediatric Department were interviewed. The questionnaire included epidemiologic data, details about the disease, timing of the second opinion consultation, reasons for seeking a second opinion and the risk/benefit of the consultation.
Results: 37 parents (25%) had sought a second opinion. There was a correlation between higher socio-economy status ($p = 0.003$) and number of educational years to the decision to go second opinion ($p = 0.001$). Most of the parents which went to second opinion also use the internet as a data source, but using the internet did not correlate with the decision ($p = 0.157$). There was no correlation between the age of parents, age of the sick child, family status, living place (urban vs. rural), the disease group, the stage of disease or using CAM (Complementary, Alternative, or Integrative Health) on the decision to go to second opinion. Non-religious parents went more to second opinion ($p = 0.003$). 26 of 75 Jewish parents go to second opinion, versus 11 of 75 Arab parents ($p = 0.031$).
Conclusions: Second opinions are an established part of health care, caregivers should express their empathy and take the initiative to discuss with parents their unmet needs, but sometimes even where ther is a successful communication, caregivers have to recognize that scientific evidence is not all that counts in the life of parents of a child with cancer that have to deal with a lifethreatening disease.

P-326

PSYCHOLOGICAL DISTRESS, CAUSATION BELIEFS AMONG CAREGIVERS OF CHILDREN WITH CANCERS IN A DEVELOPING COUNTRY: INFLUENCE ON PATHWAY TO CARE AND TREATMENT UPTAKE

A. Olagunju[1], O. Aina[1], T. Fadipe[1], T. Oyelohunnu[1], F. Sarimiye[2], T. Olagunju[3]

[1]Department of Neuropsychiatry (psychooncology), Lagos University Teaching Hospital/ College of Medicine University of Lagos, Lagos, Nigeria; [2]Department of Radiotherapy, University College Hospital, Ibadan, Nigeria; [3]HIV/Infectious Diseses Hospital, Health Service Commission, Lagos, Nigeria

Objectives: The caregivers of children with cancers often play significant roles in making decisions about pathway to care and treatment related issues. The treatment related decisons may be influenced by caregivers' belief about cancer causation and their emotional wellbeing. This study aims to investigate psychological distress and belief about causation of cancers in a developing context.
Methods: The study participants were made up of one hundred caregivers of children with histological diagnoses of cancers attending a tertiary health facility in West Africa. Eligible participants, who gave informed consent were interviewed with designed questionnaire to elicit socio-demographic profile, treatment related variables as well as pathway to care; subsequently this was followed by administration of General Health Questionnaire (GHQ-12) to ascertain psycholoical distress based on cut-off score of 3. Data Analyses was done using SPSS-17.
Results: The mean age of the caregiver was 49.02 ± 0.12, and female gender was predominant 83 (83.0%). About 42 (42.0%) caregivers had psychological distress based on GHQ-12 and upto 66 (66.0%) reported positive belief about preternatural/spiritual causation of cancers. Similarly, 70 (70.0%) had opted for one form of alternative care (spiritual deliverance, prayers, herbal preparation among others) before presenting in the hospital. Good treatment uptake correlated positively with level of education, being employed and good social support from family members ($p>0.05$). However, financial constraint and preternatural causation belief correlated negatively with good treatment uptake ($p>0.05$).
Conclusions: The care of children with cancer is significantly impacted by caregiers' related factors. Psychosocial support for caregivers, promotion of awareness campaign and targeted cancers education programs as well as cancer treatment issues are indicated.

P-327

SHARED CARE IN PAEDIATRIC ONCOLOGY: A MANAGED AND NEGOTIATED PARTNERSHIP OF TERTIARY AND SATELLITE HEALTH CARE PROVIDERS

A. Punnett[1], M. Greenberg[1], M.A. Martimianakis[2]

[1]Paediatric Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Paediatrics, The Hospital for Sick Children, Toronto, Canada

Objectives: Vast geography and limited human health resources dictate a need for collaborative care in the management of paediatric cancer patients in Canada. There is a lack of conceptual and empirical research to inform best practice in establishing and enhancing interprofessional and inter-organizational collaboration (Gagliardi, 2011). In particular, the complexity of relationships within and between professions is poorly understood (D'Amour, 2005). This study sought to examine the nature of these relational dynamics in an established paediatric oncology shared care program.
Methods: The Paediatric Oncology Group of Ontario (POGO) administers a formal satellite care program in Ontario. We conducted In-depth interviews of purposively sampled tertiary and satellite health practitioners to examine knowledge, skills and attitudes required for a successful collaborative care program. Interviews were audio- recorded, transcribed and inductively analyzed to generate emerging themes related to perceptions of interprofessional and inter-organizational interactions. Witz's model of professional closure strategies (1992) was used to explore and contextualize perceived relational dynamics.
Results: This study was approved through the local REBs of each participating institution. Twenty-three interviews (10 nurses, 3 nurse practitioners, 10 physicians) were conducted at the largest tertiary centre (SickKids) and the 6 provincial satellite centres. Unanimous commitment to the program appeared to be pivotal to navigating a number of inherent tensions identified within the working arrangement: 1) the partnership between tertiary and satellite centres is both managed and negotiated, 2) established guidelines are both necessary and overly restrictive, 3) tertiary providers balance loss of control with an evolving job profile and increasing access to tertiary services, 4) satellite providers balance increased job satisfaction with competing responsibilities and conflicting organizational agendas.
Conclusions: Providers within the shared care program navigate complex professional and organizational relationships while both maintaining and redefining traditional professional boundaries. Ongoing management and negotiation of the partnership is vial to the success and longevity of the program.

P-328

BREAST MILK FROM IMMUNE THROMBOCYTOPENIC MOTHERS CONTAINS ANTI PLATELET ANTIBODIES THAT ARE ASSOCIATED WITH PERSISTENT THROMBOCYTOPENIA IN NEONATES

N. Sharon[1], H. Hauschner[2], N. Rosenberg[2], U. Seligsohn[2], R. Mendelsohn[1]

[1]Pediatrics, Laniado Hospital, Netanya, Israel; [2]The Amalia Biron Research Institute of Thrombosis and Hemostasis, Chaim Sheba Medical Center Tel Hashomer, Ramat Gan, Israel

Objectives: Maternal immune thrombocytopenic purpura (ITP) accounts for 5% of all cases of pregnancy associated thrombocytopenia and is a common cause of neonatal thrombocytopenia. One of the common mechanism involves transfer of IgG autoantibodies against platelet receptors which are found in the blood samples of affected patients. The neonatal thrombocytopenia usually subsides within 2-3 months. The autoantibodies are often of the IgG type and therefore can cross the placenta and cause fetal and/or neonatal thrombocytopenia. Recently we observed persistence of neonatal ITP which rapidly disappeared following discontinuation of breast feeding. The aim of our current work was to discern whether breast milk of mothers with ITP contains anti-platelet antibodies and whether these antibodies may be the cause for persistent neonatal ITP.
Methods: Breast milk samples were collected from 14 women with ITP. Seven of them were thrombocytopenic during pregnancy and their neonates also had thrombocytopenia. The remaining 7 mothers had a history of ITP but not during the current pregnancy, and neither did their neonates. As controls, breast milk from 10 healthy women was also examinied. The presence of anti-platelet antibodies were evaluated by incubating washed platelets from healthy donors with breast milk or extracted milk – Ig. The type of immune globulin was defined by flow cytometry using fluorescence conjugated anti-human IgA, IgG or total Ig antibodies.
Results: In four women with active ITP with accompanying neonates with thrombocytopenia, high levels of anti-platelet IgA antibodies were observed. In the three remaining women with active ITP and 7 with a history of ITP, no or minimal concentraions of anti-platelet antibodies were detected. No anti-platlet antibodies were found in breast milk of healthy women.
Conclusions: This is the first evidence that transfer of anti-platelet antibodies from mothers with ITP to their infants via breastfeeding was associated with persistent thrombocytopenic neonates.

P-329

THE ROLE OF PRIMARY CARE IN THE MANAGEMENT OF TEENAGERS AND YOUNG ADULTS (TYA) WITH CANCER: A PRELIMINARY STUDY

M. Stevens[1], M. Ridd[2], K. Dixon[2], A. Heawood[2], A. Cameron[3]

[1]On Target, Bristol Royal Hospital for Children, Bristol, United Kingdom; [2]Social and Community Medicine, University of Bristol, Bristol, United Kingdom; [3]TYA Cancer Service, University Hospitals Bristol NHS Trust, Bristol, United Kingdom

Objectives: Cancer in TYA is rare and primary care professionals may be unfamiliar with patient needs. With improved survival, the majority of TYA will return to primary care after completion of treatment but limited involvement of family (general) practitioners (FP) with TYA pre-diagnosis and during treatment, and potential perceptions of diagnostic delay, may impact the relationship between FP and patient/family to create barriers for effective aftercare. The Bristol On Target programme showed >40% TYA specifically wanted information about what to expect from FP during and after treatment. We explored FP experiences of TYA with cancer to understand barriers and to inform strategies for their increased involvement.
Methods: FP of recently diagnosed 15-24 year old with cancer were invited to an in-depth interview. A topic guide was developed with TYA clinicians and interviews were audio-recorded and transcribed verbatim. Of 56 FP contacted, 11 participated before interviews achieved theme saturation. Data were analysed using the constant comparative method.
Results: Analysis showed that FP mostly contributed to initial referral, emotional support and on-going care for un-related/intercurrent medical problems. Lack of knowledge, prolonged periods of hospital treatment, incomplete/ineffective communication and FP fear of burdening patients with additional input, were common reasons offered for limited involvement, especially during treatment.
Conclusions: These results align with general findings from cancer survivorship research and confirm that transition from specialist cancer care to care by FP may be difficult for both patient and FP. Effective communication during/after treatment and information about TYA cancer for FP at diagnosis could help clarify expectations for both FP and patients, prevent disruption of the patient:primary care relationship, and assist FP to contribute to care in partnership with TYA cancer teams. A strategy to promote engagement between TYA and FP early after diagnosis is under development as part of the On Target programme.

SURGERY (IPSO)

P-330

ANALYSIS OF MAJOR SURGICAL PROCEDURE IN ONCOLOGIC PEDIATRIC PATIENTS WITH COAGULATION DISORDERS.

F. Albanez Souza[1], E. Meis[2], E. Machado[2], A. Ikeda[3], M. Perini[4], S. Coelho[1], A. Favre[1], T. Cortez[5], R. Vianna Carvalho[1]

[1]Pediatric Surgery, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [2]Coagulation Committee, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [3]Pediatric Oncology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [4]Physical Therapy Service, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [5]Anesthesiology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil

Objectives: Coagulation disorders are found in many patients with neoplasm. Risk factors to bleeding and/or thrombosis are augmented in patients who need a surgical procedure. The objective of these report is to analyze the frequency of these risk factors and preoperative management in patients with abdominal neoplasm who requires major surgical treatment.
Methods: Retrospective study in patients submitted to major surgical abdominal neoplasm resection in National Cancer Institution, in the period between 2011 and 2013, under 16 years old. The patients who had suspicion of coagulation disorders (bleeding previous history, laboratory coagulation disorders) were evaluated by Coagulation Committee. Non hematological patients were enrolled in this study.
Results: In this three years our pediatric oncology surgical service performed 1183 surgical procedures. 87 patients were evaluated by Coagulation Committe, 22 were submitted to major surgical treatment. The histopatological diagnosis were: neuroblastoma (4), Wilms tumor (7), germinative (3), Ewing neoplasm (2), PNET (2), desmoplastic tumor (1), paraganglioma (1), hepatoblastoma (1), soft tissue sarcoma (1). The patients were followed by specialized coagulation team, before and after surgical procedures. The initial protocol of investigation by the Coagulation Committee was to evaluate lupus anticoagulant (LAC), protein C, antithrombin III, D-Dimer, V, VII, VIII, IX, X, XI factors. We followed the Institutional Protocol to prevent bleeding and/or thrombosis, specific for each patient. No major postoperative complications have occurred.
Conclusions: Its important the access to a specialized coagulation team for the patients with coagulation disorders, specially for pediatric oncology patients. With adequate management of these patients major complications can be reduced.

P-331

SCF EXPRESSION IS ASSOCIATED WITH UNFAVORABLE PROGNOSIS IN NEUROBLASTOMA

R. Kapoor[1], S. Agarwala[1], V.K. Iyer[2], S.N. Dwivedi[3], P.P. Chattopadhyay[4], S. Ali[5], A.K. Dinda[2], M. Bajpai[1], D.K. Gupta[1], V. Bhatnagar[1]

[1]Pediatric Surgery, All India Institute of Medical Sciences, Delhi, India; [2]Pathology, All India Institute of Medical Sciences, Delhi, India; [3]Biostatistics, All India Institute of Medical

Sciences, Delhi, India; [4]Biochemistry, All India Institute of Medical Sciences, Delhi, India; [5]Molecular and Genetics Laboratory, National Institute of Immunology, Delhi, India

Objectives: To determine the prevalence and the prognostic significance of SCF expression in neuroblastoma.
Methods: SCF expression was investigated by immunohistochemistry. Univariable and multivariable analysis (Cox regression) and outcome analysis (Kaplan Meier) was done for 2-year overall survival (OS) and 1-year event-free survival (EFS) in relation to the SCF expression. Death, recurrence, progression and non-response were considered as events.
Results: Of the 91 cases, there were 67 (74%) ≥12 months of age, 62 (68%) adrenal, 42 (46%) stage-4. Histopathology upfront, was done in 54 (59%), of which 39 (72%) were unfavorable histology (UFH) tumors. SCF expression was observed in 21 (23%) of the 91 tumors. SCF expression was more commonly observed in stage-4 as compared to non-stag-4 (36% vs. 12%; $p = 0.012$) and among high grade than low grade (36% vs.0%; $p = 0.011$). No response or progressive disease was commoner in those with SCF expression (62% vs.28%; odds-ratio 4.19 (95%CI; 1.5-11.7); $p = 0.008$). Five of 21 (24%) with SCF expression died and 17 (80%) had events giving a poorer OS (29% vs. 85%; $p = 0.0046$) and EFS (7% vs. 56%; $p = 0.0001$) for those with SCF expression. Of 17 (27%) patients with SCF expression in the adrenal location, 4 (24%) died and 14 (82%) had an event giving poorer OS (21% vs.80%; $p = 0.025$) and EFS (45% vs.66%; $p = 0.0007$) for those with SCF expression. Among 42 stage-4 patients, 15 (36%) had SCF expression and among these 5 (33%) died and all 15 (100%) had an event giving poorer OS (17% vs.77%; $p = 0.02$) and EFS (40% vs.43%; $p = 0.05$) for those with SCF expression. Thirteen among the 39 (33%) with UFH had SCF expression and among these 2 (13%) died 11 (85%) had an event. The EFS (38% vs.58%; $p = 0.04$) was significantly worse for those UFH with SCF expression.
Conclusions: SCF is expressed in 23% of the neuroblastomas and its expression is an independent prognostic variable responsible for shorter event-free survival [hazard-ratio 2.48 (95%CI; 1.11-5.52); $p = 0.026$]. This difference in outcome is especially marked in those with age ≥12, stage4, adrenal and unfavourable histology tumors.

P-332

CLINICAL APPLICATION OF MULTIPARAMETER FLOW CYTOMETRY TO DIAGNOSTIC SCREENING AND CLASSIFICATION OF PEDIATRIC SOLID TUMORS

C. Ferreira-Facio[1], C. Milito[2], V. Botafogo[1], M. Fontana[1], L. S. Thiago[3], E. Oliveira[1], A. da Rocha-Filho[4], F. Werneck[4], D. Forny[1], S. Dekermacher[5], A.P. Azambuja[6], S.E. Ferman[7], P.A. Silvestre de Faria[7], M. Land[1], A. Orfao[8], E. Sobral da Costa[1]

[1]Pediatric Department IPPMG, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; [2]Department of Pathology School of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; [3]Pediatric Hematology and Oncology, Brazilian National Cancer Institute, Rio de Janeiro, Brazil; [4]Pediatric Hematology and Oncology, Servidores do Estado Hospital, Rio de Janeiro, Brazil; [5]Pediatric Surgery, Servidores do Estado Hospital, Rio de Janeiro, Brazil; [6]Pediatric Hematology and Oncology, Federal University of Parana, Curitiba, Brazil; [7]Pediatric Oncology, Brazilian National Cancer Institute, Rio de Janeiro, Brazil; [8]Flow Cytometry Service, Universidad de Salamanca, Salamanca, Spain

Objectives: Multiparameter flow cytometry (MFC) immunophenotyping has proven to be essential for rapid diagnosis, classification and monitoring of therapy in most hematological malignancies, including pediatric leukemias and lymphomas. Conversely, it remains a research tool for pediatric solid tumors. Here we evaluate a MFC panel of markers for the diagnostic screening and classification of those tumors. The proposed strategy aims at differential diagnosis between tumor *vs* reactive samples, hematological *vs* non-hematological malignancies, and the subclassification of pediatric solid tumors.
Methods: A total of 125 samples from 91 patients suspicious of pediatric cancer – 51 males (56%) and 40 females (44%) were analyzed by MFC panel following a gating strategy analysis for identification of suspicious tumor cells and further characterization into hematopoietic *vs* non-hematopoietic solid tumor. To establish the statistical significance of differences observed between groups, the Mann-Whitney U test was used (continuous variables; SPSS software program, version 18.0, SPSS Inc., Chicago, IL, USA).
Results: Seventy-two patients (79%) had cancer, 31 of whom (43%) showed metastatic disease; the remaining 19 children (21%) had inflammatory/reactive diseases. The overall concordance rate between MFC analysis and histopathological exam was of 92.2% (diagnostic samples), with 100% agreement for all reactive/inflammatory, with only 9 false negative cases diagnosed as Hodgkin lymphoma, Anaplastic Lymphoma and a metastatic nasopharyngeal carcinoma in lymph node. Moreover, clear discrimination between samples infiltrated by hematopoietic vs. non-hematopoietic tumor cells was systematically achieved. Distinct subtypes of solid tumors showed different protein expression profiles, allowing the differential diagnosis of neuroblastoma (CD56hi/GD2+/CD81hi), primitive neuroectodermal tumors (CD271hi/CD99+), Wilms tumors (over 1 cell population), rhabdomyosarcoma (nuMYOD1+/nuMyogenin+), carcinomas (CD45-/EpCAM+), germ cell tumors (CD56+/CD45-/NG2+/CD10+) and eventually hemangiopericytomas (CD45-/CD34+).
Conclusions: In summary, our results show that MFC provides fast and useful complementary data to routine histopathology for the diagnostic screening and classification of pediatric cancer.

P-333

ACUTE SURGICAL COMPLICATIONS OF ABDOMINAL LYMPHOMA: A STUDY AMONG EGYPTIAN CHILDREN OVER A PERIOD OF 20 YEARS

Y. Saad-eldin Sadek[1]

[1]Pediatric Surgery, University of Alexandria, Alexandria, Egypt

Objectives: To report and study cases of abdominal lymphoma presented with acute surgical abdomen.
Methods: All children with abdominal lymphoma treated in the Pediatric Surgery & Pediatric Oncology Departments, University of Alexandria, Egypt over a period of 20 years were reported and sudied concerning their demographic data, clinical presentation, pathological varieties, staging and the management modalities. Type of surgery and survival were recorded.
Results: A total number of 121 cases of abdominal lymphoma were were reported over a period of 20 years with a median age 5.45 years. Non-Hodgikin's lymphoma was encountered in 103 cases (85%), with lymphoblastic lymphoma was the most common followed by Burkitt's lymphoma. Primary intestinal lymphoma was encountered in 32 cases. Twenty seven of these were presented with acute surgical abdomen as follows: intussusception (19 cases), volvulus (5 cases) and intestinal perforation (3 cases). These cases were treated by right ileocaecal resection in 23 cases and ileal resection in 4 cases. All cases were treated by chemotherapy as a definitive therapy. Two years survival of all cases were correlated to the stage as follows: stage I (70.5%), stage II (50%), stage III (16.2%), and stage IV (0%).
Conclusions: Primary intestinal lymphoma in Egyptian children is a special entity of abdominal lymphoma. It is more liable to complicate and present with acute surgical abdomen. Surgey is indicated as an emergency for the acute surgical abdomen followed by chemotherapy as the definitive therapy.

P-334

ROLE OF PET- CT IN STAGING OF PEDIATRIC ROUND CELL TUMORS. CAN IT ELIMINATE THE NEED FOR BONE MARROW BIOPSY?

N. Singhal[1], S. Qureshi[2], G. Chinnaswami[3], S. Kembhavi[4], V. Rangarajan[5], S. Desai[6], S. Shah[5], P. Kurkure[3], A. Agrawal[7], M. Bhagat[8]

[1]Surgical Oncology, TATA Memorial Hospital, Mumbai, India; [2]Pediatric Surgical Oncology, TATA Memorial Hospital, Mumbai, India; [3]Pediatric Oncology, TATA Memorial Hospital, Mumbai, India; [4]Radiology, TATA Memorial Hospital, Mumbai, India; [5]Nuclear Medicine, TATA Memorial Hospital, Mumbai, India; [6]Pathology, TATA Memorial Hospital, Mumbai, India; [7]Nuclear Medicine, TATA Memorial Hospital, Mumbai, India; [8]Pediatric Surgery, TATA Memorial Hospital, Mumbai, India

Objectives: To evaluate the efficacy of PET-CT in detection of bone marrow metastases in pediatric round cell tumors (Neuroblastoma, Rhabdomyosarcoma) and to compare it with the gold standard method of bilateral bone marrow biopsy.
Also to compare the results of bilateral marrow biopsy with unilateral biopsy to determine whether unilateral biopsy is sufficient for detection of bone marrow metastases.
Methods: This is a prospective observational study and includes all treatment naive patients with histologically confirmed diagnoses of Neuroblastoma or Rhabdomyosarcoma, attending pediatric surgery outpatient department in our hospital. All the patients underwent a routine staging workup along with PET-CT. For evaluating the results of unilateral versus bilateral biopsy, findings of right sided biopsy were taken as a baseline for comparison for each patient. In cases of focal marrow positivity (PET showing a positive marrow site other than iliac crest) or discordance in results of PET-CT and bone marrow biopsy, presence of marrow metastases was confirmed with MRI scan of that region.
Results: At the time of abstract submission, of the 21 patients evaluated, there were 12 cases of Rhabdomyosarcoma and 9 cases of Neuroblastoma. There was no evidence of bone marrow metastases in 18 patients on both PET scan and bone marrow biopsy. Thus the negative predictive value of PET-CT for bone marrow metastases was 100% in our study. PET-CT detected marrow metastases in 3 patients, of these two patients also had positive bone marrow biopsy. MRI done for one patient with negative bone marrow biopsy confirmed the findings of PET scan. Of the two patients with positive bone marrow biopsy, one patient had unilaterally positive bone marrow.
Conclusions: PET-CT can obviate the need for bone marrow biopsy and its associated morbidities. Also it has the potential to be a single investigation for the staging work up of this group of patients.

P-335

OUTCOME OF ICE CHEMOTHERAPY AND SURGICAL RESECTION FOR THE TREATMENT OF RECURRENT WILMS TUMORS.

S. Agarwala[1], A. Bhatia[1], S. Bakhshi[2], M. Srinivas[1], M. Bajpai[1], M. Jana[3], S. Thulkar[3], S. Pathy[4], D.K. Gupta[1], V. Bhatnagar[1]

[1]Pediatric Surgery, All India Institute of Medical Sciences, Delhi, India; [2]Medical Oncology, BRAIRCH All India Institute of Medical Sciences, Delhi, India; [3]Radiology, BRAIRCH All

India Institute of Medical Sciences, Delhi, India; [4]Radiotherapy, BRAIRCH All India Institute of Medical Sciences, Delhi, India

Objectives: To evaluate the effectiveness of ICE (Ifosphamide+Carboplatin+Etoposide) as a salvage therapy in recurrent Wilms tumor (RWT).
Methods: Prospectively maintained data of patients of recurrent Wilms tumor managed in the pediatric solid tumor clinic from August 1999 through December 2013 was analyzed. Efficacy of ICE as a salvage regime as compared to other regimen using statistical program STATA 9. Significant difference was taken as $p < 0.05$. Kaplan Meier survival estimates for 2-year overall survival (OS) was done. Initial staging was done as per NWTS-5 protocol and treatment was done as per the AIIMS-WT-99 protocol.
Results: Of the 241 new cases of WT treated during this period, 41 (17%) recurred (40 favorable histology, 1 diffuse anaplasia). The recurrence was following treatment for stage 1WT in 3 (initially treated with Dactinomycin+Vincristin), stage 3 in 20, stage 4 in 11 and stage 5 in 7 (all other stages following 3 drugs [Dactinomycin + Vincristin+ Doxorubicin] + RT). The recurrence was bilateral in 3, local in 10 and metastatic in 28. While 11 (27%) opted for no further treatment, 2 had only re-resection (both for local recurrence following treatment for bilateral disease) and 28 received alternate chemotherapy (21 ICE;7 other protocols). Overall 18 patients underwent surgical resection for the recurrence (either upfront[2] or following chemotherapy[16]). Of the 21 who received ICE, 7 were alive giving an OS of 36% (95CI 16-57) while among the non-ICE group 11 survived (OS 49%; 95CI 22-72). The odds of survival among the non-ICE group was greater (OR 2.44; 95CI 69-86). Seven of 21 (33%) in the ICE group and 4 of 7 (57%) who received other protocols achieved disease free status.
Conclusions: One-fourth patients opted for no further treatment. ICE salvage regime resulted in disease free status far less frequently then by the other protocols and achieved OS of 36% in these intensely pretreated patients.

P-336

LONG-TERM RECURRENCES IN WILMS TUMOR: SINGLE CENTER SERIES

A. Crocoli[1], A. Serra[2], M.A. De Ioris[2], M.D. De Pasquale[2], C. Martucci[1], A. Cacchione[2], F. Diomedi Camassei[3], A.E. Tozzi[4], F. Locatelli[2], A.E. Inserra[1]

[1]Surgery, Bambino Gesù Children's Hospital - IRCCS, Rome, Italy; [2]Hematology/Oncology, Bambino Gesù Children's Hospital - IRCCS, Rome, Italy; [3]Pathology, Bambino Gesù Children's Hospital - IRCCS, Rome, Italy; [4]Epidemiology, Bambino Gesù Children's Hospital - IRCCS, Rome, Italy

Objectives: Wilms tumor (WT) is the most common renal tumor in children with an excellent outcome. Relapses occurred generally before two years from diagnosis. The aim of the study is to evaluate the rate and characteristics of long-term recurrence (LTR) in a single institution experience.
Methods: The Institutional WT register was checked in order to identify patients who presented a relapse after 3 years from diagnosis from 1999 to march 2011. Kaplan-Meier method was used for estimating overall survival (OS) and progression free survival (PFS) curve. Patients were treated according to SIOP 93-01 and SIOP 2001 Protocols.
Results: 76 patients were diagnosed during the study period. 5 years OS and PFS were 93% and 81%, respectively. Relapses occurred in 16 patients at a median time of 7,5 months from diagnosis (range 2-82 months), 56% before 12 months. In this series, a bilateral kidney involvement occurred in 16 (22%) patients while a metastatic spread in 9 (12%). Out of 16 recurrences, 3 occurred locally at 82, 76 and 51 months from the onset. Two LTRs occurred in patients with bilateral disease at onset. The later patient presented monolateral WT who underwent a nephron-sparing surgery at diagnosis because of dominant polycystic kidney disease. This patient presented a second locally recurrence at 97 months and a third metastatic spread at 122 months from diagnosis. Three LTRs are alive in complete remission at 174, 134 and 130 months from diagnosis.
Conclusions: LTRs are rare events observed in less than 4% of population but representing about 20% of relapses. These are mostly local and often associated with a bilateral tumor at onset. Notably, in this series we reported a bilateral occurrence in 22% of patients. Further analysis may confirm an increased risk of LTRs in bilateral disease as suggested by our experience. However, a prolonged follow up with ultrasonographic scans should be recommended in bilateral disease.

P-337

DIARRHEAL NEUROBLASTOMA: DIAGNOSIS AND TREATMENT

H. Wang[1]

[1]Pediatric Surgical Oncology, Beijing Childrens' Hospital CMU, Beijing, China

Objectives: The neuroblastoma cases with diarrhea as the main symptom, namely diarrheal neuroblastoma, are quite rare. Consequently, the experience for diagnosis and treatment of this disease is limited. Hereby to report a series of 6 cases of diarrheal neuroblastoma in our institute.
Methods: Six cases of diarrheal neuroblastoma from January1996 to December 2006 were analysed retrospectively. Clinicopathological features were summarized. Pathology confirmed the diagnosis. Vasoactive intestinal peptide (VIP) were detected with immunohistochemistry in the tumor tissue.
Results: Patients aged 11 to 30 months. The period from diarrhea begining to diagnosis was four months up to 1 year. Stool was loose or watery, 3-8 times each day with routine faece tests normal. Diarrhea was the first symptom and lasted permanently in five cases, and abdominal tumors were found by ultrasound finally. Two cases underwent the preoperative chemotherapy, of whom diarrhea stopped after chemotherapy in one and after surgery in the other. Three cases accepted upfront surgery and the diarrhea ended postoperation. One patient with persistent diarrhea and refractory electrolyte imbalance and passed away in the end. For one patient, whose preoperative serum potassium was 2.8mmol / L, had not been cured to normal level, cardiac arrest happened during the operation, at the exact time potassium was 1.8mmol/L. The immunohistochemical staining of VIP showed positive in the tumor tissue of 6 patients.
Conclusions: Persistent and unreasonable diarrhea may predict neuroblastoma. The metabolic disorder of the diarrheal neuroblastoma were chronic dehydration, intractable hypokalemia, chronic malnutrition and growth stagnation. Even if the preoperative serum potassium had been corrected normal, hypokalemia would still occur in the operation, which could be lethal.

P-338

ROLE OF SURGERY IN PEDIATRIC NEUTROPENIC CANCER PATIENTS PRESENTING WITH GASTROINTESTINAL OBSTRUCTION OR PERFORATION

G. Ahmed[1], A. Yones[2], M. Elshafiey[2], H. Hafez[3], Y. Madeny[3], R. Khedr[3], H. Taha[4], N. Elkinaai[4]

[1]Surgery, Children's Cancer Hospital Egypt, cairo, Egypt; [2]Surgery, NCI Egypt and Children's Cancer Hospital Egypt, cairo, Egypt; [3]Pediatric oncology, NCI Egypt and Children's Cancer Hospital Egypt, cairo, Egypt; [4]Pathology, NCI Egypt and Children's Cancer Hospital Egypt, cairo, Egypt

Objectives: Was to evaluate the causes, and impact of surgical intervention on the outcome of gastrointestinal obstruction or perforation in pediatric neutropenic cancer patients post chemotherapy
Methods: This is a retrospective study that included all neutropenic pediatric patients following chemotherapy who were referred to surgery between Jan. 2008 to Dec. 2013 because of intestinal obstruction or perforation unrelated to the primary malignancy. Clinical, radiological, intraoperative findings and outcome were evaluated
Results: Exploration was done in nine cases (eight leukemia &one Retinoblastoma), because of obstruction (seven cases) and perforation (two cases). Pathologically proven mucormycosis was found in five patients (55%), three of them with intestinal obstruction and two patients with stomach perforation. On exploration the three obstructed cases had patches of gangrenous loops adherent together and resection anastomosis was done. On the cases with gastric perforation the edges were non-viable, trimming of the edge and primary repair augmented with omental patch was done in one case and partial gastrectomy on the other case. In the remaining four cases, the cause of obstruction was due to fibrous band in two patients, intussusception in one patient, and non-specific inflammation in the last one. There was no specific clinical or radiologic presentation for mucormycosis. Two out of five cases died from progressive infection and inflammation and the other three patients recovered on postoperative maintenance antifungal therapy
Conclusions: Early and prompt surgical intervention in neutropenic pediatric oncologic patients with gastrointestinal obstruction or perforation may be life saving, although the patients' general condition may render it risky. Mucormycosis is not uncommon diagnosis in pediatric neutopenic patients have gastrointestinal obstruction or perforation, thus it should be kept in mind and appropriate antifungal agent should start as early as possible to prevent further complications.

P-339

LAPAROSCOPIC RESECTION OF THE PANCREAS IN CHILDREN WITH SOLID PSEUDOPAPILLARY TUMORS

D. Rybakova[1], P. Kerimov[1], A. Kazantcev[1], M. Rubansky[1]

[1]children oncology, Federal State Budgetary Institution «N.N. Blokhin Russian Cancer Research Center» under the Russian Academy of Medical Sciences, Moscow, Russia

Objectives: Development rational surgery for solid pseudopapillary tumor (SPT) of the pancreas and implementation of Endosurgery.
Methods: Five children with SPT were operated since 2011 to 2013. We analyzed clinical data, operation options and results of treatment.
Results: All patients were females age from 9 to 15 years (median 12y.o.). Course of the disease asymptomatic, however, was observed in 1 child pain in the epigastric region. Localization tumors in pancreas: in the tail. The size: 5,5 – 7,4 sm (M 6,5 sm). 5 children underwent laparoscopic distal pancreatectomy with splenic preservation. Time of operations: 90 – 190 min. Bleeding: 100ml. Complications occurred in 2 patients: pancreatitis with pancreatic fistula. The observation period of the patients was from 6 month to 2 years. All patients are alive without evidence of disease recurrence.
Conclusions: SPT of the pancreas is a rare disease in children, which usually occurs in females puberty. The main method of treatment is surgery, the use of endosurgery possible, but

very strictly necessary to define the indications for this type of treatment and the risk of postoperative complications.

P-340

MANAGEMENT AND LONGTERM OUTCOMES OF GIANT MEDIASTINAL GERM CELL TUMORS IN CHILDREN

K. Kumar[1], S. Agarwala[1], S. Bakhshi[2], M. Srinivas[1], M. Bajpai[1], A.K. Bisoi[3], A.K. Gupta[4], M. Jana[4], D.K. Gupta[1], V. Bhatnagar[1]

[1]Pediatric Surgery, All India Institute of Medical Sciences, Delhi, India; [2]Medical Oncology, BRAIRCH All India Institute of Medical Sciences, Delhi, India; [3]Cardiothoracic and vascular surgery, All India Institute of Medical Sciences, Delhi, India; [4]Radiodiagnosis, All India Institute of Medical Sciences, Delhi, India

Objectives: To evaluate the outcome of children with giant mediastinal germ cell tumors.
Methods: All children up to 12 years of age, with mediastinal germ cell tumors (GCTs) treated at our hospital from 2008 through 2014 were evaluated for their tumor size, malignancy, chemotherapy, surgery, complications and outcome.
Results: Twelve mediastinal GCTs were included. The age ranged from 7-144 months with 5 (42%) being $\leq$ 1 year, 3 (25%) 1-10 years and 4 (33%) $>$ 10 years of age. All except one were males (92%). The average size of the tumor was 9 cm x 6 cm. Four were occupying nearly the entire hemithorax, displacing the diaphragm inferiorly. Nine of these 12 (75%) were benign (normal (FP) while 3 (25%) were malignant (with elevated αFP). While all 12 benign GCTs were resected upfront, the 3 malignant ones received 2 courses of PEB (Cisplatin+Etoposide+Bleomycin). On neoadjuvant chemotherapy, though there was no significant reduction in size noticed, the (FP levels decreased in all the three. All patients underwent complete resection of the tumor, 8 (67%) through postero-lateral thoracotomy (5-left, 3-right) and the 4 (33%) through median sternotomy. One, a dumbell shaped thoraco-abdominal tumor through a Bochdelek hernia, required laparotomy as well as diaphragmatic repair. There were no post-operative complications and the malignant ones completed a total of 4 courses of PEB. The follow-up ranged from 6 to 72 months (mean 39.5) and all are alive and disease free.
Conclusions: In this study group, mediastinal GCT had a bimodal age distribution and male predominance. The tumors in older children were of giant size, occupying the whole of the hemi-thorax. Neoadjuvant chemotherapy in those with elevated αFP did not decrease the size of the tumors even though the (FP normalized. A complete excision led to minimal post-operative complications and ensured long term disease free survival.

P-341

RHABDOID TUMOR OF KIDNEY: DISMAL OUTCOMES AT A TERTIARY CARE CENTER IN A DEVELOPING COUNTRY

V. Khanna[1], S. Agarwala[1], S. Bakhshi[2], M. Srinivas[1], S. Thulkar[3], M. Jana[3], M. Bajpai[1], D.K. Gupta[1], V. Bhatnagar[1]

[1]Pediatric Surgery, All India Institute of Medical Sciences, Delhi, India; [2]Medical Oncology, BRAIRCH All India Institute of Medical Sciences, Delhi, India; [3]Radiology, BRAIRCH All India Institute of Medical Sciences, Delhi, India

Objectives: To evaluate the outcome of children with rhabdoid tumor of kidney (RTK).
Methods: Retrospective review from the records of children with RTK enrolled from 1988 through2013 for their presentation, chemotherapy, surgeryand outcome. Before 1999 the chemotherapy was DD4A (Vincristin+Dactinomycin+Adriamycin) while since 1999 it was RTK regime (Carboplatin+Etoposide+Cyclophosphamide).
Results: Among the 480 renal tumors treated in this period, 9 (2%) wereRTK. Age ranged from 4 to 24 months (median12) and the male:female ratio was 1.3:1. All presented with an abdominal mass, 2 (22%) also had hypertension and one (11%) hadgross hematuria. The tumor size ranged from 11-9 centimeters (mean 10.5). Seven (78%) children had stage IIIand 2 (22%) had stage IV disease with metastasis to bilateral lungs in one (11%) and bilateral lungs and liver in another. Four (44%) received neoadjuvantchemotherapy (3 DD4A and 1RTK regimen) and of these 2 could be resected (gross complete resection) while 2 died pre-operatively of progressive disease. Overall 7 (78%) patients underwent surgery (5 upfront and 2 following neoadjuvant chemotherapy) of whom 5 had gross complete resection, 2 had gross residue. Five of 7 (71%) resected had tumor spill (all upfront resection). Two died soon after resection while the remaining 5 (56%) patients received adjuvant chemotherapy and only 2 (22%) received radiotherapy. All 5 (56%) patients who underwent complete excision had early local recurrence ranging from 15 days to 4 months (median 1 month) post-excision. The other 4 (44%) had progressive disease (2 following incomplete resection and 2 without resection). All 9 patients died with period of survival ranging from 2-6 months from diagnosis (median 2 months).
Conclusions: RTK is a rare pediatric renal tumorof very young children. They had very high incidence of tumor spill during upfront resection. They demonstrated very early recurrence or rapid progression and death within median of 2 months of diagnosis despite aggressive chemotherapy and complete surgical resection.

P-342

PAEDIATRIC TESTICULAR TUMOURS: A SINGLE-INSTITUITION EXPERIENCE

F.X. Li[1], J.H.Y. Chua[1], K.L. Narasimhan[1]

[1]Paediatric Sugery, KK Women's and Children's Hospital, Singapore, Singapore

Objectives: To describe a single-institution's series of paediatric testicular tumours and our experience with testis-sparing surgery (TSS).
Methods: Following IRB approval, a retrospective clinical chart review was conducted for patients with primary testicular tumours diagnosed between January 2001 and July 2012. Data on clinical presentation, demographics, pre-operative investigations and surgical procedures were collated and analysed using conventional statistics.
Results: Nineteen tumours were analysed and 89% (17) were of germ cell origin. Median age at diagnosis was 20 months (1-197). The most common presentation was a painless scrotal swelling (15,79%). All patients underwent testicular exploration via inguinal approach. Orchidectomy was performed with high ligation of the cord. In select cases of benign pathology, TSS was done. Nine patients had benign tumours (7 teratomas, 2 epidermoid cysts) and 10 lesions were malignant (5 yolk sac tumours (YST), 3 mixed malignant germ cell tumours (GCT), 1 follicular lymphoma, 1 rhabdomyosarcoma). In GCT, pre-operative Alphafetoprotein was elevated in all malignant subtypes when corrected for age. All except one malignant GCT were stage 1 at diagnosis and orchidectomy alone was curative (100% event-free survival at 88 months). The last patient had stage 4 YST and received adjuvant chemotherapy according to BEP protocol. He has remained disease-free for 9 years. TSS was performed for 6 of the 9 benign GCT. Of these, all had post-operative ultrasound demonstrating viable remaining testicular tissue. At least 1 child had undergone puberty and demonstrated growth of the remaining testicular tissue. None of the patients with benign GCT had tumour recurrence at median follow-up of 60 months (18-135).
Conclusions: Majority of paediatric testicular tumours are of germ cell origin. These tumours have an excellent prognosis even in advanced disease or delayed diagnosis. TSS is therefore a feasible option and completion orchidectomy can be employed in cases of recurrence. With close imaging surveillance, TSS can perhaps also be offered to selected patients with malignant GCT.

P-343

PERIOPERATIVE TUMOR RUPTURE CONFERS POOR SURVIVAL IN WILMS TUMOR

K. Svojgr[1], K. Pycha[2], R. Kodet[3], V. Smelhaus[1], J. Koutecky[1], J. Snajdauf[2], J. Stary[1], J. Malis[1]

[1]Pediatric Hematology and Oncology, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic; [2]Pediatric Surgery, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic; [3]Pathology and Molecular Medicine, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic

Objectives: Wilms tumor (WT) is the most common tumor of kidney in childhood. In the present study, we focused on preoperative and perioperative ruptures of tumors and their impact on survival.
Methods: From 7/1988 to 5/2009 239 patients with WT were treated at our institution. Event free survival (EFS) and overall survival (OS) was analyzed using Stat View statistical program.
Results: Patients were treated according to protocols: SIOP 9 (94 patients), SIOP 93 (80) and SIOP 2001 (65). Median follow-up is 12.5 years (3-21). 120 patients of 239 (50%) were treated with neoadjuvant CHT, 119 patients (50%) underwent primary nephrectomy. EFS and OS patients treated with neoadjuvant CHT or primary nephrectomy did not differ (EFS 76.6% versus (vs.) 79.8%, P$>$0.05; OS 85.8% vs. 86.5%, P$>$0.05). 29 patients out of 239 (12%) suffered from tumor rupture, EFS and OS did not differ in comparison to non-ruptured cases (EFS 76.6% vs. 78.8%, P$>$0.05; OS 83.3% vs. 86.5%, P$>$0.05). Preoperative tumor spillage was diagnosed in 21 cases; all the patients underwent primary nephrectomy. Perioperative tumor spillage occurred in 8 cases, 7 patients suffered from tumor spillage during primary nephrectomy (7 out of 98, 7%), only 1 patient suffered from tumor spillage when nephrectomy was performed after neoadjuvant CHT (1 out of 120, 0.8%, P = 0.02). Four patients (50%) with perioperative tumor rupture had metastatic disease at diagnosis in comparison to 2 patients with spontaneous tumor spillage (10.5%, P = 0.03). EFS of 21 patients with spontaneous tumor rupture is 90% in comparison to 37% with perioperative tumor rupture, P = 0.001, OS is 100% vs. 37% P
Conclusions: Patients suffering from perioperative tumor spillage had more likely metastatic disease and poor prognosis at our institution. Our findings should be confirmed in a multicenter study.
Supported by MHCZ – DRO, University Hospital Motol, Prague, Czech Republic 00064203.

P-344

DOES THE ADDITION OF TOPICAL VANCOMYCIN DECREASE THE INCIDENCE OF SURGICAL SITE INFECTION IN BONE TUMORS?

A. Puri[1], A. Gulia[1], M.B. Suman[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: A retrospective audit compared a consecutive group of patients operated for bone tumors who received only perioperative antibiotics (Group A) against a similar group that had additional topical vancomycin sprinkled in the wound prior to closure (Group B), to determine if addition of topical vancomycin decreases the incidence of surgical site infection (SSI).
Methods: 221 patients operated between Jan 2011 and Dec 2011 (Group A) and 183 patients operated between April 2012 and Dec 2012 (Group B) were analysed. Any patient needing operative intervention for wound discharge was considered infected. All patients had a one year follow up to determine incidence of SSI.
Results: The overall rate of SSI was 7% (29 of 404 patients). 17 (8%) of Group A and 12 (7%) of Group B patients had SSI – p = .669. In a subgroup analysis of patients with endoprosthetic reconstruction, 9 of 97 (9%) of Group A patients and 7 of 74 (9%) Group B patients had SSI. Similarly 3 of 76 (4%) Group A patients and 2 of 64 (3%) Group B patients with internal fixation implants (plates / IM nails), had SSI.
Conclusions: Addition of topical vancomycin prior to wound closure in patients operated for bone tumors does not decreases the incidence of surgical site infection (SSI). A longer follow up may determine its efficacy in reducing the incidence of late infections.

P-345

EARLY SURGICAL INTERVENTION IMPROVES CHANCE OF SURVIVAL IN NEUTROPENIC PATIENTS WITH CLOSTRIDIUM SEPTICUM SEPSIS

A. Zeinab[1], K. Ampofo[2], K. Korgenski[2], R. Meyers[3]

[1]Pediatric Oncology, University of Utah and Primary Children Hospital, Salt Lake City, US; [2]Pediatric Infectious Disease2, University of Utah and Primary Children Hospital, Salt Lake City, US; [3]Pediatric Surgery, University of Utah and Primary Children Hospital, Salt Lake City, US

Purpose: Due to our identification of high mortality rates in neutropenic patients with *Clostridium septicum* sepsis, we sought to identify prognostic and/or interventional measures that could be associated with improved outcome.
Method: Retrospective review of patients diagnosed with *C. septicum* infection from 1/2003 to 3/2014 with collection of prognostic and interventional measures that might be associated with outcome.
Results: Six patients were identified, 5 were female. Median age at infection was 13.5 years (range 3.5-21.2 years). Three had Acute Lymphoblastic leukemia, 2 Acute Myeloid leukemia and one Rhabdoid brain tumor. All were receiving myelosuppressive chemotherapy All patients were severely neurtopenic and 5 were not yet in remission. *C. septicum* were isolated by culture from all patients with 5 from blood and 1 from biopsy tissue. All patients presented with septic shock, 4 had clinical features of severe enterocolitis, one with abdominal wall and perirectal necrotizing fasciitis (); and another with erector spinae myonecrosis. All patients were treated with broad spectrum antibiotics and hospitalized in intensive care. Surgery was performed in 4 patients, 3 patients underwent surgical resection/debridement, and one had decompression exploratory laparotomy for compartment syndrome. Two patients survived, one with extensive erector spinae myonecrosis following extensive debridement surgery, and the other resection of perforated terminal ileum. The remaining four patients died within 4 hours to 6.5 days of first positive *C. septicum* culture.
Conclusion: In immuncompromised pediatric oncology patients, *C. septicum* infection is rapidly and highly fatal. High index of suspicion, particularly in patients with severe abdominal pain, septic shock, together with prompt therapeutic intervention by instituting anti-anaerobic antimicrobial coverage and early surgical intervention are critical in improving the chance for survival.

PSYCHOSOCIAL

P-346

TOWARDS A DYADIC UNDERSTANDING OF PARENTAL COULES' MARITAL SATISFACTION IN THE PEDIATRIC CANCER CONTEXT

W. Burns[1], S. Sultan[1], K. Péloquin[2], S. Marcoux[3], P. Robaey[3]

[1]Hemato-Oncology, CHU Sainte-Justine, Montreal, Canada; [2]Psychology Department, Université de Montréal, Montreal, Canada; [3]Centre de recherche, CHU Sainte-Justine, Montreal, Canada

Objectives: In the context of pediatric cancer, parents have various caregiving and support roles in the child's rehabilitation (Hutchinson et al, 2009; Long & Marsland, 2011), thus their well-being (including their conjugal well-being) is of vital importance. This research provides a dyadic understanding of the martial satisfaction of mothers and fathers of acute lymphoblastic leukemia (ALL) patients through predictors including individual mood and perceived family well-being.
Methods: Couples completed the Family Well-Being Assessment (family well-being) and the Profile of Mood States-Bipolar Form (mood states) at diagnosis and three months later, as well as the Locke-Wallace Marital Adjustment Scale (marital satisfaction) at 1-year (n = 72) and 2-years post diagnosis ($n = 61$). Specifically, this data comes from a cohort of parents of children treated for ALL at the CHU Sainte-Justine.
Results: Analyses based on the Actor-Partner Interdependence Model (APIM; Kenny et al., 2006) demonstrated that there are different marital satisfaction predictors for mothers and fathers of pediatric cancer patients. Mothers' marital satisfaction at 1 and 2-years post diagnosis was predicted by her family well-being variables at diagnosis and 3-months (actor effects); whereas fathers' marital satisfaction was predicted by his mood (actor effects) and his partners' role conflict and fatigue at diagnosis and 3-months (partner effects).
Conclusions: These research findings indicate that predictors of marital satisfaction for mothers and fathers of children with leukemia differ. This suggests the importance of using dyadic models to examine the relational adjustment of the parental couple and account for potential partner effects and gender effects. Thus, clinical interventions designed to help these couples should be tailored to address their specific needs and continued support should be provided throughout the cancer trajectory.
Acknowledgements: CRSH-UdM "small grants", Fondation CHU Sainte-Justine; Le Centre de recherche interdisciplinaire sur les problémes conjugaux et les agressions sexuelles (CRIPCAS)

P-347

INTEGRATED ASSESSMENT MAP (I AM) – A DOMAIN BASED HOLISTIC FRAMEWORK

J. Cargill[1], V. Gupta[1], S. Hewett-Avison[2], A. Cameron[1], P. Beynon[3], S. Dolby[4]

[1]Teenage and Young Adult Cancer Service, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; [2]Teenage and Young Adult Service, Teenage Cancer Trust, London, United Kingdom; [3]OnTarget Programme, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom; [4]Psychological Health Services, University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom

Objectives: Peer Review standards require that all patients are offered a holistic assessment of their needs. Within the Teenage and Yound Adult (TYA) population this is seen as a priority given the range and complexity of needs. The South West TYA service operates an online Multidisciplinary Advisory Team (MDAT) and so a framework to capture the holistic needs of TYA's and for meeting guidance was required.
Methods: A collaborative approach was used to develop the Integrated Assessment Map (IAM) and a multi-domain model was created to provide a structure to ensure that all TYA's were offered an assessment that incorporated the impact of diagnosis of cancer additional to treatment within a bio-psycho-social-educational-vocational framework. The domains used in the IAM model are; Physical impact, Emotional impact, Beliefs &Spirituality, My support network, Intimate relationships & fertility, My lifestyle-health, Education Training & Work, Accommodation & finance, My lifestyle-Activities/Interests. A scoring system was developed with a score assigned to each domain

- Level 1 – Universal: No additional input
- Level 2 – Targeted: Some additional input
- Level 3 – Specialist: significant input

The IAM is completed at stages throughout the pathway to allow for individual tracking by professionals and patients, and as a tool to guide service development.
Results: Internal service evaluation has been completed. The IAM is used consistently when discussing the needs of TYA's via the online Multi-Disciplinary advisory Team (MDaT) meeting and provisional data has been examined for service development purposes. A review and 'next steps' phase has begun, considering validation and publication.
Conclusions: The IAM provides the TYA service with a quantifiable measure of the TYA's support needs at various points in their pathway. It ensures the young person is at the centre of their care planning and that all areas of support are discussed at the appropriate time.

P-348

HISTORY OF RELAPSED DISEASE IN PEDIATRIC BRAIN TUMOR SURVIVORS: PSYCHOSOCIAL OUTCOMES AND QUALITY OF LIFE

C. Chow[1], C. Liptak[1], P. Manley[2], C. Recklitis[2]

[1]Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, USA; [2]Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: Advancement in medical treatment has allowed for improved survival rates for pediatric brain tumor patients, even after relapse. Although pediatric brain tumors survivors are at-risk for psychosocial challenges, little is known about how relapse history affects psychological outcomes and quality of life. This study examined the associations between disease relapse, psychological functioning, and quality of life in adolescent and young adult (AYA) survivors of pediatric brain tumors.
Methods: Participants were 84 adolescents (age 12-18) who completed the Beck Youth Inventory-II and 79 young adults (age 19-30) who completed the Brief Symptom Inventory-18 and the SF-12. Parents completed the Child, and Adolescent Behavior Checklists for respective age groups. Clinicians rated participants on the Global Assessment of Functioning (GAF) following semi-structured clinical interviews. Previously established cut-off scores were used to identify cases of clinically significant distress. Disease and treatment variables were taken from the medical record.
Results: Fourteen percent (23/162) of participants experienced relapse and 48% (11/23) of relapsed participants had a low grade glioma. Clinically significant anxiety was significantly more common in survivors with relapse history than in those with no history of relapse (33.3%

vs. 10.5%, p = 0.005). There were no significant relationships between relapse history and patient-reported depression or QOL, parent-reported behavior problems or clinician GAF ratings. Anxiety was not significantly related to time since diagnosis (p>0.05).
Conclusions: Relapse can be considered a risk factor for clinically elevated anxiety in AYA brain tumor survivors. Anxiety symptoms were present regardless of length of time since diagnosis. Results point to the importance of using self-report anxiety measures to capture this distress. Early identification of at-risk survivors could allow for implementation of empirically validated treatment for anxiety, particularly for low grade glioma patients, who may experience multiple relapses.
Acknowledgement of funding: Children's Brain Tumor Foundation (Recklitis), Brain Tumor Network (Liptak)

P-349

ETHNIC DIFFERENCES IN COPING, SOCIAL SUPPORT AND QUALITY OF LIFE AMONG PARENTS OF CHILDREN WITH CANCER

I. De Paepe[1], J. Van Der Werff Ten Bosch[1], C. Schotte[2]

[1]Pediatric oncology, UZ Brussel, Brussels, Belgium; [2]Clinical Psychology, UZ Brussel, Brussels, Belgium

Objectives: Pediatric cancer is widely accepted to drastically impact the parents' quality of life. Adaptive coping skills and social support are seen as important protective factors (e.g., Greening & Stoppelbein, 2007). Despite our multicultural society, pediatric cancer research on ethnic differences in parents' coping and social support is scarce. The current study investigated (a) mean level differences in coping strategy, social support and quality of life between Caucasians and immigrants and (b) whether the impact of coping and social support on quality of life was moderated by ethnicity.
Methods: Validated questionnaires on coping, social support and quality of life were administered from two matched samples of parents (23 Caucasians, 21 north Africans).
Results: Mean-level differences were uncovered through MANOVA analyses. As for coping, immigrants were found to score higher on positive reappraisal ($p < 0.10$) and on putting into perspective ($p < 0.01$). In terms of social support, immigrants generally reported receiving equal or more social support than Caucasians ($p < 0.10$). At the same time, they also reported a lower satisfaction with social support as well ($p < 0.01$). Also, immigrants seemed to have a lower quality of life due to a higher incidence of physical complaints (pain ($p < 0.05$) and sleep ($p < 0.01$)) and depression symptoms ($p < 0.05$). Linear regression analyses were performed to investigate the impact of coping and social support on quality of life. The degree of experienced social support was no significant predictor; yet, satisfaction with social support was found to be an important predictor of quality of life ($p < 0.01$). None of these associations were moderated by ethnicity.
Conclusions: In conclusion, the current childhood cancer investigation uncovered several important ethnic differences in parents' coping and especially in (satisfaction with) social support. More profound investigation with larger groups of parents is warranted in order to guarantee support tailored to the needs of each person regardless of their ethnic origin.

P-350

ATTENTION BIAS MODIFICATION THERAPY (ABMT) AS A MODERN TECHNIQUE FOR PAIN MANAGEMENT IN CHILDREN WITH CANCER

M. Firoozi[1]

[1]Department of Psychology, University of Tehran, Tehran, Iran

Introduction: The purpose of Attention Bias Modification Therapy (ABMT) is to implicitly shape anxiety related biases in attention orienting. Continuing pain problems in children with cancer are often assumed to be excessively attentive for their symptoms, and this is referred to as hyper-vigilance. This model assumes that fearful children become increasingly vigilant for signs of bodily threat, which in turn leads to avoidance behavior, increased disability and maladjustment to cancer treatments.
Methods: ABMT uses the dot-probe task as a therapeutic tool by computer program. Potential applications of attention bias modification (ABMT) for acute (injection pain) in the children were investigated. In this study 98 children with cancer who were under daily injection were recruited and randomized to receive 8 session of ABMT or placebo. Children were followed up 3 months later.
Results: Participants who were randomized to receive ABMT reported better coping to injection pain (P = 0.043) and adherence of self management program for control pain (P = 0.003) and show better communication for nurses who did the injection (P = 0.01) than those who received placebo.
Conclusion: The results of these studies show that there is potential in the application of ABMT to pain conditions, and a positive effect of ABMT on clinical outcomes suggests that this technique is worthy of future study as an intervention for pain patients.

P-351

PSYCHOSOCIAL PROFILE OF PEDIATRIC BRAIN TUMOR SURVIVORS WITH NEUROCOGNITIVE COMPLAINTS

M. Grootenhuis[1], M. de Ruiter[1], A. Schouten-van Meeteren[2], D. van Vuurden[3], H. Maurice-Stam[1], C. Gidding[4], L. Beek[5], B. Granzen[6], J. Oosterlaan[7]

[1]Pediatric Psychosocial Department, Emma Children's Hospital Academic Medical Centre, Amsterdam, Netherlands; [2]Department of Pediatric Oncology, Emma Children's Hospital Academic Medical Centre, Amsterdam, Netherlands; [3]Department of Pediatrics, VU Medical Center, Amsterdam, Netherlands; [4]Department of Pediatric Oncology/Hematology, Radboud University Medical Center, Nijmegen, Netherlands; [5]Department of Medical Psychology, Wilhelmina Children's Hospital UMC, Utrecht, Netherlands; [6]Department of Pediatrics, Maastricht University Medical Centre, Maastricht, Netherlands; [7]Department of Clinical Neuropsychology, VU University Amsterdam, Amsterdam, Netherlands

Objectives: With more children surviving a brain tumor, neurocognitive consequences of the tumor and/or its treatment become apparent. We studied the psychosocial functioning of this growing group of pediatric brain tumor survivors (PBTS).
Methods: Psychosocial functioning of PBTS (8-18 years) with neurocognitive complaints was compared to normative data on the following domains: Health Related Quality of Life (HRQOL), self-esteem, social-emotional functioning, executive functioning, (one-sample t-tests) and fatigue (sibling control group, independent samples t-test). We included self-, parent-, and teacher-report questionnaires where appropriate.
Results: Eighty-two PBTS (mean age = 13.4 years, SD = 3.2, 49% males) and 43 healthy siblings (mean age = 14.3, SD = 2.4, 40% males) were included. PBTS reported decreased physical, psychological and generic HRQOL (*d*s 0.39 to 0.62, *Psd* = 0.57, *Pd* = 0.81, *Pd*s 0.35 to 0.43, *Psd* = 0.69, P
Conclusions: PBTS show increased psychosocial problems, as reported by themselves, parents and teachers, with small to large effect sizes. Better understanding of psychosocial functioning in the growing group of PBTS with neurocognitive complaints, will help to provide tailored support to this group of vulnerable children.

P-352

LIFE GOALS IN PATIENTS WITH CANCER: A SYSTEMATIC REVIEW WITH IMPLICATIONS FOR ADOLESCENT AND YOUNG ADULT PATIENTS

S.E. Hullmann[1], S.L. Robb[1], K.L. Rand[2]

[1]School of Nursing, Indiana University, Indianapolis, USA; [2]Department of Psychology, Indiana University-Purdue University Indianapolis, Indianapolis, USA

Objectives: One characteristic of adolescent/young adult (AYA) development is the identification and pursuit of life goals; unknown is how cancer affects life goals during this developmental stage. A critical examination of existing research is needed to establish what is currently known, and to inform subsequent study design. Purposes of this systematic review were to: 1) identify theoretical models used to examine cancer patient life goals, 2) identify life goal constructs being examined and their assessment, and 3) summarize what is known about the impact of cancer on life goals.
Methods: Our systematic review examined research on life goals in patients with cancer published between 1993 and 2013. Inclusion criteria were: 1) cancer population, 2) original research article, and 3) assessed life goals. Based on these criteria, 156 articles were screened and 32 included in the final review. Theoretical models, goal constructs, assessment methods, and findings were summarized and informed discussions centered on AYA life goals.
Results: Self-regulation was the most commonly applied theoretical model (28%), and nearly half (44%) used theories not replicated in other studies. Goal constructs included self-identified life goals, change in life goals, goal disturbance/hindrance, and goal adjustment. Goal assessment methods included validated questionnaires (47%), author-developed questionnaires (31%), and semi-structured interviews (22%). Review study findings suggest: 1) cancer hinders ability to achieve pre-diagnosis goals and changes life priorities (i.e., greater focus on social and health-related goals), and 2) goal adjustment is related to better psychosocial/physical health outcomes.
Conclusions: Review findings offer theoretical frameworks and validated questionnaires for inclusion in subsequent research. Cancer negatively impacts patient goal achievement, and interventions targeting goal adjustment may improve patient outcomes. However, representation of AYA in the reviewed study samples was low, and research specific to AYA life goals is needed to elucidate the impact of the cancer experience on patients during this unique developmental stage.

P-353

ON THE CHILD'S OWN INITIATIVE - PARENTS COMMUNICATE WITH THEIR DYING CHILD ABOUT DEATH

L. Jalmsell[1], T. Kontio[2], M. Stein[2], J.I. Henter[3], U. Kreicbergs[2]

[1]Centre for Research Ethics and Bioethics, Uppsala University, Uppsala, Sweden; [2]Women and Child Care, Sophiahemmet University, Stockholm, Sweden; [3]Women and Child Care, Karolinska Institutet, Stockholm, Sweden

Objectives: Open and honest communication has been identified as an important factor in providing good palliative care. Parents having lost a child to cancer in some cases regret not having talked to their child about death. Still, there is no easy solution to if, when and how

parents and a dying child should communicate about death. This study reports on how parents communicated about death with their dying child.
Methods: Nation-wide questionnaire with bereaved parents having lost a child to a malignancy during a six-year period in Sweden. Parents were asked how they communicated with their child about death and if they used fairy-tales, drawings, films, music or other activities as facilitators of the communication. In addition, parents were asked to elaborate on their answer with written comments. Both quantitative and qualitative content analyses have been used.
Results: 449/561 (80%) parents returned the questionnaire. Using fairy tales was the most commonly reported mean of communication, regardless of the age of the dying child. Parents with children younger than four, used music and drawings to communicate, less often than parents with older children. 67 parents provided free-hand comments revealing that often it was the child who initiated communication about death. Analysis revealed four categories as to how communication about death occurred, 1) *communicating about deathby using narratives*, 2) *talking about friends and family that had died, or about death itself*, 3) *talking about life after death*, and 4) *preparing for death through practical preparations*.
Conclusions: There are many ways in which a parent can communicate about death with his or her dying child. In our study many used fairy-tales or other means to facilitate the communication about a difficult subject. Providing appropriate literature and/or movies at the pediatric wards may help parents and children in their communication at minimal risk of causing harm.

P-354

STABILITY OF TWO SHORT DISTRESS MEASURES AS APPLIED TO PARENTS OF SURVIVORS OF CHILDHOOD BRAIN AND OTHER SOLID TUMOURS

T. Leclair[1], Y. Samson[2], A.S. Carret[2], S. Sultan[2]

[1]Psychology Department, Universite de Montreal, Outremont, Canada; [2]Hemato-Oncology, CHU Sainte-Justine, Montreal, Canada

Objectives: To estimate the stability of the Distress Thermometer-Parents (DT-P) and the Anxiety and Depression Scales of the Edmonton Symptom Assessment System-Revised (ESAS-R -A, -D) with parents of survivors of childhood brain tumours and other solid tumours.
Methods: Fifty-six parents completed distress questionnaires immediately after a usual follow-up appointment of their child (M0) and a month later (M1). Parents rated children's HRQoL and life events on separate scales.
Results: The DT-P and the ESAS-R -A and -D demontrated high test-retest reliability in a stable clinical situation ($rs > .65$). Changes in children's HRQoL and life events were associated with changes on distress measures. DT-P and ESAS-R -A and -D scores were associated with scores of other validated distress measures ($rs > .60$).
Conclusions: The DT-P and the ESAS-R -A and -D may be stable measures of parental distress. The results support the use of these instruments in caregivers. It is important to study test-retest correlations in single-item distress measures since it is the only way to ascertain the reliability of these measures.

P-355

A MULTI-SITE EVALUATION OF SUMMER CAMPS FOR CHILDREN WITH CANCER AND THEIR FAMILIES

A. Martiniuk[1], Y. Wu[2], M. Amylon[3]

[1]Faculty of Medicine, The University of Sydney, Sydney, Australia; [2]Faculty of Medicine, The University of Utah, Utah, USA; [3]Faculty of Medicine Pediatric Oncology, Stanford University, Stanford, USA

Objectives: More children are surviving childhood cancer. Children with cancer and their families often attend specialized summer camps (therapeutic recreation) through their cancer treatment journey. Evaluations of these programs are emerging over the recent decade. Previous evaluations have infrequently used standardized measures, and typically enrol small sample sizes drawn from one summer camp. To address these gaps, this study sought to use standardized outcome measures, and to enrol a large sample size from multiple centres to enable stratification of outcomes by sub-groups.
Methods: A cross-sectional study in 2012 at 19 camps in North America was used to evaluate summer camps for children with cancer and their siblings. Outcomes were measured using the 29-item Pediatric Camp Outcomes Scale (PCOS) which uses a Likert Scaling to score. This study had approval by the Stanford Ethics Review Board and participants signed consent forms.
Results: A total of 2,286 campers ($N = 1215$ females) were enrolled in this study. Of these campers, 1,332 were patients and 951 were siblings. Participants (patient or sibling): "on" treatment were 444 (20%), relapsed 294 (14%) and 1st year at camp 535 (24%). The mean score on the PCOS emotional subscale was 29.8 ($SD = 4.5$); social subscale was 39.8 ($SD = 5.3$); physical subscale was 20.6 ($SD = 3.2$) and self-esteem was 22.3 ($SD = 2.8$). The PCOS total mean score was 112 ($SD = 12.6$).
Conclusions: This study uses the standardized PCOS tool to measure outcomes for children attending camp. This allows for comparison of data across camps and across specialty camp types (eg cancer, diabetes etc). The findings demonstrate that camp helps campers feel improved emotional, social, and physical functioning, and helps children improve their self-esteem. Strongest scores were observed for the emotional and social functioning subscales. Ultimately it is hoped that these increased skills gained at camp will help build coping and resiliency for children who have been diagnosed with cancer.

P-356

TWO OVERLOOKED CONTRIBUTORS TO ABANDONMENT OF CHILDHOOD CANCER TREATMENT IN KENYA: PARENTS' SOCIAL NETWORK AND EXPERIENCES WITH HOSPITAL RETENTION POLICIES

S. Mostert[1], F. Njuguna[2], S.C. Langat[2], A.J.M. Slot[1], J. Skiles[3], M.N. Sitaresmi[4], P.M. van de Ven[5], J. Musimbi[2], R.C. Vreeman[3], G.J.L. Kaspers[1]

[1]Pediatric Oncology-Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Pediatrics, Moi Teaching and Referral Hospital, Eldoret, Kenya; [3]Pediatrics, Indiana University School of Medicine, Indianapolis, USA; [4]Pediatrics, Dr Sardjito Hospital, Yogyakarta, Indonesia; [5]Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, Netherlands

Objectives: Principal reason for childhood cancer treatment failure in low-income countries is treatment abandonment. Two often neglected factors may contribute to abandonment: 1) Lack of information and guidance by doctors, along with beliefs of those surrounding parents, can increase misconceptions regarding cancer and its treatment, 2) National policy in public hospitals by which patients are retained after doctor's discharge until medical bills are settled. This study explored parents' social network and experiences with hospital retention policies in a Kenyan academic hospital.
Methods: Home-visits were conducted to interview parents of childhood cancer patients who had been diagnosed between 2007-2009 and abandoned treatment.
Results: Retrospective chart review revealed 98 childhood cancer patients had abandoned treatment. During 2011-2012, 53 families (54%) could be reached and 46 (87%) interviewed. Community members surrounding parents (grandparents, relatives, friends, villagers, church-members) believed that the child was bewitched (61%), advised parents to seek alternative treatment (74%), and stop medical treatment (54%). Parents discussed with other parents of cancer patients that child's life is in God's hands (87%), trauma of forced hospital stays (84%), importance of completing treatment (81%), financial burden of treatment (77%), and incurability of cancer (74%). These discussions influenced their perceptions of cancer treatment and its usefulness (65%). Thirty-six families (78%) had no health-insurance and nineteen of these parents (53%) could not pay their medical bills and were not allowed to take their child home. Parents felt desperation (95%), powerlessness (95%), sadness (84%), and that their child was imprisoned (80%) during the retention period. Most parents (87%) felt hospital retention must cease.
Conclusions: The beliefs of those surrounding parents may influence their perceptions of cancer treatment and contribute to abandonment. Hospital retention policies are highly distressing for parents and may contribute to both treatment delays and treatment abandonment. These factors jeopardize treatment outcomes for children and require attention and modification.

P-357

EXAMINING THE EFFECTS OF CHILDHOOD CANCER ON THE PARENTAL SUBSYSTEM

N. Moules[1], A. Estefan[1], G. McCaffrey[1], D. Tapp[1], D. Strother[2]

[1]Nursing, University of Calgary, Calgary, Canada; [2]Hematology Oncology and Blood and Marrow Transplant Program, Alberta Children's Hospital, Calgary, Canada

Objectives: This study investigated the effects of childhood cancer on the parents' relationship. Some past studies report that childhood cancer can have a negative effect on the relationship and others that it can even strengthen it. Though it may not ever be known whether or not the relationship suffers or strengthens, what is little understood is *how* the cancer experience affects the relationship between the parents and what might health care professionals do to support the relationship.
Methods: Twenty-three unstructured interviews were conducted to a total of 29 participants. Data were analyzed using hermeneutic phenomenology methods of interpretation. The participants included parents of children who were 1) treated and cured and live with little or no side effects; 2) treated but live with long term effects; 3) did not survive.
Results: The state of the relationship prior to cancer had, in many situations, important implications on how the relationship fared during and after the cancer experience. This cannot be the only predictor however, as some challenged relationships thrived and repaired as a result of the experience. The strongest finding in this study is that the relationship can be affected in intense ways, even to the surprise of the couples and they offered advice to other couples facing this experience. The participants also had advice to offer health care professionals about things that are helpful and not helpful to say and do regarding supporting them as a couple.
Conclusions: The relationship between the parents has profound effects on the health and well being of the child and any support that can be offered in this area is preventative healthcare.

Acknowledgements: Kid's Cancer Care Foundation Chair Funding, Alberta Children's Hospital Foundation.

P-358

DETAILED PSYCHOAFFECTIVE STATUS IN A LONG TERM PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) SURVIVORS COHORT: DESCRIPTION AND PREDICTION

A.-J. Pépin[1], C. Laverdiére[2], D. Sinnett[2], S. Lippé[2], S. Sultan[2]

[1]Psychology, Université de Montréal, Montreal, Canada; [2]Hemato-oncology, CHu Sainte-Justine, Montreal, Canada

Objectives: Survivors of pediatric ALL are at increased risk of mental health difficulties. Previous research suggests that emotional patterns could be specific in this population. Although rates for broad psychiatric conditions have been studied, no description of individual emotional symptoms has been offered. Describing psychoaffective symptoms is essential to orient further treatment. The objective of this study is to present a detailed description of psychoaffective status in a sub-group of a large pediatric ALL survivors cohort. We describe positive and negative emotions, depression and anxiety symptoms (including concerns), mental quality of life and fatigue.
Methods: The present sample consists of 70 survivors from an ongoing cohort follow-up (Sainte-Justine UHC, Montreal). Mean age is 21yrs (range = 14-34 yrs). Self-reported questionnaires include the Distress Thermometer, Depression and Anxiety modules of the Beck Youth Inventory, the Brief Symptom Inventory-18, the Assessment of Survivor Concern, the PedsQL Generic Scale and the PedsQL Fatigue Scale. We describe this statistically and use effect sizes to compare the sample with external norms.
Results: A minority of survivors reported significant distress (26%). Anxiety (29%) was more frequently reported than depression (9%). Anxiety affects were more frequently reported (jittery, nervous, anxious, upset, scared). Fatigue was particularly high in the sample. ALL survivors reported fewer concerns about there health, cancer relapse and death, than other survivors samples. Exploratory results suggest that risk status and treatment history were associated with symptoms of anxiety and patterns of fatigue.
Conclusions: These results suggest that the symptomatic pattern of this population could be marked by a relatively high number of anxiety and fatigue symptoms but fewer depression symptoms.

P-359

IDENTIFYING CAUSES OF MISSING APPOINTMENTS AND IMPLEMENTING INTERVENTIONS IN REAL TIME INCREASES TREATMENT COMPLIANCE AND REDUCES ABANDONMENT RATES FOR CHILDHOOD CANCER IN EL SALVADOR

C. Salaverria[1], N. Rossell[1], S. Fuentes Alabi[1], F. Vasquez[1], A. Hernandez[1], C. Lam[2], R. Ribeiro[3]

[1]Pediatric Oncology, Fundación Ayúdame a Vivir/Hospital Nacional de Niños Benjamin Bloom, San Salvador, El Salvador; [2]Department of Oncology and International Outreach Program, St. Jude Children's Research Hospital, Memphis, USA; [3]Department of Oncology, St. Jude Children's Research Hospital, Memphis, USA

Objectives: In El Salvador, about 200 new cases of pediatric cancer are diagnosed each year and survival rates are approaching 70%. Although treatment is available at no cost, abandonment of therapy has been high (13%) during the last decade. The reasons for abandonment are not clear. In 2011, a procedure designed to detect missing appointments, register their root causes, and intervene in a timely fashion was implemented.
Methods: Absences to medical appointments in any of the areas of the pediatric oncology unit were informed to the medical team daily. Patient demographics and reasons for the absences were determined and registered. Cases of lymphoblastic leukemia (ALL) in induction therapy were contacted within 24 hours from the notification. All other cases were contacted within 48 hours and patients who had completed treatment within a week. Reasons for absences were obtained through telephone or in person interviews. If a patient failed to show up after initial contact, local health clinics and municipalities were contacted to conduct a search of the patient. Law enforcement was used as a last resort in patients in first line treatment with good prognosis.
Results: Absences were efficiently registered and families reasons behind absences were detected and proper interventions conducted. Categories for reasons of absences were established with cultural and social context considered. Abandonment rates dropped from 13% to 3%. Institutional costs were reduced.
Conclusions: The relationship between adherence and abandonment of treatment needs to be addressed; information of the first might shed light on abandonment showing possible similarities as well as differeneces between the two. Analysis of the impact of absenteeism on survival needs to be further explored. Abandonment of therapy is not necessarily a result of non-adherence in this study.

P-360

FAMILY PSYCHOSOCIAL FUNCTIONING AFTER RECENT DIAGNOSIS WITH CHILDHOOD CANCER

S. Schepers[1], S.M. Sint Nicolaas[2], H. Maurice-Stam[1], H.N. Caron[3], G.J.L. Kaspers[4], P.M. Hoogerbrugge[5], C.M. Verhaak[2], M.A. Grootenhuis[1]

[1]Psychosocial Department, Academic Medical Center, Amsterdam, Netherlands; [2]Department of Medical Psychology, Radboud University Medical Center, Nijmegen, Netherlands; [3]Department of Pediatric Oncology, Academic Medical Center, Amsterdam, Netherlands; [4]Department of Pediatric Oncology & Hematology, VU University Medical Center, Amsterdam, Netherlands; [5]Department of Pediatric Oncology, Radboud University Medical Center, Nijmegen, Netherlands

Objectives: Being diagnosed with childhood cancer is a stressful event for the entire family, which puts them at risk for developing psychosocial problems. We aimed to determine psychosocial functioning in parents (of patients 0-18 years), patients (8-16 years), and siblings (8-16 years) after a very recent diagnosis of childhood cancer and to compare this with scores from the healthy population.
Methods: Psychosocial functioning was assessed online one month post-diagnosis in n = 116 families (response rate 60%). The Hospital Anxiety and Depression Scale (HADS) was used for parents. The parent-report of the Strengths and Difficulties Questionnaire (SDQ) was used for patients ($N = 54$) and siblings ($N = 30$). HADS and SDQ scores were compared with Dutch reference groups by t-tests for means and χ^2-tests for percentages in the clinical range.
Results: Parents of children with cancer scored significantly higher than the reference group ($p < 0.0001$) on anxiety and depression. The percentages of parents in the moderate to severe range were higher than in the reference group ($p < 0.0001$); anxiety 14.2% vs 7.7%; depression 16.3% vs 3.6%. No significant differences were found for the mean SDQ-scores of patients and siblings compared with the norm. One fifth of the patients (20.4%) and siblings (20.0%) scored in the borderline to clinical range of the SDQ.
Conclusions: Parentsreported high levels of anxiety and depression. Even though on average patients and siblings (8-16 years) psychosocial functioning is comparable to the norm, a considerable proportion of children seems to struggle. Structural and early attention for family problems at diagnosis is necessary, such that early (preventive) intervention is possible.

P-361

PSYCHOSOCIAL AND ALLIED HEALTH WORKFORCE: QUANTIFYING WORKFORCE RATIOS FOR PAEDIATRIC ONCOLOGY SERVICES. HOW DO WE PLAN FOR OUR FUTURE?

A. Shelly[1], J. Williamson[1], P. Downie[1], S. Hirst[2]

[1]Paediatric Integrated Cancer Service, Paediatric Integrated Cancer Service, Melbourne, Australia; [2]Sheila Hirst Consulting, Sheila Hirst Consulting, Melbourne, Australia

Objectives: Management of paediatric oncology requires extensive multidisciplinary staffing. A recent audit of activity in Victorian primary treating centres, for the period 2006-07 to 2009-10, revealed significant increases in usage for inpatient activity (^26%), chemotherapy (^38%) and radiation therapy (^50%). Within the context of this increasing service usage, together with increasing birth rates, treatment complexity and survival, a project was undertaken to estimate patient to staff ratios for psychosocial and allied health workforce for Victorian paediatric oncology primary treating centres.
Methods: Workforce ratios were estimated for nine psychosocial and allied health groups. Where available, ratios were informed by industrial awards, guidelines and/or models of care. Professional disciplines identified tasks required for newly diagnosed children at key pathway points. Time was allocated to each task, for each level of care, using a risk adaptive approach (low, moderate and high risk/need).
Results: The methodology used in this project allowed for the calculation of ratios of newly diagnosed children per annum to 1 full-time equivalent (FTE). Ratios were calculated for art, music and play therapy, educational play therapy, dietetics, mental health, neuropsychology, occupational therapy, pharmacy, physiotherapy and social work. For example, a ratio of 83 newly diagnosed children to 1 FTE Neuropsychologist is recommended. For Mental Health clinicians, a ratio of 67 newly diagnosed children to 1FTE is recommended.
Conclusions: Limited national and international models are available to estimate paediatric oncology psychosocial and allied health workforce ratios. These ratios will assist the primary treating centres to plan to meet the future workforce needs for Victorian children and adolescents with cancer. In addition, the methodology used may assist other states in Australia, as well as overseas health services, to plan for oncology psychosocial and allied health workforce in the future.

P-362

COMMUNICATING RESULTS OF MEDICAL IMAGING TESTS IN PAEDIATRIC ONCOLOGY: OPINIONS AND NEEDS OF RADIOLOGISTS: A SURVEY

A.M.J.B. Smets[1], E.M.A. Smets[2], G.A. Tytgat[3], H.N. Caron[3], J. Stoker[1], M.A. Grootenhuis[4]

[1]Radiology, Emma Childre's Hospital/Academic Medical Center, Amsterdam, Netherlands; [2]Medical Psychology, Emma Childre's Hospital/Academic Medical Center, Amsterdam, Netherlands; [3]Paediatric Oncology, Emma Childre's Hospital/Academic Medical Center, Amsterdam, Netherlands; [4]Paediatric Psychology, Emma Childre's Hospital/Academic Medical Center, Amsterdam, Netherlands

Objectives: Discovering a malignancy, or progression or recurrence of a malignancy during an imaging test is a stressful event for a radiologist. Radiologists often have no previous relationship with patients and only have limited time to build rapport which hampers communication of such results. Moreover, skills for breaking bad news may be limited as communication training is not mandatory in the radiology curriculum. We conducted a survey investigating opinions, attitudes and needs regarding discussing imaging results with parents of children with cancer.
Methods: A questionnaire was presented to all members of the European Society of Paediatric Radiology. Radiologists who have children with cancer among their patients were asked to anonymously answer 42 questions about their background, practice, opinions and needs regarding communicating results to parents of children with cancer.
Results: From the 121 radiologists with an interest in oncology, 74, representing 22 countries, responded. Seventy percent of respondents reported that parents of pediatric cancer patients frequently ask for results. Sixty-six percent of respondents agreed they have a role in discussing results directly with parents. Thirty-four percent reported not feeling comfortable discussing worrisome results. Fifty-three percent of respondents indicated they had never received training in communication skills. Seventy-two percent would sign up if training in communication skills was available to them. Seventy-five percent reported being unaware of a policy or guidance on disclosing results within their department or institution.
Conclusions: Parents of children with cancer frequently ask radiologists to discuss results of imaging tests with them and many radiologists agree they have a role in doing this. A substantial percentage of radiologists does not feel comfortable discussing bad news and reports there is a lack of guidelines. Our findings suggest there is room and need for guidelines and training regarding communication between radiologists and patients.

P-363

FEASIBILITY TESTING HELP: AN ONLINE INFORMATION INTERVENTION FOR PARENTS SHARING INFORMATION ABOUT ACUTE LYMPHOBLASTIC LEUKAEMIA WITH THEIR CHILD

C. Vindrola[1], G. Bryan[1], G. MacIntyre[2], N. Ranasinghe[2], T. Say[3], F. Gibson[4], A. Richardson[5], R. Taylor[6], N. Crichton[7], V. Harding[8]

[1]Children's Nursing, London South Bank University, London, United Kingdom; [2]Parent representative, User of Paediatric Oncology Cancer Services, London, United Kingdom; [3]Haematology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [4]Children's Nursing, London South Bank University and Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [5]Faculty of Health Sciences, University of Southampton and University Hospitals Southampton NHS FoundationTrust, Southampton, United Kingdom; [6]Children's Nursing, University College London Hospitals NHS Foundation Trust and London South Bank University, London, United Kingdom; [7]Faculty of Health and Social Care, London South Bank University, London, United Kingdom; [8]Medical Illustration, University College London Institute of Child Health, London, United Kingdom

Objectives: Our previous research identified that parents of children with Acute Lymphoblastic Leukaemia (ALL) felt that they received minimal support to facilitate the acquisition of knowledge about the disease, especially the period close to diagnosis. We developed an online intervention named HELP (Harmonising Education about Leukaemia for Parents) to facilitate easy access to information about leukaemia. This resource is aimed at parents. At SIOP 2011, we presented an early description of what an intervention might look like. At SIOP 2012, we presented the basis for HELP and explained its initial development. This paper will focus on how we have feasibility tested and validated the intervention with families and health professionals prior to its evaluation in the second phase of the study.
Methods: After the development stage, feasibility testing and validation took place in five sequential steps. Firstly, our family advisory group provided comments on the content, look and feel of the website. Next, a group of clinicians and parents at one hospital were invited to use HELP and provide comments. Thirdly, health professionals at each of the other four sites reviewed the intervention, provided comments and advise on any hospital specific changes. The intervention was revised to reflect these comments. Finally, a health professional reviewed the intervention to validate all the information.
Results: Feasibility testing and validation of the intervention was a lengthy but important step in the development of HELP. Trials and tribulations in the recruitment of families on treatment and busy health professionals to take part in research will be discussed. The final version of HELP will be presented.
Conclusions: In the second phase of the study, HELP will be tested in a prospective two group non-randomised study. We anticipate HELP will increase parents' knowledge, confidence and competence, decrease stress and make communication with professionals easier.

P-364

EXPLORING CANCER WORRY PREDICTORS IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCERS

R. Wang[1], I. Syed[2], P. Nathan[3], R. Barr[4], Z. Rosenberg-Yunger[5], A. Klassen[4]

[1]School of Medicine, Queen's University, Kingston, Canada; [2]Health Research Methodology, McMaster University, Hamilton, Canada; [3]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada; [4]Department of Pediatrics, McMaster University, Hamilton, Canada; [5]School of Health Services Management, Ryerson University, Toronto, Canada

Objectives: The experience of cancer in childhood can influence the psychosocial wellbeing of AYA (adolescent and young adult) survivors, who report having cancer-related worries years beyond the completion of their treatment. Cancer worry has been shown to be an important barrier/facilitator in transition to long-term followup care and also impacts psychosocial adjustment in survivors. Despite its importance, there is a lack of research on cancer worry in this population. The aim of this study was to investigate the relationship between patient, cancer, and treatment-related factors and cancer worry in AYA childhood cancer survivors.
Methods: Between July 2011 and January 2012, AYA survivors aged 15 to 26 were recruited either in person or through mail from three Canadian pediatric hospitals. 250 participants (75.5% response rate) completed a questionnaire booklet that included a newly developed psychometrically sound 6-item Cancer Worry Scale (CWS). Selection of predictors for cancer worry were based upon review of literature and guided by expert opinion. Univariate analysis was used to identify predictors significantly related with CWS scores, which were then included in a multivariable regression model.
Results: In the multivariate analysis, females AYA survivors reported significantly greater cancer worries than males, scoring on average 9.4 points lower on the CWS (($=-9.4$; $P < 0.001^*$; 95% CI: -14.4 to -4.5). Level of treatment intensity was also significant, as survivors who received the most intense therapy were significantly more worried than patients who received the least intensive therapy (($=-18.5$; $P < 0.012^*$; 95% CI: -31.16 to -5.89). These predictors contributed to a good fit in the multivariable regression model ($F_{12,221} = 2.696$, $p < 0.002^*$).
Conclusions: Our study identified two important factors associated with increased cancer worry in the AYA population. These results can help identify survivors who are most likely to worry and further direct appropriate programs to mitigate the burden of cancer worry on their transition process and overall wellbeing.

E-POSTER PRESENTATIONS

ACUTE LYMPHOBLASTIC LEUKAEMIA

EP-001

EVALUATING IRON OVERLOAD AT THE END OF THERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

S. Acar[1], S. Gözmen[1], S. Bayraktaroglu[2], T.H. Karapinar[1], Y. Ay[1], Y. Oymak[1], B. Demirag[1], D. Ince[1], G. Özek[1], Y. Aydinok[3], C. Vergin[1]

[1]Pediatric Hematology-Oncology, Dr. Behçet Uz Childen's Hospital, Izmir, Turkey; [2]Radiology, Ege University, Izmir, Turkey; [3]Pediatric Hematology-Oncology, Ege University, Izmir, Turkey

Objectives: The aim of this study is to determine the hepatic iron overload by using R2 MRI and to evaluate the influence of hepatic iron overload on liver function tests in children with acute lymphoblastic leukemia (ALL).
Methods: Medical charts of30 patients (19 males, 11 females) with diagnosis of ALL were recorded. Age at diagnosis and at the time of R2 MR, risk group of ALL, treatment protocol, amount of transfused blood products were noted from the patients'records. Serum iron parameters, TORCH and hepatit markers at the end of the therapy were noted from patiens' records. We performed R2 MRI study in the first 3 months after therapy to evaluate the liver iron burden. We repeated serum iron, serun ferritin, serum transferrin and total iron binding capacity between12 to 18 months after the end of the treatment in patients having high ferritin.
Results: Twenty patiens were in standart risk group, 8 patients were in intermediate risk group, 8 patients were in high risk group. There was no patient having severe hepatic iron overload. Eight (27,5%) patients had mild and 1 (3,4%) patient had moderate iron everload. High Risk Group had the highest number of red blood cell products. Iron overload was higher in patients having more than 100 ml/kg red blood cell products. Transferrin saturation, ferritin levels and amount of transfusions per year were positively correlated with the amount of liver iron overload. Repeated ferritin measurements between 12 to 18 monts after the cessation of the therapy were found to be statistically decreased in patients with high ferritin levels. No abnormal liver function tests were found.
Conclusions: There was 30.9% of our patients had mild-moderate iron overload at the end of thrapy. There was no correlation between liver iron overload and liver function tests. Control measurements of ferritin between 12 to 18 months after the cessation of therapy were significantly decreased.

EP-002

LOW DOSE RASBURICASE FOR TREATMENT AND PREVENTION OF TUMOUR LYSIS SYNDROME IN ACUTE LYMPHOBLASTIC LEUKEMIA: SINGLE CENTRE EXPERIENCE

S. Agarwal[1], V. Chinnabhandar[1], N. Radhakrishnan[1], A. Kumar[1], D. Thakkar[1], D. Tarangini[1], A. Sachdeva[1]

[1]Pediatric Hematooncology, Sir Ganga Ram Hospital, Delhi, India

Objectives: Tumour lysis syndrome (TLS) is an oncological emergency that requires early recognition and intervention. Rasburicase is used widely for both prevention and treatment of TLS at a dose of 0.15-0.2mg/kg/day for 5-7 days. Due to financial constraints, it is difficult to administer rasburicase in the prescribed dose. We observed the effect of single dose of rasburicase (0.1-0.2 mg/kg) used at our center in management of TLS
Methods: A retrospective analysis of ALL/Lymphoma patients who had features of TLS from Jan 2006 -Jan 2014 was done. Biochemical markers were analyzed before and after rasburicase administration
Results: 34 patients suffering from ALL/Lymphoma developed features of TLS during the study period. Rasburicase was used only in 17 children because of financial constraints.13 out of 17 patients had ongoing TLS at admission and 4 developed it after chemotherapy was started. Age range 0.8 to 15 years; Dose range (weight based) 0.1mg/kg to 0.2mg/kg. Range of Uric acid 4.8mg/dl to 12.6mg/dl.
Range of Creatinine 0.3mg/dl to 1.5mg/dl. Baseline median UA and creatinine levels were 8.9mg/dl and 0.8 respectively. Median serum UA levels 6, 12, 24 hours after rasburicase administration were 8.4, 5.5,2.4mg/dl. All patients had a significant reduction in uric acid levels on the first day, and creatinine, phosphate, and potassium reduced propotionately as well. Only 1 patient had to undergo hemodialysis of all the patients who were given rasburicase, due to rising creatinine. However, 4 patients had to undergo hemodialysis in whom rasburicase could not be given.
Conclusions: Financial constraints in developing countries poses a great challenge in management of cancer cure and there is a pressing need to develop cost efficacious yet effective modalities of treatment. Our study suggests that a single dose rasburicase is effective in managing TLS. It effectively reduces the need for renal replacement therapy.

EP-003

COMPARATIVE ANALYSIS OF HDAC 2,4,5,7,8, AND 9 M-RNA EXPRESSION LEVELS IN PEDIATRIC ACUTE LEUKEMIA PATIENTS IN BEFORE AND AFTER CHEMOTHERAPY COMPARE TO HEALTHY CONTROLS

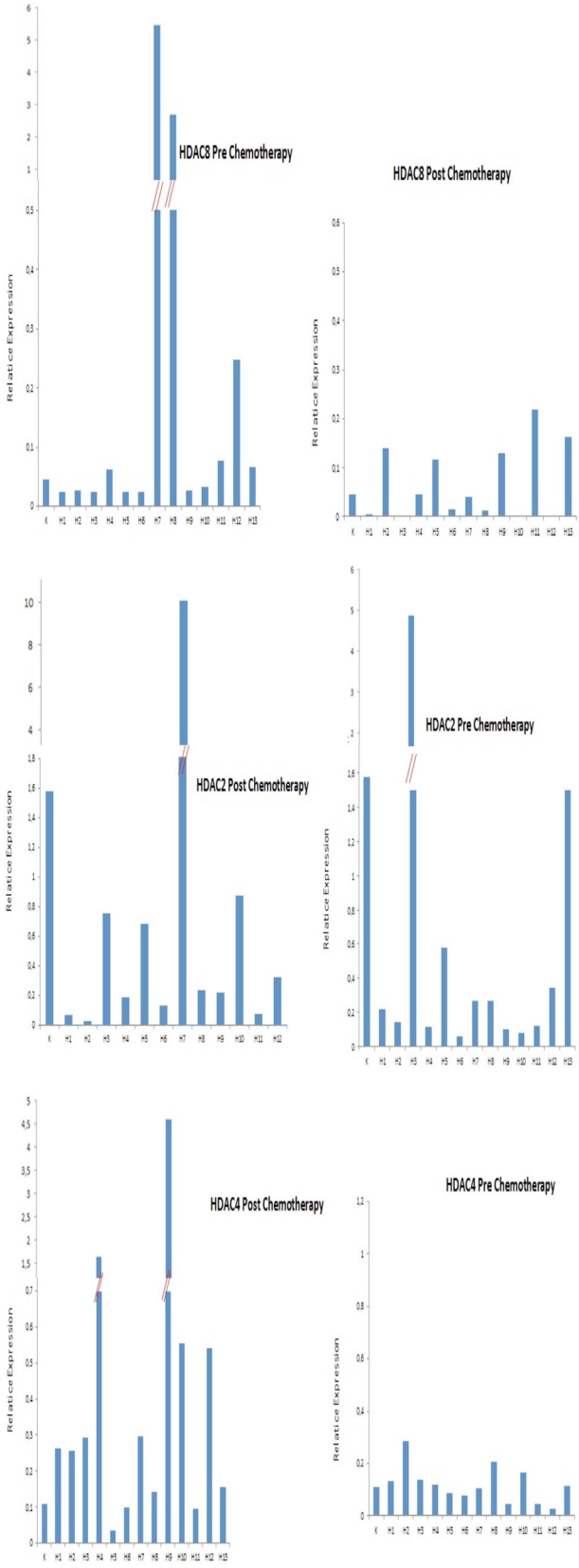
D. Akin[1], D. Aslar[1], M. Mumcuoglu[1], U. Ezer[1], E. Kurekci[2], N. Akar[3]

[1]Cancer Research and Genetik Laboratory, LOSEV Foundation for Children with Leukemia, Ankara, Turkey; [2]Department of Pediatric Haematology, Gulhane Military Medical Academy, Ankara, Turkey; [3]Department of Pediatric Clinical, TOBB-ETU Hospital, Ankara, Turkey

Objectives: HDACs are involved in both nucleosomal changes chromatin structure remodeling, important in gene transcription and oncogenesis regulation. Mutations and abnormal expression of HDAC have been observed in types of cancers, including haematological malignancies. This study aims evaluting mRNA expression of HDACs (2,8,4,5,7,9) in childhood leukemia samples pre-postchemotherapy.
Methods: The study population consists of 13 patients 1to15 years old, admitted to hospital with a diagnosis is of acute leukemia. RNA isolation was performed using RNA isolation kit. Expression data was analyzed using RelativeBasicQuantification software provided with LightCycler480II.

Sex	Age	Diagnosis	Karyotype
M	1y	Pre B-ALL	tri 4,10,14,17,21
F	3y	ALL	Normal Karyotype (46,XX)
M	3y	ALL	Normal Karyotype (46,XY)
F	2y	CALLA+ALL	Normal Karyotype (46,XX)
F	9y	T-ALL	AML relapse
F	16y	My+ Pre B hücreli ALL	Relapse, chimerism, t(9;22) + CNS relapse- 2 HKHN -2 KI
M	6y	my+Pre-B-ALL	Normal Karyotype (46,XY), t(12:21)
M	5y	Pre B-ALL	Normal Karyotype (46,XY), t(9;22)
F	6y	Pre B-ALL	Normal Karyotype (46,XX), t(4:11)
F	8y	AML-M3	t(15:17)
M	6y	AML-M3-APL	t(15:17)
M	9y	AML	ex t(9;22), t(8:21) –molecular relapse

Results:



Interestingly our results indicate differing leves of HDACs expression amongs patients while controls remain relatively consistant. Pre-posttherapy samples of HDAC2 showed lower levels of expression when compared to controls except for two patients. We observed dramatic

increases in posttherapy samples are opposed to pretherapy samples for HDAC4 expression. HDAC8 showed great variants in expression both for pre-post samples. HDAC5 expression were high compared to controls for pre therapy samples and decreased to control levels in postsamples. HDAC7 expression demonstrated that no significant changes in either preor postsample, except for one patient. We observed low levels of HDAC9 expression in samples at both experimental time points. One patient diagnosed with My+PreBcell ALL, with t (9;22), CNS relapse and two bone marrow transplants showed unusually high HDAC7 expression in the pretherapy sample. Another patient who had high levels of HDAC4, relapsed and died duringtreatment. One preBcell ALL patient showing MLL translocation had high levels of HDAC2. While another preB-cell ALL patient with normal karyotype showed high HDAC2 expression in posttherapy high HDAC8 expression pretherapy samples. Lastly a PreBcell ALL patient with t (12;21) showed high HDAC8 expression in pretherapy.
Conclusions: Some studies have been conducted in haematological malignancies for HDAC expression. In this study we analyzed expression changes of HDAC2,4,5,7,8, and9 in pediatric leukemia samples pre-post threapy. We found HDAC4,5and9 expression changes are important in pediatric leukemia since these genes have a role in cell differentiation, angiogenesis and regulation pathways.

EP-004

REDUCING SIDE EFFECTS OF SEVERE ASPARAGINASE REACTIONS (ANAPHYLAXIS): A POSSIBLE ROLE FOR USE OF METHYLENE BLUE AFTER GIVING EPINEPHERINE TO QUICKLY REDUCE ANGIOEDEMA AND HYPOTENSION

P. Anderson[1], C. Murphy[1], K. Arnold[1], M. Devine[1], J. Kaplan[1]

[1]Pediatrics, Carolinas HealthCare System, Charlotte, USA

Objectives: L-asparaginase is an effective drug for acute lymphoblastic leukemia and lymphoma with a safety profile which includes severe allergic reactions. These usually occur after repeat dosing and are associated with life-threatening symptoms including angioedema (hives, lip, mouth and throat swelling, hoarseness, wheezing, and difficulty breathing) and hypotension. Anaphylaxis treatment currently involves administration of epinephrine then other supportive measures. To more rapidly reduce reaction severity, we have started using an additional measure, methylene blue, which inhibits angioedema and hypotension.
Methods: In 2014, review of literature shows many papers supporting use of methylene blue to treat anaphylaxis; methylene blue inhibits guanylyl cyclase and nitric oxide associated vasopermeability. Methylene is commercially supplied as 100 mg blue liquid in 10 mL vials containing 10 mg/mL. Each vial costs about $11 US. Recommended dose is 2mg/kg and is given as a rapid iv bolus over 1-2 minutes. Timing is after the epinephrine is given.
Results: Input from pediatric oncologists, nursing, pharmacy, and Emergency Department resulted in improved pathways of care for reactions to L-asparaginase. These are now characterized as 1) skin only (e.g. hives) or 2) more serious in which prompt administration of epinephrine and team care is started. For 'skin only' reactions, no epinephrine is recommended and diphenhydramine (0.5 mg/kg iv), hydrocortisone (1mg/kg iv) and famotidine (1 mg/kg iv) are given. For severe reactions, a methylene blue bolus infusion is given immediately after 0.01 mg/kg IM epinephrine and additional measures are done including albuterol nebulization, oxygen & pulse oximetry, diphenhydramine, hydrocortisone, famotidine, and hospital admission for monitoring via the Emergency Department. We also encourage parents to take a cell phone picture, so future caregivers can better understand the severity of rash and/or lip&face swelling.
Conclusions: Methylene blue is an inexpensive and effective means to ameliorate severe L-asparaginase reactions.

EP-005

DEMOGRAPHICS AND DISEASE RESPONSE EVALUATION IN PEDIATRIC HIGH RISK ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS AT A TERTIARY CARE CENTRE

S. Anwar[1], M. Faizan[1]

[1]Paeds Hematology/Oncology, Children Hospital, Lahore, Pakistan

Objectives: The main objective of the study is to discuss presentation and outcome of children with acute lymphoblastic leukemia (ALL).
Methods: We present a retrospective study, looking at demographics and outcome of children with ALL presented to the hematology and oncology department of the children's hospital Lahore between January 2009 and December 2009. Children with Bone Marrow biopsy proven ALL were included and data regarding age, gender, risk categorization and outcome were recorded and analyzed. Children were stratified as high risk who were <2 and >9 years of age, BFM-risk factor 1.2 or above, CNS disease and mediastinal mass on presentation. Lahore Group Protocol for acute lymphoblastic Leukemia LALL01 (BFM and UKALLXI based) was used for treatment.
Results: A total of 198 patients were included. Seventy percent were males. Majority 141 (66.6%) were between 2-8.9 years of age while 44 (22.2%) patients were of 9 years and above. One hundred and sixteen (60%) had high risk disease and only 55 (27%) with standard risk. Initial WBC was >100,000/mm3 in 35 (17.6%), 50,000-100,000/mm3 in 14 (7%) and 47 (23.7%) had 10,000-50,000/mm3. BFM risk factor was 1.2 and above in 66 (33.3%), 14 (7%) patients had CNS disease and 5% mediastinal mass on presentation. Seventy eight (40%) patients had completed treatment, 44 (22.2%) left against medical advice and 38 (19.1%) died. Twenty nine (14.6%) had relapse and among them 76% relapsed while on treatment.
Conclusions: High risk disease is the most common presentation of ALL in children at our centre with initial High WBC count, massive organomegaly and male predominance. Abandonment is another major factor affecting the overall survival rate. However overall survival is almost 50% in our treated patients.

EP-006

SAFETY OF NALBUPHINE ON NEURAL TISSUES IN THE RATS AND ITS EFFICACY IN THE TREATMENT OF ACUTE HERPETIC PAIN IN PEDIATRIC WITH ACUTE LYMPHOBLASTIC LEUKEMIA

J. Attia[1], M. Kamel[2], R. Yousef[3]

[1]Anesthesia and I.C.U, Faculty of medicine, Minia, Egypt; [2]Pharmacolgy department, Faculty of medicine, Minia, Egypt; [3]Pathology department, Faculty of medicine, Minia, Egypt

Objectives: Acute lymphoblastic leukemia (ALL) was previously shown to cause severe impairment in the immunity and in turn makes children more susceptible for viral infection especially herpes zoster that is manifested by severe pain. The main purpose of this study was to evaluate: firstly, the safety of nalbuphine experimentally on the neural tissues of the rats and secondly, the efficacy of the caudal injection of nalbuphine with minimal dose of oral paracetamol as an analgesic in pediatric patients with ALL suffering from acute herpetic pain.
Methods: Two studies were performed. In Study 1, Evaluation the safety of nalbuphine HCl on neural tissues experimentally in rats. The treated groups were injected with nalbuphine (0.5, 1, 2, 4 and 5 mg/kg) intrathecally each after one day for 14 days. The longitudinal section of the cerebellum and transverse section of spinal cord excised from each animal for histological examination. In Study 2. The study was conducted on 30 children. Nalbuphine was injected caudally in dose of 5 mg, each dose every 48 h for a period of 14 days, and paracetamol was administrated in dose of 7.5 mg/kg once every 4 hours,
Results: The results revealed that nalbuphine showed no pathological changes in both cerebellum and spinal cord. On the other hand, the protective effect of nalbuphine with minimal dose of paracetamol was associated with a significant analgesic effect in ALL children Its analgesic effect was assessed by facial pain scale (FPS), behavioral pain assessment (BPA) with motor block effect assessed by Bromage score.
Conclusions: These findings show that nalbuphine caudally injected induced proper analgesic effect with minimal dose of paracetamol in acute herpetic pain in pediateric patient with ALL.

EP-007

TOXICITY DURING HIGH DOSES OF METHOTREXATE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

B. Choneska Jovanova[1], S. Glamochanin[1], K. Martinova[1], Z. Trajkova Antevska[1], S. Kocheva[1], A. Jovanovska[1]

[1]Hematology and oncology, University Clinic for Children diseases, Skopje, Macedonia

Objectives: Intensification of systemic chemotherapy with inclusion of high doses methotrexate (MTX) has contributed to the improvement of event free survival in children acute lymphoblastic leukemia (ALL) and has helped to reduce cranial radiation for mostly patient. Despite this benefit, this agent might cause serious toxicity, even life treating events during the treatment. Because of that, prediction, early detection and management of toxic effects during therapy with high doses of MTX is still great challenge for every pediatric oncologist. The aim of our study was to evaluate the incidence of toxic effects of chemotherapy with high doses MTX ($5g/m^2$) and to compare them with toxicity during application of lower doses MTX ($2g/m^2$)
Methods: Retrospective record review was done in 77 children with standard risk ALL treated in our department. Forty five of them were treated with $5g/m^2$ and 32 of them were treated with $2g/m^2$ (historic group). Toxicity was registered according the protocol for acute toxicity, part of the ALL BFM 95 protocol.
Results: Toxicity of high doses MTX was predominant in the group treated with 5g/m2. Most significant toxic effects were hepatotoxicity 77% versus 25% ($p = 0.000013$), oral mucositis 35.56% versus 18.75% ($p = 0.023$) and myelosupresion. Anemia gradus 3 was present in 37.78% versus 6.25%, trombopenia gr 3 in 28.8% versus 12.5% and patient of the study group have experienced more episodes of neutropenia 99 versus 32. Bacterial and viral infections were predominant in the study group due to severe myelosupresion.
Conclusions: In our study toxic effects were more common in the study group due to application of higher doses MTX. Variationes in toxicity between the patients in the study group are probably due to the genetic differences in the drug metabolism. Current researches are dedicated on discovering markers which will be able to predict the risk for appearance of MTX toxicity.

EP-008

MOLECULAR CYTOGENETIC ABNORMALITIES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA–EXPERIENCE FROM A TERTIARY CARE CENTER IN NORTH INDIA

Y.R. Chopra[1], M. Ramzan[1], R. Sharma[1], S. Katewa[1], S. Yadav[1]

[1]Pediatric Hematology Oncology and Bone Marrow Transplant Unit, Fortis Memorial Research Institute, Gurgaon, India

Objectives: The aim of the study was to determine the frequency of cytogenetic abnormalities in childhood ALL patients coming to tertiary care hospital in developing country.
Methods: Retrospective study (2013- 2014). Inclusion criteria - 61 ALL patients in our follow-up, Age<16yrs of age. Multiplex reverse transcriptase polymerase chain reaction (Multiplex RT PCR) analysis and conventional cytogenetic were performed to detect the chromosomal abnormalities
Results: Cytogenetic analysis was done in 40 of 61 children with ALL, in rest could not be done in view of financial constraint. Twenty (17 B cells, 3 T cells) had normal cytogenetic. Twenty of them had clonal chromosomal abnormalities. Numerical imbalances consisted of hypodiploid (< 46 chromosomes, no cases), hyperdiploid (> 47 chromosomes, 14cases out of which 13 were B cell ALL and 1 was T cell ALL) and pseudodiploidy (46 chromosomes, 6 cases, All were B cell ALL). Chromosomal translocations detected by Multiplex RT PCR were observed in 9 patients. Five children had t (9:22) and 4 had t (12:21) positivity. MLL rearrangement was present in 1 infant. Complex cytogenetic were seen in 3 children. Ten out of 61 children relapsed, on BFM 95 protocol. In 6 cytogenetics could not be done, 2 had normal cytogenetics, 1 had t (12:21) (Standard risk) and 1had t (9:22) (High risk).
Conclusions: In 1/3rd (20/61) cytogenetics could not be performed and so complete risk stratification was hindered. Six children relapsed and cytogenetics was not known which can be confounding factor for risk stratification, management and prognosis and should be aimed in every patient.

EP-009

MTOR RELATED PROTEIN EXPRESSION IN CHILDHOOD ALL

M. Csóka[1], K. Nemes[1], A. Márk[2], M. Hajdú[2], Z. Váradi[1], A. Sebestyén[2]

[1]2nd Dept of Pediatrics, Semmelweis University, Budapest, Hungary; [2]1st Dept of Pathology and Experimetal Cancer Res, Semmelweis University, Budapest, Hungary

Objectives: Improvement of treatment of childhood ALL may depend on the development of targeted therapies. mTOR kinase, a central mediator of several signaling pathways, has recently attracted remarkable attention as a potential target in pediatric ALL. However, limited data exists about the activity of mTOR.
Methods: In the present study, the amount of mTOR activity dependent phospho-proteins was characterized by ELISA in human leukemia cell lines and in lymphoblasts from childhood ALL patients (n = 49). Expression was measured before and during chemotherapy and at relapses. Leukemia cell lines exhibited increased mTOR activity, indicated by phospho-S6 ribosomal protein (p-S6) and phosphorylated eukaryotic initiation factor 4E binding protein (p-4EBP1). Elevated p-4EBP1 protein levels were detected in ALL samples at diagnosis; efficacy of chemotherapy was followed by the decrease of mTOR activity dependent protein phosphorylation. Optical density (OD) for p-4EBP1 (ELISA) was significantly higher in patients with poor prognosis at diagnosis, and in the samples of relapsed patients.
Results: Our results suggest that measuring mTOR activity related phospho-proteins such as p-4EBP1 by ELISA may help to identify patients with poor prognosis before treatment, and to detect early relapses.
Conclusions: Determining mTOR activity in leukemic cells may also be a useful tool for selecting patients who may benefit from future rapalog treatments.
Supported by OTKA K81624 and K84262.

EP-010

ANALYSIS OF ADVERSE EVENTS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL) TREATED WITH PROTOCOL ALL IC BFM 2002 – SINGLE-CENTRE RETROSPECTIVE STUDY

K. Derwich[1], P. Marciniak-Stepak[1], O. Zajac-Spychala[1], M. Baranska[1], J. Wachowiak[1]

[1]Pediatric Oncology Hematology and Transplantology, Poznan University of Medical Sciences, Poznan, Poland

Objectives: The aim of this study was a retrospective analysis of adverse events in children with ALL treated with protocol ALL IC BFM 2002 between 2002 and 2013 at our department.
Methods: According to ALL IC BFM 2002 criteria 196 patients (90 females, 106 males) 1-18 years of age (med. 5.04 yrs) were classified to SR- 56 (29%), IR- 73 (37%) or HR- 66 (34%) group. Remission on time was achieved by 190 (97%) patients. At a median follow-up was 70,9 months (range: 19.8-128.5 months). Results of the treatment were analysed as pEFS and pRFS.
Results: Among adverse events 26 (13.3%) relapses were observed within 1.1-69.5 months (med. 23.5 months) from the diagnosis. There were 9 (34.6%) very early, 5 (19.2%) early and 12 (46.2%) late relapses: 12 (46.1%) in BM (SR: 4, IR: 3, HR:5), 4 (15.4%) in CNS (SR: 1, IR:1 HR:2), 1 (3.8%) in testis (HR), 1 (3.8%) in mediastinum (HR) and 8 (30.8%) mixed relapses: 6 BM-CNS (SR: 1, IR: 3, HR: 2), 1 CNS-testicular (IR) and 1 BM-CNS-abdominal (SR). There were 26 (13.3%) deaths: 1 (3.8%) early death; 14 (53.8%) due to treatment complications (9 in I CR (IR: 2, HR: 7), 5 in II CR (IR:2, HR:3)), 10 (38.5%) due to leukaemia relapse/progression (SR:3, IR:2, HR:5), 1 (3.8%) in car accident. 159 patients are in I CR 159 (81.1%) and 11 in II CR (5.6%).
Conclusions: An analysis has shown that BM, CNS and mixed relapses were seen in high proportion of patients from SR and IR groups. High rate of deaths (mainly in HR group of patients) was noticed due to treatment complications.

EP-011

CLINICO-HEMATOLOGICAL PROFILE OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN: AN EXPERIENCE FROM JAMMU (INDIA)

S. Digra[1], S.S. Slathia[1], R. Harish[1]

[1]Pediatrics, Government Medical College, Jammu, India

Objectives: To study the clinico-haematological profile of children presenting with ALL.
Methods: All the children hospitalized with ALL in the Department of Pediatrics, Government Medical College, Jammu during a period of 6 years were included in this retrospective study and their clinical and hematological profile was analyzed in detail.
Results: A total of 62 patients were diagnosed as ALL with male to female ratio of 2.4:1. Majority (77.4%) of children with ALL were less than 10 years of age. Out of 62 patients of ALL, 51 were ALL-L1, 10 ALL-L2 and 1 ALL-L3. 43 ALL- L1 and 5 ALL-L2 patients were less than 10 years of age. Fever, pallor, bleeding manifestations, hepato-splenomegaly, lymphadenopathy, generalized weakness, weight loss and bone pains were present in 65%, 61%, 55%, 53%, 45%, 24%, 21% and 19% respectively. 73% of ALL patients had hemoglobin less than 6 gm% while 20% and 7% had hemoglobin of 6-10gm% and more than 10 gm% respectively. 45% of these patients had decreased and 16% had increased Mean Cell Volume and Mean Cell Hemoglobin. Increased total leucocyte counts between 10000-50000/dl were seen in 37% patients, while counts more than 50000/dl were seen in 35% of patients. Leucopenia was seen in 24% of patients and rest had normal counts. 89% patients had thrombocytopenia. 48% had lymphoblasts and 5% had atypical cells in their peripheral blood films.
Conclusions: We found that in this region ALL-L1 FAB is common under the age of 10 years. Fever, anemia, bleeding manifestations, hepato-splenomegaly and lymphadenopathy were the commonest presenting features. Majority of them had leukocytosis and thrombocytopenia at the time of presentation.

EP-012

BONE MARROW EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR, VEGF RECEPTOR-1 AND VEGF RECEPTOR-2 IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

V. Dinand[1], S. Sharma[1], N. Rao[2], M. Kalra[1], P. Gupta[3], S. Preeti[2], N. Radhakrishnan[1], A. Sachdeva[1]

[1]Pediatric Hematology Oncology & BMT, Sir Ganga Ram Hospital, Delhi, India; [2]Research Department, Sir Ganga Ram Hospital, Delhi, India; [3]Histopathology Department, Sir Ganga Ram Hospital, Delhi, India

Objectives: Angiogenesis plays an important role in hematological malignancies. Vascular endothelial growth factor (VEGF) promotes angiogenesis via interaction with VEGF receptors-1 and -2. Blood levels of VEGF and its receptors have shown some prognostic significance in pediatric acute lymphoblastic leukemia (ALL). We assessed the significance of sVEGF and bone marrow (BM) expression of VEGF, VEGFR-1 and VEGFR-2.
Methods: Sixty-six children with newly diagnosed with ALL, 5 children with relapse, and 9 in remission after completion of ALL therapy were prospectively enrolled (2008-2012). Controls included 50 healthy children and 10 normal BM biopsies. sVEGF level was measured at presentation of ALL (new and relapsed), at the time of remission induction, and at the end of ALL therapy. Immunochemistry for VEGF, VEGFR-1 and VEGFR-2 was done on BM biopsies at those time points.
Results: Untreated leukemia BM samples (n = 43) showed strong VEGF and VEGFR1 expression in >90% of blast cells. Conversely, most normal BM (n = 10) had moderate VEGF and VEGFR1 expression in 50-89% of mononuclear cells. VEGFR-2 expression was moderate in leukemic samples, in 50-89% of blast cells, contrasting with normal samples which showed strong VEGFR-2 expression in 50-89% of hematopoietic cells. After remission induction (n = 24) and at the end of treatment (n = 9), immunochemistry results were comparable with BM controls. Median (interquartile range) sVEGF was significantly lower in untreated ALL [15.9ng/ml (8.6-30.4)] and relapsed cases [21.5ng/ml (10.9-36.1)] as compared to controls [50.0ng/ml (30.3-73.6)] and to old ALL cases enrolled after treatment completion [48.0ng/ml (15.8-68.9)], p
Conclusions: BM expression of VEGF and VEGFR-1 is strong in ALL blasts, while VEGFR-2 is mainly expressed by normal mononuclear cells. Overexpression reduces with hematological remission.

EP-013

PREDICTORS OF ACUTE CHEMOTHERAPY-ASSOCIATED TOXICITY IN CHILDREN WITH ALL

B. Djurdjevic-Banjac[1], N. Krstovski[2], D. Janic[2], J. Predojevic-Samardzic[1], L. Dokmanovic[2], D. Malcic[1], J. Lazic[2], P. Rodic[2]

[1]Department of Pediatric Hematology and Oncology, Children's Hospital Banja Luka, Banja Luka, Bosnia and Herzegovina; [2]Department of Pediatric Hematology and Oncology, University Children's Hospital Belgrade, Belgrade, Serbia

Objectives: Success in treating childhood acute lymphoblastic leukemia (ALL) was achieved mainly due to intensification of cytotoxic therapy. We analyzed possible predictors of acute chemotherapy-associated toxicity in this population.
Methods: In this short study, we reviewed the medical records of children at the age of 1-18 years who were diagnosed with ALL and treated according to ALLIC BFM 2002 protocol at two academic medical centers from December 2002 to May 2010. Clinical and biological characteristics, disease characteristics at diagnosis and intensity of the chemotherapy of the patients were analyzed as the possible predictors of toxicity.
Results: The retrospective study included 123 patients with ALL at the average age of 7.11 years (median 5.5 years) and toxicity data. 98.35% of the patients had at least one toxic complication during the treatment. Age ($p = 0.973$), sex ($p = 0.847$), body mass index ($p = 0.994$), initial leukocyte count ($p = 0.979$), organomegaly ($p = 0.894$) and CNS status ($p = 0.608$) at diagnosis, imunophenotypic ($p = 0.929$), molecular ($p = 0.994$), and cytogenetic ($p = 0.908$) features of leukemia were not associated with higher toxicity. Presence of central venous catheter was not associated with total toxicity as well as the infections as the most common complication ($p = 0.056$, $p = 0.181$). Dose-intensity of the chemotherapy was only associated with higher incidence of the entire toxicity ($p = 0.047$), particularly infections ($p < 0.001$). Cycles of chemotherapy in high-risk patient group (HR) with high-dose of cytarabine and methotrexate were significantly associated with higher toxicity ($p < 0.001$).
Conclusions: In our sample, we have shown that the intensity of chemotherapy was the only predictor of chemotherapy-associated toxicity and that the patients in the high-risk group with most intense chemotherapy have higher rates of total toxicity, particularly infections. This group of patients requites increased intensive supportive care.

EP-014

CORRELATION BETWEEN DIAGNOSIS DELAY AND RISK STRATIFICATION OF B-PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

M. Dwinata[1], E. Supriyadi[2], M. Juffrie[2]

[1]Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia; [2]Department of Pediatrics, RSUP Dr. Sardjito, Yogyakarta, Indonesia

Objectives: To understand the correlation of diagnosis delay with the risk stratification of B-precursor ALL in children.
Methods: Fifty eight patients diagnosed as precursor B ALL from 2008 to 2011 in Pediatric Department, RSUP Dr. Sardjito, Yogyakarta, Indonesia were observed.
Results: Among 58 medical record analyzed, 46 patients were classified as standard risk ALL and 12 patients were classified as high risk ALL. The mean of diagnosis delay was 58 days. Analysis using mean of delay as cut-off showed no significant correlation ($p = 0.3$), but the odd ratio was 1.99 (CI = 0.55-7.22).
Conclusions: There is 2 times increased risk to become high risk ALL after 58 days of delay. Further study with bigger sample size should be conducted to confirm the result.

EP-015

PREVALENCE OF CMV INFECTION IN ALL PATIENTS

M.A. Ehsani[1], M. Karahroudi[1], A.A. RahabariManesh[1], M. Aghajani[1], Z. JaliliTahmasebi[1], E. Shahgholi[1], A.P. Meisami[2], A. Mehrvar[3], M. Tashvighi[3]

[1]Pediatric Hematology and Oncology, Tehran University of Medical Sciences (TUMS), Tehran, Iran; [2]Community Medicine, Tehran University of Medical Sciences (TUMS), Tehran, Iran; [3]Pediatric Hematology and Oncology, MAHAK charity hospital, Tehran, Iran

Objectives: CMV is an opportunistic infection that may be lethal in immunocomprimized patients
Methods: All ALL patients who were admitted in Bahrami Hospital (TUMS), Tehran, Iran between March 2011 and March 2013 were prospectively followed. Eligible patients had a previous diagnosis of ALL and had been treated with UK-ALL-X protocol.
Only patients who were at least one year post-induction chemotherapy were included. None of the patients received hematopoietic SCT. Patients with a positive result for CMV viremia according to a (PCR) *and* with clinical or other laboratory findings suggestive of CMV disease were treated with oral valganciclovir (10 mg/kg twice daily) for 6 weeks. After discharge from the hospital, the first follow up was at 2 weeks after completion of the 6-week course of treatment. Four weeks after completion of treatment, patients were re-evaluated for clinical improvement and repeat PCR. CMV serology was performed at the time of initial diagnosis of CMV infection. Patients with viremia but without evidence of CMV disease did not receive treatment; these patients were followed closely. A Chi-square test (with Fisher's exact test when needed) was used to compare proportions between groups. A p value of <0.05 was considered statistically significant.
Results: Total of 171 patients (males: 49.1%) with a median (range) age of 8 (2-17) years were included. Median (range) values for Hb, WBC, platelets, ALT, and AST were 9.8 (7.9-13.6) g/dL, 4.7 (1.5-11.2) $x10^9$/L, 235 (36.8-470) $x10^9$/L, 32 (10-133) U/L, and 33 (15-83) U/L, respectively. Two (1.2%) patients had hepatosplenomegaly. A total of 10 (6.4%) patients had CMV viremia ($p = 1.00$). Males and females comprised 3 and 7 of the 10 viremic patients, respectively ($p = 0.33$).
Conclusions: In this study Anti-CMV IgM sensitivity was 100% and its specifity 98.77, and PPV = 83.3. It is suitable test for screening and detect the infection.

EP-016

EARLY COMPLICATIONS AND OUTCOME OF CHILDREN WITH LEUKEMIC HYPERLEUKOCYTOSIS: EXPERIENCE FROM A DEVELOPING COUNTRY

A.S.B. Syed[1], Z. Fadoo[1], A. Haq[1], S. Ashraf[2], M. Alam[1], M. Khan[2]

[1]Pediatric Hematology & Oncology, Aga Khan University & Hospital Karachi Pakistan, Karachi, Pakistan; [2]Pediatric Hematology & Oncology, Children Cancer Hospital, Karachi, Pakistan

Objectives: We studied the presenting clinical and laboratory features, early complications, and outcome of children with acute leukemia and hyperleukocytosis who were diagnosed and treated in two medical centers of Karachi between January 2009 and December 2013.
Methods: This was a descriptive, observational, non-interventional, retrospective analysis.
Results: Hyperleukocytosis was found in 146 (17.9%) out of 812 patients diagnosed as acute leukemia, precursor T cell ALL in 77 (52.7%), precursor B cell ALL in 61 (41.8%), acute myeloid leukemia in 5 (3.4%) and chronic myeloid leukemia in 3 (2.1%). Age group was 1-5 years in 61 patients (41.8%) and above 10 years in 56 (38.4%), more common among males 111 (76.0%). Half, 72 (49.3%) had symptoms for >30 days. Seventeen patients (11.6%) had CNS involvement. Therapeutic interventions were hydration/allopurinol in 138 (94.5%) patients. Leukapheresis was done in 4 patients, one of whom expired. Median hemoglobin was 7.35 g/dL (range 2.0 g/dL to 13.1 g/dL). Median total leukocyte count was 181.0×10^9/L (range 102×10^9/L to 782×10^9/L). Median platelet count was 30×10^9/L (range 5×10^9/L to 558×10^9/L). Median LDH was 3184 IU/L (range 520 IU/L to 26024 IU/L). Median uric acic was 5.98 mg/dL (range 1.5 mg/dL to 43.4 mg/dL). Median phosphate was 4.3 mg/dL (range 0.9 mg/dL to 16.6 mg/dL). BCR ABL translocation was positive in 14 patients (9.6%). 30 patients (20.5%) expired after their first admission. The major cause of death was infection in 10 (30%), respiratory complication with infection in 7 (23.3%), CNS with respiratory complications and infection in 3 (10%), only renal complication in 2 (6.6%).
Conclusions: Early death and complications can be prevented by early referrals, timely and appropriate antibiotics, management of tumor lysis syndrome, timely use of ICU modalities and leukapheresis whenever required.

EP-017

NON-CODING RNAS: A NEW FIELD IN THE PHARMACOGENETICS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

E. Lopez-Lopez[1], I. Martin-Guerrero[1], A. Gutierrez-Camino[1], J. Uriz[2], A. Navajas[3], P. Garcia-Miguel[4], A. Garcia-Orad[1]

[1]Genetics Physical Anthropology and Animal Physiology, University of the Basque Country, Leioa, Spain; [2]Department of Paediatrics, Hospital Donosti, San Sebastian, Spain; [3]Department of Oncohaematology, Hospital Cruces, Bilbao, Spain; [4]Department of Oncohaematology, Hospital La Paz, Madrid, Spain

Objectives: Acute lymphoblastic leukemia (ALL) treatment can produce severe toxicity. In the last years, pharmacogenetic studies have been performed in order to search for markers of toxicity in pediatric ALL. However, up to date, *TPMT* is the only marker in ALL with clinical guidelines for drug dosing. The majority of the studies by now have focused in coding regions (1.5% of the entire genome). A promising field in pharmacogenetics are regions that do not codify proteins but may have a regulatory function, such as non-coding RNAs (ncRNAs). Alterations in the ncRNA expression or in their function have been associated with drug response in different cancers. These alterations in ncRNAs could be due to genetic polymorphisms. The aim of the present study was to evaluate whether polymorphisms in ncRNAs lead to drug response.
Methods: We analyzed blood samples from pediatric B-cell ALL patients during complete remission treated with the LAL/SHOP protocol. We selected all the SNPs described in pre-miRNAs with a MAF > 1% and SNPs in long non coding RNAs (lncRNAs) dysregulated in cancer, using the VeraCode GoldenGate Genotyping assay from Illumina.
Results: In a preliminary study including 46 SNPs in miRNAs and 152 patients, we found for the first time an association between polymorphisms in mir-300 and mir-453 and toxicity in B-ALL. Taking into account these results, we have extended the study increasing the number of patients and SNPs to a total of 362 SNPs: 235 in 222 pre-miRNAs and 127 in 16 lncRNAs. We have obtained very promising results.
Conclusions: Genetic variants in ncRNAs could be new toxicity markers in the treatment of pediatric ALL.
This project was supported by RETICS (RD/12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13, SAI10/03, and 2006111015).

EP-018

NEW SUSCEPTIBILITY MARKERS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: NON CODING RNAS

A. Gutierrez-Camino[1], E. Lopez-Lopez[1], I. Martin-Guerrero[1], N. Garcia de Andoin[2], A. Navajas[3], P. Garcia-Miguel[4], A. Carbone Bañeres[5], A. Garcia-Orad[1]

[1]Genetics Physical Anthropology and Animal Physiology, University of the Basque Country, Leioa, Spain; [2]Department of Paediatrics, University Hospital Donostia, San Sebastian, Spain; [3]Department of Oncohaematology, University Hospital Cruces, Bilbao, Spain; [4]Department of Oncohaematology, University Hospital La Paz, Madrid, Spain; [5]Department of Oncohaematology, University Hospital Miguel Servet, Zaragoza, Spain

Objectives: Evidence for an inherited genetic risk for pediatric acute lymphoblastic leukemia (ALL) has been provided in several studies. Most of them focused on coding regions. However, those regions represent only 1.5% of the entire genome. The expression of non coding RNAs (ncRNAs), specifically microRNAs (miRNAs) and long non coding RNAs (lncRNAs), has been shown to be dysregulated in ALL, suggesting that they may have a role in ALL risk. Changes in ncRNA function may occur through genetic variants. Therefore, the aim of this study was to evaluate whether polymorphisms in ncRNA contribute to a predisposition for childhood ALL.
Methods: We analyzed blood samples of B-cell ALL patients during complete remission and healthy controls. For the study, we selected all the SNPs described in pre-miRNAs with a MAF $> 1\%$ and SNPs in dysregulated lncRNA in cancer, using the VeraCode GoldenGate Genotyping assay from Illumina.
Results: In a preliminary study of 213 patients and 387 healthy controls and 46 SNPs in miRNAs we found for the first time an association between polymorphisms in mir-499, mir-449b and mir-612 and susceptibility in B-ALL. Taking into account these results, we have increased the number of patients to 317 and the number of SNPs to 362. We selected 235 SNPs in 222 pre-miRNAs genes, and 127 SNPs that cover 16 long-non coding RNAs.
Conclusions: Our results suggest that SNPs in non-coding RNAs may affect B-ALL susceptibility and may represent novel markers of B-ALL susceptibility.
This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13, S-PE12UN060).

EP-019

THERAPEUTIC POTENTIAL OF DASATINIB AGAINST BCR-ABL1-NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA

H. Goto[1], S. Goto[1], N. Miyagawa[1], T. Sarashina[1], T. Yokosuka[1], F. Iwasakai[1], S. Hamanoue[1], K. Fukuda[1], H. Shimbo[1], J. Nagai[1]

[1]Division of Hemato-Oncology/Regenerative Medicine, Kanagawa Children's Medical Center, Yokohama, Japan

Objectives: Src has recently been suggested to be a therapeutic target in both BCR-ABL1-positive and negative acute lymphoblastic leukemia (ALL). To investigate therapeutic potential of Src-inhibition, the effects of dasatinib on survival of BCR-ABL1-negative ALL cells were studied.
Methods: Cytotoxicity of imatinib or dasatinib in childhood ALL clinical samples ($n = 15$, including 2 BCR-ABL1-positive) and cell lines ($n = 7$, including 1 BCR-ABL1-positive) was studied by the WST-8 assay. In the clinical samples, the ALL cells were defined to be sensitive if% survival of cells after 4 days incubation with 10 (M of the drug was lower than 30%. The expression of pSrc or pAkt was analyzed by the phosflow assay. The combination effects of dasatinib and anti-leukemia drugs were evaluated by the improved isobologram assay.
Results: In the clinical ALL samples, 3 (20%) or 7 (46.7%) were sensitive to imatinib or dasatinib, respectively. Two BCR-ABL1-positive clinical samples were sensitive to both drugs. The 6 BCR-ABL1-negative ALL cell lines responded to dasatinib with IC50 values varied from 6.1 nM to >1 (M. None of BCR-ABL1-negative cell lines responded to imatinib. Dasatinib reduced pSrc expression, followed by subsequent decrease pAkt in ALL cells. The levels of reduction of pSrc or pAkt did not correlate with dasatinib-sensitivity among ALL cell lines. Among and-leukemia drugs, clofarabine showed the synergistic effects with dasatinib in several different concentration ratios in dasatinib-sensitive YCUB-8 cells.
Conclusions: Dasatinib is suggested to have the therapeutic role in some BCR-ABL1-negative ALL. The combination use with other drugs such as clofarabine might enhance the anti-ALL effects of dasatinib.

EP-020

A PROSPECTIVE RANDOMIZED TRIAL OF L- ASPARAGINASE VERSUS PREDNISOLONE IN PREVENTION OF TUMOR LYSIS SYNDROME IN ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS WITH HYPERLEUCOCYTOSIS

S. Gulia[1], B. Arora[1], G. Narula[1], G. Chinnaswamy[1], P.G. Subramamanium[2], S.D. Banavali[1]

[1]Pediatric Oncology, TATA Memorial Hospital, Mumbai, India; [2]Hemato-pathology, TATA Memorial Hospital, Mumbai, India

Objectives: Patients withAcute Leukaemia presenting with hyperleucocytosis develop life threatening complications. Although, leukapheresis has been the standard of care for prevention of these complications, it is expensive and not widely available. Rapid cytoreduction in these patients using steroids significantly increases the risk of tumor lysis syndrome (TLS). In view of the above, there is a need to have a safe and cost effective cytoreductive method for management of hyperleucocytosis with minimal occurrence of TLS. We hypothesize that L-asparaginase causes adequate cytoreduction with minimal TLS as compared to prednisolone in acute leukemia patients with hyperleucocytosis.
Methods: This is a prospective, randomized trial where ALL patients, with hyperleucocytosis (WBC count$>100{,}000/mm^3$), between age group 1-21 years were randomized to receive either L-asparaginase ($10{,}000IU/m^2$ on alternate days) or Prednisolone ($40\ mg/m^2$/day). The medications were continued till WBCs $< 25{,}000/mm^3$ or 120hrs after enrollment whichever was earlier. If there was less than 50% fall in blood counts after 72 hours of study, patients were taken off study. All patients received standard TLS prophylaxis measures. Primary outcome variables were incidence of laboratory/clinical TLS and secondary outcome variable was rate of cytoreduction.
Results: Amongst97 patients included, 49 were randomized to receive L-Asparaginase and 48 received Prednisolone. The median age is 9 years (1- 21 years). Median WBC count at presentation is $253000/mm^3$ (100- 694 x 10^3). While 14/49 patients in L-Asparaginase arm developed Laboratory TLS, the same was noted in 22/48 patients who received prednisolone ($p = 0.887$). One patient in prednisolone arm developed clinical TLS while none was noted in the other group. At 48 hours 31/48 patients in Prednisolone arm achieved adequate cytoreduction (WBC< 50% from baseline) compared to 24/49 in L-Asparaginase arm
Conclusions: Interim analysis of our study does not show any difference in the incidence of laboratory TLS between L-Asparaginase or Prednisolone in ALL patients with hyperleucocytosis.

EP-021

BASAL CELL CARCINOMA AFTER TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AND CONCISE REVIEW OF THE LITERATURE

F. Gumruk[1], S. Unal[1], M. Cetin[1]

[1]Division of Pediatric Hematology, Hacettepe University Medical School, Ankara, Turkey

Objectives: The cumulative incidence of secondary malignancies related to treatment of childhood ALL have been reported to be 1-10% depending on the differences in anti-leukemic treatment and follow-up duration. Herein, we report two patients who developed basal cell carcinoma (BCC) within the previous radiation field of pediatric ALL treatment and review of the literature on BCC following childhood leukemia.
Methods: A computerized literature search of electronic databases-Medline and Embase identified all published studies on the subject from the start date of the database to February 2014. The general search structure for electronic databases was (childhood or synonyms) AND (basal cell carcinoma) AND (secondary). The patients with a primary diagnosis of leukemia were included into the literature review after electronic search.
Results: Case 1 is a 29 year-old woman who developed BCC of the scalp 17 years after the successful treatment of childhood ALL. The patient was diagnosed as having B-cell ALL at the age of 12 years and was treated with chemotherapy, intrathecal treatment and 2400 cGy prophylactic cranial radiotherapy for 15 days. She developed BCC at the age of 29 years. Case 2 presented with hyperpigmented macule of 3 cm diameter at the age of 31 years-old, with a latency period of 17 years after initial diagnosis of ALL. She has previously received prophylactic cranial radiation during treatment for leukemia. The pathological evaluation confirmed BCC. In the literature there are 42 patients who developed BCC subsequent to leukemia treatment. Besides, among CCSS data 213 of 13,132 childhood malignancies developed BCC, subsequently, including leukemia as primary malignancy.
Conclusions: Basal cell carcinoma as a secondary malignancy following ALL is rare, but may occur more often among patients who have previously received radiation therapy.

EP-022

PHARMACOLOGICAL EFFECT OF EZH2 INHIBITOR IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA.

A. Iannotta[1], M. Ramaglia[1], A. Lombardi[2], V. D'Angelo[1], M. Caraglia[2], M.C. Affinita[1], C. Fusco[1], M. Di Martino[1], D. Di Pinto[1], M. Oreste[1], C. Indolfi[1], P. Indolfi[1], F. Casale[1]

[1]Women Child and General Specialized Surgery, Second University of Naples, Naples, Italy; [2]Biochemistry Biophysics and General Pathology, Second University of Naples, Naples, Italy

Objectives: Polycomb group (PcG) proteins are highly conserved epigenetic effectors that maintain the silenced state of genes involved in critical biological processes. Evidence suggests that over-expression of the histone metil transferasi Enhancer of Zeste Homologue 2 (EZH2) is strongly associated with haematologic cancer progression and poor outcome. 3-Deazaneplanocin (DZNep) is the first molecular inhibitor of EZH2. We have studied pharmacological effect between DZNep and a conventional chemotherapic agent Daunoblastina (DNB) in pediatric T-cell Acute Lymphoblastic Leukaemia (T-ALL).
Methods: Jurkat cell line and blast cells of pediatric T-ALL were grown in RPMI and treated with DNB and DZNep, single and in combination to 24h, 48h and 72h. Cell viability was analyzed by MTT and Trypan blu assay. Apoptotic cell death and cell cycle were analyzed by

Annexin-V–FITC staining and PI fluorescence. EZH2, Bcl-2 and Procaspase 8 were analyzed by western blotting assay.
Results: Our data demonstrated a synergistic effect (CI_{50}/48h = 0.88 and CI_{50}/72h = 0.80 Biosoft CalcuSyn software) on Jurkat growth inhibition by DNB/DZNep with about a 50% decrease of the sub-G0/G1 peak, presumably due to apoptosis, and a parallel increase of cells in G2/M phase. These results were confirmed by annexin analysis with an increase (26%) of early apoptosis. Moreover, we have found a 60% and 40% decrease of procaspase 8 expression in single treatment with DZNep and in combination with DNB, respectively. Therefore we observed a complete decrease of Bcl-2 protein respect to single treatment with DNB. Samples treated with DNB/DZNep evidenced an inhibition of EZH2.
Conclusions: EZH2 inhibition may offer the opportunity of a novel treatment approach that could be considered in combination with conventional chemotherapy to eradicate ALL stem cells. A better understanding of the complex epigenetic regulatory network controlling EZH2 expression and target genes would facilitate the design of novel therapeutic interventions.

EP-023

FURTHER UNRAVELING OF CHILDHOOD LEUKEMIA GENETIC BOTTLENECK PHENOMENON RELATED TO TEL-AML1: THE POSTULATION BY A MATHEMATICAL MODEL

I. Ivanovski[1], O. Djuric[2], P. Ivanovski[3]

[1]Institute for Mother and Child Healthcare, Medical Faculty University of Belgrade, Belgrade, Serbia; [2]Institute of Epidemiology, Medical faculty University of Belgrade, Belgrade, Serbia; [3]University Childrens Hospital, Medical Faculty University of Belgrade, Belgrade, Serbia

Objectives: Childhood leukemia prevention.
Methods: We did comprihensive browsing of articles in leading leukemia research journals, on the etiology of childhood leukemia and we constructed our own view on leukemia bottleneck etiology.
Results: TEL-AML1 (ETV6-RUNX1) is formed prenatally in 1% of newborns. But only one child out of a hundred children born with this gene develops leukemia (bottleneck phenomenon). In other words, out of a hundred children born with TEL-AML1 only one child is at risk for leukemia development which means that TEL-AML1 is inevitable, but not sufficient for overt leukemia. There is a stringent requirement for a second genetic abnormality for leukemia development. In most cases of TEL-AML1$^+$ leukemia, translocation t (12;21) is complemented with loss of normal TEL gene, not involved in the translocation, on contralateral 12p. The loss of normal TEL gene, i.e. loss of heterozygosity (LOH) at 12p occurs postnatally during mitotic proliferation of TEL-AML1$^+$ cell in mitotic crossing over (MCO) process. MCO is very rare event with a frequency rate of 10-6 in a 10 kb region. Since minimally deleted regions always affect at least some part of the TEL transcriptional framework, follows that reported frequency of $\sim 10^{-6}$ MCO in a 10 kb locus are valid for MCO frequency at 12p in naïve TEL-AML1$^+$ cells.
Conclusions: The exploration and identification of environmental exposure (s) that cause proliferation of TEL-AML1$^+$ cell in which approximately 10^6 mitoses are generated to cause 12pLOH i.e. TEL deletion, and/or introduction of mitotic crossing over inhibitors may contribute to childhood leukemia prevention.

EP-024

ANALYSIS OF PROGNOSTIC RISK FACTORS FOR PEDIATRIC ACUTE LEUKEMIA WITH FUNGEMIA

J. Jiang[1]

[1]Hematology and Oncology Center, Bei Jing Children's Hopspital, Beijing, China

Objectives: To investigate the epidemiology of fungemia and provide evidence for clinical therapy.
Methods: A retrospective survey was done with the 42 cases of fungemia in our hospital from Jan 2002 to Jan 2011
Results: 40 cases candida fungemia accounted for 95.2% in 42 fugemia. The main pathogen agent was non-Candida albicans in candida fungemia, which were candida albicans (14.3%), candida parapsilosis (38.1%), candida glabrata (35.7%), candida tropicalis (2.4%). 11 uneffective cases accounted for 26.2%. Multiple-factor analysis showed that neutropenia time>7 days, antibiotic using time>7 days and fungal infection history correlated with bad prognosis. Our study also showed that chemotherapy regiments including hormone, combining with other organs fungal infection and non-Candida albicans were risk factors of bad prognosis.
Conclusions: The main pathogen agent of fungimia is candida, especially non-Candida albicans. Neutropenia time>7 days, antibiotic using time>7 days and fungal infection history correlate with bad prognosis.

EP-025

NEUROLOGIC COMPLICATIONS DUE TO CHEMOTHERAPY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS TREATED WITH ALL IC BFM 2009 – SINGLE CENTER EXPERIENCE

M. Jovic[1], D. Micic[1], M. Kuzmanovic[1], A. Jovanovic[1], R. Kravljanac[2], S. Gazikalovic[3]

[1]Department of Pediatric Hematology, Mother and Chiled Health Care Institute, Belgrade, Serbia; [2]Department of Neurology, Mother and Chiled Health Care Institute, Belgrade, Serbia; [3]Department of Radiology, Mother and Chiled Health Care Institute, Belgrade, Serbia

Objectives: This study presents retrospective analyses of 8 acute lymphoblastic leukemia (ALL) patients who developed neurologic complications due to chemotherapy.
Methods: From April 2010 up to February 2014 the diagnosis of ALL was established in 63 patients. Among them, 8 patients (12.7%), whose age ranged between 14 months and 9 years, developed 11 complications. Diagnosis was made upon following procedures: computed tomography (CT) - 7 patients, magnetic resonance images (MRI) - 3 patients, EEG - 8 patients, lumbar puncture (LP) - 2 patients, MTHFR c677T mutation – 1 patient and biochemical analysis including the screening for hemostasis performed in all patients.
Results: The most common clinical manifestation was seizure, which occurred in 5 patients (6 episodes). Sagittal sinus thrombosis was diagnosed in one of them. Acute encephalopathy was noticed in two patients, in two year old male during the induction treatment and in three year old female due to hypoglycemia provoked with 6-mercaptopurine during maintenance therapy. Posterior reversible encephalopathy syndrome was diagnosed in one female with acute onset of hemiparesis. The most peculiar complication was observed in two year old male who developed persistent chemical arachnoiditis after the first lumbar puncture. During the maintenance therapy, after the 5th prophylactic lumbar puncture, acute ataxia with right sided hemiparesis has occurred. CT scan showed multifocal parenchimal calcifications, and MRI confirmed the presence of calcifications with massive edema in basal ganglia. After the investigations (homozygous for c677t MTHFR mutation) we concluded that this was the case of methotrexate toxicity. Complete recovery was achieved in 6 patients (75%) and two patients (25%) developed neurologic sequels (delayed speech development and milde hemiparesis).
Conclusions: Neurologic complications due to chemotherap in ALL patients are not rare. By better diagnosis, close follow –up and effective treatment of underlying causes the morbidities and mortalities of these complications can be decreased.

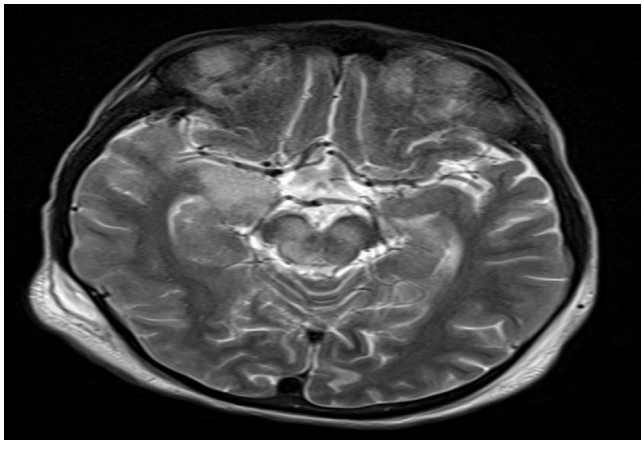
EP-026

CNS COMPLICATIONS IN CHILDHOOD LEUKEMIA: ROLE OF MRI IN DIAGNOSIS AND MANAGEMENT

S. Kakkar[1], P. Sobti[2], C. Kakkar[3], K. Saggar[3]

[1]Paediatrics, Dayanand Medical College, Ludhiana, India; [2]Paediatrics, Christian Medical College, Ludhiana, India; [3]Radiodiagnosis, Dayanand Medical College, Ludhiana, India

Objectives: To illustrate the MRI patterns of various CNS complications in Childhood Leukemia.
Methods: MRI studies of 16 children with acute leukemia who presented with seizures, altered sensorium or focal neurological deficits were reviewed. The children were divided into two categories; the first group included the children who had complications related to leukemia and second group therapy related complications.
Results: Of the 16 children, 6 children had complications directly related to leukemia which included leukemic infiltration (n = 1), microinfarcts (n = 1), stroke (n = 2), cortical venous thrombosis (n = 1), limbic encephalitis as a paraneoplastic manifestation (n = 1). The second group included chemotherapy induced leucoencephalopathy (n = 2), vasculitis (n = 1), posterior reversible encephalopathy syndrome (n = 2), infections (n = 4), thrombotic microangiopathy (n = 1).



Conclusions: A wide range of abnormalities affect the brain and central nervous system in a leukemic child and MRI plays a substantial role in early diagnosis and management of these conditions.

EP-027

INDUCTION RELATED MORTALITY AND MORBIDITY IN CHILDREN TREATED WITH ACUTE LYMPHOBLASTIC LEUKAEMIA: SINGLE CENTER EXPERIENCE FROM A LOWER MIDDLE INCOME COUNTRY

M. Khan[1], M. Shahzad[1], S. Riaz[1], F. Naz[1], A. Rashid[1]

[1]Pediatric Oncology, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan

Objectives: Outcome during induction phase of therapy (IP) for acute lymphoblastic leukemia (ALL) is reduced to 1-2% in developed countries. But in resource poor settings, morbidity and mortality during IP are still very high. Main objective of this study was to review the outcomes of children with ALL during IP who were treated at Shaukat Khanum Memorial Cancer Hospital Lahore.
Methods: Medical records of all newly diagnosed childhood ALL patients during Jan 2011 to June 2013 were retrospectively reviewed from their first clinic visits till the start of consolidation, abandonment or death. Patients' characteristics and details about diagnosis, chemotherapy, course of illness, re-evaluation bone marrow morphology and complications of therapy were recorded. For those who died, cause of death was assessed by thorough data review.
Results: Of 162 cases reviewed, median age at presentation was 3 years with male to female ratio of 1.7:1. Precursor B ALL was diagnosed in 91% whereas 8% patients had precursor T disease. Bulk disease was present in 40% cases. Standard (84%) and high risk (16%) patients were treated with 3 and 4 drugs induction respectively. Mortality rate during IP was 19% (n = 29). Cause of death was attributed to infectious etiology in all patients and 79% (n = 23) deaths occurred during or after 4th week of IP. Hypocellular marrow was reported in 57% of patients assessed at day 8/15 (n = 17). Of those successfully completing IP (n = 123), common reasons for admission were febrile neutropenia, diarrhea, oral mucositis, pneumonia and sepsis. Severe malnutrition and bulk disease were found to be statistically significant factors with p-values of 0.021 and 0.001 respectively.
Conclusions: Infection was the commonest cause for morbidity and mortality in IP of ALL therapy. Better infection control strategies and supportive care can improve outcome. Nutritional rehabilitation of severely malnourished children and chemotherapy modifications during IP may be other considerations.

EP-028

EXPRESSION OF CD133-2, AS A PROSPECTIVE MARKER, PREDICTING MINIMAL RESIDUAL DISEASE (MRD) LEVEL AT DAY 15, IN CHILDREN WITH CD45-DIM B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

M. Khvedelidze[1], A. Shengelaia[1], T. Javakhadze[1]

[1]Hematology/Oncology, Children Central Hospital, Tbilisi, Georgia

Objectives: To address predictive value of CD133-2 receptor expression on CD45-dim B-ALL cells at initial diagnosis, in the context of minimal residual disease monitoring at day 15 in children with B-ALL.
Methods: Nine newly diagnosed children with CD45-dim B-ALL were assessed for MRD levels on the day 15 of remission induction. We arbitrarily assigned the patients to either relatively 'high or low CD133-2'groups based on percentage of CD133-2 positive events at initial diagnosis. Phenotyping was performed in agreement with ALL-ICBFM-2009 recommendations using 4-color flow cytometry, with an acquisition number of at least 300.000 nucleated cells per tube and MRD of 30 cellular events was considered as positive.
Results: Among study subjects there were four males and five females with an average age of 3.1 (95%CI: 1.9 – 4.3). Median percentage of CD133-2 positive cells in 'low CD133-2' group were defined as 0.8% (Interquartile range (IQR): 0,115 – 1.70) and as 42.85% (IQR: 29,01 – 70) in 'high CD133-2' group gated on CD19+ ALL cells. Comparison between these groups revealed statistically significant difference in minimal residual disease levels at day 15 (p = 0.02); Median percentage of MRD in 'high CD133-2' group was 1.75% (IQR: 1.18 – 6.6), while a median of 0.04% of residual leukemic cells (IQR: 0.04 – 0.08) was observed in 'low CD133-2' group. Correlation analyses revealed significant positive correlation between CD133-2 and CD45 receptor expression (Mean Fluorescent Intensity) at diagnosis ($r^2 = 0.86$; p = 0.029). Percentage of CD133-2 positive B-ALL cells also positively correlated with leukocyte count at initial diagnosis ($r^2 = 0.83$; p = 0.04)
Conclusions: Study showed that, CD133-2 receptor expression at initial diagnosis might be exercised as a surrogate marker to predict MRD levels at day 15 in children with CD45-dim B-ALL, although further, larger cohort studies are needed to address this question.

EP-029

ASSOCIATION BETWEEN IMMUNOPHENOTYPING AND PROGNOSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

S. Köker[1], F. Genel[2], N. Gülez[2], Y. Oymak[1], S. Gözmen[1], Y. Yaman[1], G. Özbek[1], D. Ince[3], C. Vergin[1]

[1]Pediatric Hematology and Oncology, Dr. Behçet Uz Childen's Hospital, Izmir, Turkey; [2]Pediatric Immunology, Dr. Behçet Uz Childen's Hospital, Izmir, Turkey; [3]Pediatric Oncology, Dr. Behçet Uz Childen's Hospital, Izmir, Turkey

Objectives: Acute lymphoblastic leukemia (ALL) is the most common malignancy in childhood. Immunophenotyping has become important for determining the subgroups of ALL. We aimed to determine the features of subgroups according to immunophenotype, the correlation between clinical and other laboratory and their effects on prognosis retrospectively.
Methods: Sixty-six males and forty females receiving TR-ALL 2000 BFM between 2008-2012 were included in the study.
Results: The mean age was 5.9 ± 3.8 years. The distribution was; 1% pro-B, 44% common B, 38% pre-B, 7.5% pre-T, 5.5% cortical T and 4% mature T. Pre-B ALL had a higher rate compared to literature. Male gender was dominant in T cell ALL when compared with B cell ALL group. T cell ALL was seen more frequent in group with patients older than 6 years of age. Leukocyte count higher than 20000/mm3 at diagnosis was more common in T cell ALL group. Lymphadenopathy larger than 2 cm was more common in T cell ALL group when compared with common B and pre-B cell groups. Mediastinal involvement was high in T cell ALL when compared with common B cell group. Co-expression was found in 20 cases with no statistical difference in subgroups. CD33 was determined as the most common marker showing co-expression. No negative effect related with myeloid antigen co-expression in terms of clinical and medical prognosis was found. Overall relapse rate was 13.6%. Death rate was 41.7% and 2.6% in relapse and non-relapse groups respectively. WBC count, organomegaly, lymphadenopathy, prednisone response in day 8, marrow in day 15, relapse and risk subgroups had significant impact on overall survival. WBC count higher than 20×10^9L was the only factor influencing the survival by multivariate analysis.
Conclusions: Immunophenotyping by flow cytometry is of importance in the diagnosis of ALL, in determining of the immunophenotype subgroups and risk groups and in planning of the therapy.

EP-030

IMPROVED OUTCOME FOR CHILDREN AND ADOLESCENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN THE LAST DECADE: A REPORT FROM THE SLOVAK REPUBLIC

A. Kolenova[1], M. Makohusova[2], Z. Subova[3], E. Bubanska[4], I. Oravkinova[5], J. Horakova[3], V. Mrazova[2], D. Sejnova[6], E. Kaiserova[1]

[1]Department of Pediatric Hematology and Oncology, Comenius University - Medical School and University Children's Hospital, Bratislava, Slovakia; [2]Department of Chemistry, University of SS. Cyril and Methodius, Trnava, Slovakia; [3]Department of Pediatric Hematology and Oncology, University Children's Hospital, Bratislava, Slovakia; [4]Department of Pediatric Hematology and Oncology, University Children's Hospital, Banska Bystrica, Slovakia; [5]Department of Pediatric Hematology and Oncology, University Children's Hospital, Kosice, Slovakia; [6]Department of Pediatric Hematology and Oncology, University Children's Hospital, Bratislava, Slovakia

Objectives: To analyze event-free (EFS) and overall survival (OS) among children and adolescents with acute lymphoblastic leukemia (ALL) treated with International BFM Intercontinental trial (ALL IC 2002) therapy in the Slovak Republic between 2002 and 2012.
Methods: In total, 280 children and adolescent age 1 to 18 years were treated with ALL IC BFM 2002 based therapy from 2002 to 2012, which was divided into two periods. During 2002-2007, when patients were actively enrolled in the ALL IC-BFM 2002 trial, and during 2008-2012 when the trial was closed and patients were treated with the same therapy without randomization.
Results: Five-year EFS and OS rates were 79% (+/- 2.6%) and 86% (+/- 2.1%), respectively, similar to results obtained in the ALL-BFM 95 trial, which was the basis for ALL IC BFM 2002 therapy. The EFS ($p < 0.003$) and OS ($p < 0.009$) were significantly better than the prior Slovak experience in 1997-2001. Survival improved in standard and intermediate risk groups, including males and females; those age 1 to 6 years, and older; in those with B-cell or T-cell immunophenotype, and is also excellent for those with ETV6/RUNX1 translocation and hyperdiploidy and with good response in peripheral blood on day 8 and in bone marrow on day 15 and 33. The rate of death in induction, cumulative incidence of death in complete remission and of relapse decreased. However, outcome was suboptimal for patients in the high risk goup.
Conclusions: Current EFS and OS rates for children and adolescents with ALL in the Slovak Republic now approach those obtained in Western Europe as a result of clinical trial participation, and gaining clinical experience with intensive BFM type treatment.

EP-031

HIGH-HYPERDIPLOIDY AND FAVORABLE PROGNOSIS IN B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

M. Kourti[1], A. Athanassiadou[2], M. Lambrou[1], A. Taparkou[3], V. Sidi[1], K. Stamatopoulos[2], D. Koliouskas[1]

[1]Pediatric Oncology Department, Hippokration General Hospital, Thessaloniki, Greece; [2]Hematology and HSCT Department, Papanikolaou General Hospital, Thessaloniki, Greece; [3]First Pediatric Department, Aristotle University of Thessaloniki, Thessaloniki, Greece

Objectives: High hyperdiploidy (HeH) (51-67 chromosomes), in pediatric B-cell precursor acute lymphoblastic leukemia (ALL) is generally associated with favorable prognosis. We performed a retrospective analysis of B-ALL patients with HeH who were treated in our department in the last 5 years and their cytogenetic analysis was available.
Methods: Prettreatment bone marrow samples were cultured and analyzed by standard cytogenetic methods. A total of 20 children (11 females and 9 males) displayed G-banded karyotypes with 51-67 chromosomes who were also informative for molecular studies, were included for analysis.
Results: The most frequently gained chromosomes were X (100%), 21 (95%), 14 (55,5%), 17 (55,5%), 6 (50%), 4 (38,8%%), 18 (38,8%) and 10 (38,8%). Triple trisomy (+4, +10,+17) were identified in 33,33% cases. The triple trisomy-positive cases had a median of 57 chromosomes (range, 51-65), whereas the negative cases had a median of 54 chromosomes (range, 51-57) Translocation-positive high hyperdiploidy (t-HeH) was identified in only 2 cases with t (12;21). None of the HeH cases had evidence of extramedullary (central nervous system, mediastinal mass or testes) leukemia at diagnosis. Median age at diagnosis was 4.7 years (range: 1.5-13 years). Median WBCx10^9/L was 2.100 (range: 1200-17000). Only 3 cases were stratified as high-risk patients because they were prednisone poor responders and their minimal residual disease (MRD) in bone marrow on day 15 was LOG-1 but on day 33 they all achieved complete remission with MRD of LOG-4. All patients are in continuous complete remission with event-free and overall survival of 100%.
Conclusions: Our results are consistent with literature that HeH is the largest cytogenetic subgroup in childhood B-cell ALL and is associated with other favorable clinical features. The impact of triple trisomy (+4, +10,+17) in the context of high hyperdiploidy warrants further investigation.

EP-032

RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA – A SINGLE CENTER EXPERIENCE FROM A DEVELOPING WORLD

A. Kumar[1], V. Chinnabhandar[1], A. Gupta[1], N. Radhakrishnan[1], A. Sachdeva[1]

[1]Pediatric Hematology-Oncology and Bone Marrow Transplant Centre, Sir Ganga Ram Hospital, Delhi, India

Objectives: Data about relapsed ALL is lacking from developing world. Here, we have analysed our centre's relapsed ALL data to see its pattern and treatment outcomes
Methods: Retrospective data analysis was done among patients with ALL from 2005-2013, treated on a modified UK-ALL XI protocol. Relapse defined as presence of >25% blast cells in bone marrow (BM), or on histology, or cytological documentation of blasts in extra-medullary (EM) sites after achievement of complete remission. Based on the time of relapse, they were categorized as very early (within 18 months from diagnosis), Early (after 18 months but within 6 months of completion of therapy) and late (more than 6 months of completion of therapy)
Results: 41 (11.6%) patients relapsed among the 353 patients with ALL. Median age was 4 years (range 0.16-20). Male preponderance (66%) seen. Majority of them (80%) were of B cell type. Among them one case had CNS diasease at diagnosis and 5 of them presented with initial high TLC. Molecular work up showed BCR-ABL n = 4, TEL-AML n = 4, MLL n = 2, Hyperdiploidy, n = 2. 16 (34%) and 11 (27%) respectively had isolated BM and CNS relapses. One each had testicular and ocular relapse.6 (15%) had combined BM and CNS relapse and 6 (15%) had combined BM and testicular relapse.56%-very early,26.8%-early and 17%-late relapses.33 out of 41 opted for therapy and were treated on BFM-REZ 96 protocol.16 patients are alive at a median follow up of 0.65 years (0.1-4.3 years). Our relapse rates were 11.6% and 2nd CR was achieved in 70%.12 died (5-sepsis,3-refractory disease,4-second relapse).27% patients were lost to follow up or died of sepsis.2 year OS 51.7 ± 11.4%,2 year EFS 27.2 ± 8.9%
Conclusions: It is feasible to treat children with relapsed ALL in the developing world but sepsis treatment abadonment are barriers to improving survival.

EP-033

INCIDENCE OF HYPERGLYCEMIA DURING REMISSION INDUCTION CHEMOTHERAPY FOR PAEDIATRIC ALL, A HOSPITAL BASED STUDY

R. Laila[1], A. Islam[2], A. Bhuiya[3], K. Nahar[2], A. Saha[4]

[1]Paediatrics, United hospital, Dhaka, Bangladesh; [2]Paediatrics Haematlogy and oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [3]Nephrology, Birdem, Dhaka, Bangladesh; [4]Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Objectives: To see incidence of hyperglycemia during remission induction phase of chemotherapy treatment in case of ALL in children
Methods: Prospective observational study. About 50 newly diagnosed ALL patients age range of 1 to 15 years were studied. Study period was 6 months. Hyperglycemia was defined as > 2 random glucose determines of >200 mgldl during the first 28 days of induction phase chemotherapy.
Results: Out of all patients, only 4 (8%) developed hyperglycemia during remission induction. No significant differences was noticed between two groups (hyperglycemic group, non hyperglycemic group) regarding age distribution ($P > 0.05$) and body weight ($P > 0.05$). Hyperglycemia mostly experienced during second week (75% patient) and third week (25% patient). This condition persists <7 days in 75% patients and > 7-days in 25% patients.
Conclusions: Around 8% ALL Patients during induction remission phase of chemotherapy experienced hyperglycemia. They recover when drugs like L -asparaginase, corticosteroid are withdrawn. These patients had no longer long term adverse eflects.

EP-034

OUTCOME AND PROGNOSTIC FACTORS FOR TEL-AML1 POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN KOREAN CHILDREN: A SINGLE INSTITUTION STUDY

J.W. Lee[1], P.S. Jang[1], N.G. Chung[1], D.C. Jeong[1], B. Cho[1], H.K. Kim[1]

[1]Pediatrics, The Catholic University of Korea, Seoul, Korea

Objectives: The *TEL-AML1* fusion is the most frequent genetic abnormality in children with acute lymphoblastic leukemia (ALL), and is associated with a favorable outcome. However, its incidence differs according to patient ethnicity, and its prognostic relevance may also differ.
Methods: In this study, we studied the outcome and prognostic features of 50 patients with *TEL-AML1* (M:29 F:21) who were diagnosed at the Department of Pediatrics, The Catholic University of Korea from May, 2005 to June, 2011. Independent variables studied included patient age and WBC count at diagnosis, minimal residual disease positivity at the end of remission induction (MRD), and cytogenetic features including presence of complex karyotype, or additional 12p translocations or inversions besides *TEL-AML1* (12p abnormalities).
Results: Median patient age at diagnosis was 4.5 years (range: 1.8-13.6), with only 4 patients (8%) diagnosed above the age of 10 years. Median WBC count at diagnosis was 11,500 (range: 1,000-134,580). A complex karyotype was found frequently at diagnosis (24/50, 48%). Eight patients relapsed (16%) at a median of 27.4 months from diagnosis (range: 18.3-39.3), including 7 with BM, and 1 patient with isolated CNS relapse. Five-year event-free survival was 84.0 ± 5.2%. All 7 patients with BM relapse received allogeneic transplant; all 7 subsequently relapsed and died of disease progression. Five year overall survival was 74.8 ± 12.3%. In univariate study, WBC count $\geq$ 50,000 ($P = 0.024$), MRD at end of induction ($P = 0.029$), and 12p abnormalities ($P = 0.001$) predicted relapse. In multivariate study, only 12p abnormalities was a significant factor for relapse ($P = 0.011$).
Conclusions: A significant portion of our *TEL-AML1* cohort relapsed. Of note, relapses occurred relatively early after diagnosis, in contrast to Western studies which reported a tendency for late relapses. Considering the extremely poor prognosis once relapse occurs, studies should be undertaken to clarify additional genetic lesions in *TEL-AML1* patients that predict a poor prognosis.

EP-035

CLINICAL SIGNIFICANCE OF DYNAMIC MONITORING MINIMAL RESIDUAL DISEASE IN CHILDHOOD B LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA

H. Li[1]

[1]Hemotology/Oncology, Children's hospital of Shanghai, Shanghai, China

Objectives: To study the clinical significance of dynamic monitoring minimal residual disease (MRD) using flow cytometric detection of abnormal immunophenotype in childhood B lineage acute lymphoblastic leukemia.
Methods: 134 patients were enrolled in the research from January 2005 to December 2011. MRD targets were filtered preliminarily by flow cytometry, and then were dynamic monitored at specified time. The overall treatment plan is reference to Shanghai Children's Leukemia Cooperative Group protocol. Divided the patients into low?middle and high risk groups depends on risk factors including day 35 and 55MRD level. All datas were analyzed by SPSS 16.0.
Results: In this study,49 patients belonged to low risk (36.6%), 46 patients to middle risk (34.3%) and 39 to higher risk (29.1%), Five year EFS was 85.60 ± 5.0%,69.2 ± 7.2%, 63.0 ± 7.0%, respectively. There were significant statistic differences between low and high risk groups ($P = 0.024$).128 patients achieved complete remission after induction therapy, with a 5-year event-free survival (EFS) 73.4 ± 3.9%. 109 patients with MRD targets, 25 patients without, 5-year EFS were 77 ± 4.1%, 56.7 ± 10.5%, respectively. Univariate analysis confirmed that MRD target were significantly different in both groups ($P = 0.019$). MRD detection at day 35: MRD<0.01% were 77 patients with a 5 year relapse free survival (RFS) 80 ± 5.5%, MRD $\geq$0.01% were 21 cases with a 5-year RFS of 60 ± 12.1% ($P = 0.036$). 21 patients with MRD $\geq$0.01% at day 35 while 18 turn to normal at day 55 (85.7%), 2 relapsed, 3 still abnormal, all of them relapsed. There were significant statistic differences in two groups ($P = 0.008$).
Conclusions: The prognosis of low risk patients were significant better than middle and high risk group patients. 5 year EFS of ALL patients with MRD markers was higher than those without MRD marker. There is an important clinical significance for dynamic monitoring MRD to adjust the treatment timely. MRD on day 35 and 55 were important prognostic factors for ALL patients. The prognosis for MRD continued positive is poor.

EP-036

PROGNOSTIC FACTORS AND TREATMENT OUTCOME OF THE PEDIATRIC INTERMEDIATE AND HIGH RISK T-LYMPHOBLASTIC LYMPHOMA/ LEUKEMIA-A REVIEW OF 30 CASES

Q. Kai[1], L. Yang[1]

[1]Pediatric Hematology/Oncology, Sun Yat-Sen Memorial Hospital Sun Yat-Sen University, Guangzhou, China

Objectives: To evaluate the prognostic factors and the therapeutic effectiveness of 30 cases of pediatric intermediate risk (IR) and high risk (HR) T-LBL/ALL treated with three various chemotherapeutic regimens including Sums lymphoblastic lymphoma-08, GZ2002 ALL and GD2008 ALL.
Methods: 30 patients in our department from 2002 to 2012 were retrospectively studied. Evaluate patients' 3-year overall survival (OS) rate, 3-year event-free survival (EFS) rate, recurrence rate and mortality rate with Kaplan-Meier analysis; compare inner-group patients' OS and EFS difference and survival curve with Log-Rank test, all data was processed by SPSS 17.0.
Results: Among the 30 cases, OS and EFS for MLL gene negative cases (n = 26) and MLL gene positive cases (n = 4) were 52.5% vs 0% and 45.6% vs 0%, respectively; while for cases whose LDH level≤400U/Lat first visit (n = 22) and whose LDH level>400U/L (n = 8), OS and EFS were 57.5% vs 31.7% and 35% vs 31%, respectively. Among 25 T-ALL cases, OS and EFS for prednisone good response (PGR) (n = 16) and prednisone poor response (PPR) (n = 8) cases were both 57.5% vs 32.5%; while on day 33 of induction chemotherapy, OS and EFS for M1 (n = 23) and M2 (n = 2) cases were 50.4% vs 0% and 44.3% vs 0%, respectively. For cases classified as IR (n = 12) and HR (n = 18), OS and EFS were 54.5%vs 36.5% and 43.6% vs 36.5%, respectively. After a median follow-up of 36.4 months (3∼108 months), OS and EFS were 46.7% and 42.1%, respectively.
Conclusions: MLL gene positive, LDH level≥400U/L at first visit, PPR and bone marrow shows no remission on day 33 of induction chemotherapy, the higher the risk degree, all these are poor prognostic factors resulting in lower survival rate. Successfully screening the risk factors is benefit for designing the prognostic analytical model and choosing the optimal solutions for the patients.

EP-037

IMMUNOGENICITY OF INTRAVENOUS ASPARAGINASE ERWINIA CHRYSANTHEMI IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA OR LYMPHOBLASTIC LYMPHOMA

B. Benson[1], Y. Lu[2], M. Eller[3]

[1]Clincial Development, Jazz Pharmaceuticals Inc, Palo Alto CA, USA; [2]Biostatistics, Jazz Pharmaceuticals Inc, Palo Alto CA, USA; [3]Research and Clinical Development, Jazz Pharmaceuticals Inc, Palo Alto CA, USA

Objectives: L-asparaginase (ASNase) is an important component of multiagent chemotherapy for pediatric acute lymphoblastic leukemia (ALL). Like other large proteins, ASNases can induce a host response, stimulating development of anti-ASNase antibodies. Implications of immunogenicity on the therapy can range from no effect to alterations in pharmacokinetics (PK), efficacy, and/or safety profiles. The objective of this analysis was to characterize the immunogenicity profile of ALL patients receiving *Erwinia* ASNase following hypersensitivity to *Escherichia coli*–derived ASNase.
Methods: Patients received *Erwinia* ASNase 25,000 IU/m^2 intravenously 3 times weekly in combination with chemotherapy. Serum samples for antibody testing were collected at trough ASNase activity levels (predose and 48 hours postdose 5), and were evaluated for antidrug antibody (ADA) with a screening assay (ELISA) and a confirmatory assay (competitive inhibition). Samples positive in the confirmatory assay were tested for neutralizing antibodies (NAbs).
Results: Thirty patients aged 1–17 years (mean 7.9 years) were enrolled, and 16 completed the study; 12 discontinued due to adverse events. Most patients were male (63.3%) and had precursor-B-cell ALL (76.7%). Seven patients screened positive for ADA (ADA+); 4 were confirmed positive. None of the confirmed ADA+ patients tested positive for NAbs. Comparison of PK between the ADA+ and ADA negative (ADA-) patients was limited by the fact that only 2 PK samples were taken after patients became antibody positive and the trough asparaginase activity levels were low. Ten patients experienced hypersensitivity reactions during the study; 7 were ADA- and 3 were ADA+. Six of the ADA- and 3 ADA+ patients discontinued following the hypersensitivity reaction; the fourth ADA+ patient did not experience a hypersensitivity reaction but refused further treatment.
Conclusions: In ADA+ patients the presence of anti-*Erwinia* ASNase antibodies was commonly associated with hypersensitivity reactions, although many patients who experienced hypersensitivity reactions did not have anti-*Erwinia* ASNase antibodies.
Study funded by Jazz Pharmaceuticals plc or its subsidiaries.

EP-038

THE 14-BASE PAIR DEL-DEL GENOTYPE OF THE HLA-G 3' UNTRANSLATED REGION IS ASSOCIATED WITH PEDIATRIC T- CELL LYMPHOBLASTIC LEUKEMIA

R.S. Almeida[1], R.G. Gomes[1], A.M.L. Ramos[2], E.A.V. Marques[2], T.C. Fonseca[2], E.A. Donadi[3], F. Pedrosa[2], N. Lucena-Silva[1]

[1]Imunologia, Centro de Pesquisas Aggeu Magalhães-FIOCRUZ, Recife, Brazil; [2]Oncologia Pediátrica, Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil; [3]Imunologia Clínica, Universidade de São Paulo Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto, Brazil

Objectives: HLA-G antigen modulates the immune response in health and disease and the presence of polymorphic sites at the 3'untranslated region (UTR) of the gene seems to be involved in antigen expression. In cancer, HLA-G expression has been associated with worse outcome, but lesser is known in leukemia. We investigated the genetic variability of a *HLA-G* gene segment in children with T lineage acute lymphoblastic leukemia (T-ALL) as a possible prognostic marker.
Methods: 47 T-ALL children referred to the Pediatric Oncology at the Instituto de Medicina Integral Professor Fernando Figueira, in Recife, Northeastern of Brazil, were studied. At diagnosis, blast bone marrow was characterized by morphology and immunophenotyping and minimal residual disease (MRD) was investigated using flow cytometry in Day 19 and 49. Polymorphic sites at the *HLA-G* 3'UTR were determined by *in vitro* gene amplification and sequencing. Allele and genotype frequencies were estimated by Genepop software, and compared with data from 91 healthy children using Prism software.
Results: Children were 8.6 ± 4.7 years and the proportion of males:females was 3. Twelve of 47 died, 6 within 30 days. MRD was measured in 16 children, from which 6 presented values above 1% of blast in Day 19, none was positive in Day 49. The *HLA-G* 3'UTR 14-base pair (bp) DEL-DEL genotype ($P = 0.051$; OR = 2.4) were overrepresented in T-ALL children, and 14-bp INS-INS ($P = 0.030$; OR = 0.4) underrepresented. Comparing the 12 children who died with the 35 alive, proportion of complete remission (6/12 x 34/35 cases) and relapse (4/12 x 0/35) were different. There were no differences on age ($P = 0.961$), leucocyte counting (211,300 ± 73,930 x 171,000 ± 30,370; $P = 0.464$), presence of mediastinal mass or hepatic and spleen enlargement ($P = 1.00$). The 14-bp DEL-DEL genotype frequency was also the same in both groups.
Conclusions: The *HLA-G* 3'UTR 14-bp DEL-DEL genotype was associated with T-ALL in children, but not with the disease outcome.

EP-039

END OF INDUCTION THERAPY OUTCOMES OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN ETHIOPIA

M. Celiker[1],

[1]Pediatric, Tikur Anbessa Hospital, Addis Ababa, Ethiopia

Objectives: We examined the data on induction therapy for acute lymphoblastic leukemia (ALL) in children at Tikur Anbessa Hospital in order to determine the outcome and variables determining it.
Methods: All children presenting with new or relapsed ALL were included in this examination between April 2013 and February 2014. Those with incomplete records were excluded.
Results: Fifty nine evaluable children (ages 1.5 to 14 years, median 7.0 years) with ALL received induction chemotherapy on 67 occasions (55 newly diagnosed and 12 relapsed ALL.) At the end of induction, 35 patients were alive, 19 patients died, and 14 patients abandoned (52, 31, and 17% respectively). Mortality and abandonment rates for those on 3-drug induction (n = 40) were 18 and 22%, respectively, with 60% of the patients being alive at the end of induction. Mortality rate was 41% and abandonment rate was 18% for those receiving 4-drug induction (n = 27) with 41% of the patents alive at the end of induction. Among high risk ALL patients (n = 42), survival, mortality and abandonment rates for all patients were 51, 30, and 17%; for those receiving 3-drug induction (n = 15) were 73, 13, and 13%; and for those receiving 4-drug induction (n = 27) were 41, 41, and 18%, respectively. Infection and bleeding were the primary reason for mortality with similar rates in all groups (average 58% for infection and 27% for bleeding.) Socioeconomical constraints and hopelessness were the primary reasons for abandonment and this was somehow higher among those considered standard risk ALL (28%.)
Conclusions: Intensive chemotherapy leads to significantly lower survival rates in children with ALL in Ethiopia. These observations underline the importance of making an honest assessment of the settings and ascertainment of proper supportive care when making therapeutic decisions in low and middle income countries.

EP-040

CLINICAL ANALYSIS OF THREE CASES OF FUNGAL ESOPHAGITIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

H. Mai[1], H. Cai[1], D. Dai[1], D. Bai[1], Q. Yang[1], X. Yuan[1], C. Li[1]

[1]Hematology and Oncology, Shenzhen Children's Hospital, Shenzhen, China

Objectives: To summarize the experience of diagnosis and treatment of fungal esophagitis in children with acute lymphoblastic leukemia (ALL).

Methods: Retrospectively reviewed the clinical manifestations, diagnosis and treatment of fungal esophagitis in three children with acute lymphoblastic leukemia during chemotherapy.
Results: Three patients with ALL had symptoms of epigastric pain, vomit or discomfort of the precordial area during and after chemotherapy. They were diagnosed fungal esophagitis by gastroscopy. One case had fever and neutropenia. The regimen for chemotherapy in all patients included dexamathasone. All cases were given antifungal drugs including fluconazole, micafungin and itraconazole for two to four weeks. They all recovered based on endoscopy results.
Conclusions: Gastroscopy can be performed to make diagnosis of fungal esophagitis when ALL patients have symptom of epigastric pain or discomfort of the precordial during chemotherapy. Gastroscopy can be a useful way to find out the site of fungal infection when patient is febrile and neutropenic. Antifungal drugs are effective for fungal esophagitis.

EP-041

FLOWCYTOMYTRIC PATTERN AND PROGNOSTIC SIGNIFICANCE OF CELL SURFACE PHENOTYPE IN ACUTE LYMPHOBLASTIC LEUKEMIA IN PAEDIATRIC PATIENTS-A RETROSPECTIVE ANALYSIS AT A REGIONAL CANCER CENTRE IN KASHMIR, INDIA

M. Mir[1], A. Aejaz Shiekh[1]

[1]Medical & Paediatric Oncology, Sheri-Kashmir Institute of Medical Sciences (SKIMS) SrinagarJammu&Kashmirindia, Srinagar, India

Objectives: Acute lymphoblastic leukemia (ALL) is a heterogeneous disease with biologically and clinically distinct subsets. The immunophenotype of leukemic cells at diagnosis reflects the level of differentiation achievd by the clone. Aim of the study was to review the flowcytometric pattern of ALL and its prognostic sigfnificance in paediatric patients.
Methods: This retrospective study was carried out at the Department of Medical and Paediatric Oncology, Regional Cancer Centre, Sher-i-Kashmir Institute Of Medical Sciences, Srinagar, Jammu and Kashmir, India. The clinical, hematological and flowcytometric data of the patients was reviewed over a four years period from January 2009 to December 2012.
Results: Out of 167 ALL patients registered during the study period, 118 (70.65%) were paediatric patients and 49 (29.35%) were adult ALL. Flowcytometry was available in 109 (92.37%) children with ALL. There were 68 male and 50 female children (M:F,1.3:1).B-cell ALL constituted 67.25% and T-cell ALL were 29.64%. Early pre B cell was common (54.7%) followed by pre B cell (40.2%) and mature B cell (6.1%) among B cell phenotype. In T cell phenotype, mature T cell was common (88.3%) followed by pre T cell ALL (11.7%). Mixed phenotype ALL was present in 3.11%. CALLA positivity was present in 67.33% and 3.4% were ph+ve ALL. Early Pre B cell ALL had favourable prognosis with complete response rate of 67.33%, followed by Pre B cell ALL (64.22%). In T cell ALL mature T cell had complete response rate of 13.66% followed by pre T cell ALL 3.4%. Treatment failure rates were higher in T cell type ALL (75.23%) compared to B cell phenotype. (33.23%).
Conclusions: Immunophenotyping plays a central role in the determination of clinically relevant subsets. Although intensive therapy may blur some prognostic distinctions, consideration of toxicity/efficacy ratios and the persistence of definable high-risk groups requires the continued use of immunophenotyping in the diagnosis and classification of ALL.

EP-042

SUCCESSFUL TREATMENT WITH DASATINIB IN A CASE OF RELAPSED ALL WITH NOVEL ATF7IP-PDGFRB FUSION GENE.

N. Miyagawa[1], T. Sarashina[1], T. Yokosuka[1], K. Fukuda[1], F. Iwasaki[1], S. Hamanoue[1], K. Kobayashi[2], H. Gotou[1]

[1]Division of Hemato-Oncology/Regenerative medicine, Kanagawa Children's Medical Center, Yokohama, Japan; [2]Pediatric Hematology and Oncology Research, National Research Institute for Child Health and Development, Tokyo, Japan

Objectives: BCR-ABL1 positive acute lymphoblastic leukemia (ALL) has poor response and prognosis for conventional chemotherapy, however outcome can be improved with the addition of first and second generation tyrosine kinase inhibitors. Recently, new high risk subtypes of BCR-ABL1 negative ALL were identified which have similar expression profile to BCR-ABL1 positive ALL and have genetic alterations that activate kinase signaling including rearrangement of platelet derived growth factor receptor ((PDGFRB). We report the first patient of ALL with ATF7IP-PDGFRB who received allogeneic stem cell transplantation (allo-SCT) and treatment with dasatinib.
Methods: A 11-year-old male who achieved first complete remission (CR) by conventional chemotherapy suffered from first bone marrow (BM) relapse of B cell precursor ALL during maintenance therapy. Chromosomal karyotype analysis of relapsed blast cells showed 45, XY, t (5;12) (q33:p13),-7. Using samples at relapse, we performed the mRNA sequence analysis and the in vitro drug testing with the WST-8 assay.
Results: The mRNA sequence analysis identified an in-frame transcript fusing exon 13 of ATF7IP with exon 11 of PDGFRB. Furthermore, the in vitro drug testing revealed sensitivity to dasatinib. REZ-BFM style chemotherapy could not provide a reasonable efficacy. We therefore altered to ECM therapy (etoposide, cytarabine, mitoxantrone), and as a result, second hematological-CR was achieved after 2 cycles of the therapy. ATF7IP-PDGFRB was still detectable in BM by reverse transcription polymerase chain reaction (RT-PCR). Subsequently we performed allo-SCT with 1 HLA-DR allele mismatched cord blood. His neutrophil recovered at day25, and BM showed 99% donor type at day30. Treatment with dasatinib was started from day 62 against positive ATF7IP-PDGFRB in BM at day30 and day61. ATF7IP-PDGFRB in BM decreased after dasatinib and finally became undetectable by RT-PCR at day 146.
Conclusions: Dasatinib may be effective for relapsed ALL with PDGFRB rearrangement.

EP-043

PHILADELPHIA POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN: EXPERIENCE FROM A SINGLE CENTREIN INDIA

R. Mohammed[1], C. Yogiraj[1], S. Rajat[1], K. Satyendra[1], Y. Satya Prakash[1]

[1]Pediatrics Hematology Oncolgy and BMT Unit, Fortis Memorial Research Institute, Gurgaon, India

Objectives: Philadelphia Positive Acute Lymphoblastic Leukemia (Ph+ve ALL) is an aggressive disease with poor prognosis in children. Our objective was to determine the outcome of the Ph+ve ALLin childhood from Northern India.
Methods: Sixty one cases of pediatric acute lymphoblastic leukemia were studied retrospectively.
Results: Ph+ve ALL was found in five cases (8.2%). Of the 5 patients, three were male and two werefemale with a median age of 10 years (range,6 months to 12 years). Four were treated on BFM-95 protocol and one on UKALLXI protocol. Imatinib mesylate (375 mg/m^2 was started daily at the time of diagnosis. All went in remission and later achieved complete molecular remission. However during maintenance therapy 3 patients started having rising value of quantitative BCR-ABL values at 18 months, 25 months and 31 months from diagnosis. As all these 3 children had no siblings and no matched unrelated donor was available so in these three Imatinib was stopped and after taking informed consent of parents Dasatanib was started at a dose of 100 mg/m2/day in two divided doses and maintenance therapy of oral 6-Mercaptopurine and Methotrexate was continued. All these 3 patients achieved reduction in BCR-ABL quantitative PCR after 3 months and molecular remission after 6 to 9 months after starting dasatinib. One patient stopped Dasatinibafter 8 months on its own and started on herbal medicine, is in molecular remission. One had isolated CNS relapse. Rest two patients are on Imatinib and in molecular remission. Two patients on Dasatinib had acquired WHIMsyndrome during therapy and one patient on Imatinib had fracture, excessive callus formation and mal-union of humerus. Four patients had growth delay with short statured for their age.
Conclusions: Dasatanib is an useful alternative drug for Imatinib resistant Ph+ve ALL. Side effects need to be monitored carefully while patients on Dasatinib or Imatinib.

EP-044

COLLABORATION AMONG DIFFERENT ONCOLOGY CENTERS IN A MIDDLE INCOME COUNTRY CAN IMPROVE RISK STRATIFICATION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

S. Muwakkit[1], A. El Trabulsi[1], M. Salman[1], R. Mahfouz[2], P. Noun[3], H. Khalife[4], R. Farah[5], G. Gemayel[4], N. Kabbara[4], N. Yassin[6], N. Sbeity[6], R. Saab[7], M. Abboud[7], H. El-Solh[7]

[1]Department of Pediatric and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; [2]Department of Pathology and Laboratory Medicine, American University of Beirut, Beirut, Lebanon; [3]Department of Pediatrics, Geitaoui Lebanese Hospital, Beirut, Lebanon; [4]Department of Pediatrics, Rafic Hariri Governmental General Hospital, Beirut, Lebanon; [5]Department of Pediatrics, Saint George Hospital University Medical Center, Beirut, Lebanon; [6]Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon; [7]Department of Pediatrics and Adolescent Medicine, American University of Beirut, Beirut, Lebanon

Objectives: Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood. Optimally, treatment strategies differ among different risk cases. The Children Cancer Center of Lebanon at American University of Beirut offers to all newly diagnosed Lebanese children with ALL the chance to get risk-specific treatment by providing analysis of bone marrow (BM) flow cytometry, molecular and cytogenetic testing free-of-charge. Costs were covered through fund raising at the national level.
Methods: We identified patients with ALL younger than 18 years, diagnosed between 04/2002 and 12/2012; retrospective chart review was conducted to collect patients' laboratory data. This review included Lebanese patients newly diagnosed with ALL and treated at Lebanese hospitals.
Results: 338 patients were identified (191 (57%) males); 9 (2.6%) patients were <1 year of age, 254 were between 1-10 years, and 75 (22%) ≥10 years; initial WBC was ≥50,000 in 80 (23.6%) patients, 82.5% had B-lineage and 17.5% had T-lineage ALL; DNA index was ≥1.16 in 18.5%. Metaphase cytogenetics revealed normal karyotype in 50%, >50 chromosomes in 10%, 47-50 chromosomes in 8% and <46 chromosomes in 3%. The rest failed cytogenetic testing. Molecular studies (RT-PCR) were done for 242 patients; 18% had t (12:21), 6.5% had t (1:19), 2% had t (9:22), and 3% had t (4:11).

Conclusions: The high karyotype failure rate is attributed to the long waiting time between BM performance and delivery to cytogenetics lab. Our future plans include performing Day 15 MRD studies for all patients as well as the use of a uniform treatment protocol. Offering free-of-charge examination of BM for Lebanese pediatric ALL patients was important for risk stratification of patients in order to offer them risk-adapted therapy, thus the best chance of cure. Our experience can serve as a good model for other middle and low-income countries for collaboration, implementing uniform treatment protocols and hopefully improving survival of children with ALL.

EP-045

TREATMENT RELATED DEATH IN RELAPSED CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

T. Oskarsson[1], S. Söderhäll[1], J. Arvidson[2], E. Forestier[3], T. Frandsen[4], N. Carlsen[5], M. Hellebostad[6], A. Glomstein[7], P. Lähteenmäki[8], M. Heyman[1]

[1]Pediatric oncology, Karolinska University Hospital, Stockholm, Sweden; [2]Pediatric oncology, Uppsala University Hospital, Uppsala, Sweden; [3]Pediatric oncology, Umeå University Hospital, Umeå, Sweden; [4]Pediatric oncology, Rigshospitalet University Hospital, Copenhagen, Denmark; [5]Pediatric oncology, Odense University Hospital, Odense, Denmark; [6]Pediatric oncology, Ullevål hospital, Oslo, Norway; [7]Pediatric oncology, Rikshospitalet University Hospital, Oslo, Norway; [8]Pediatric oncology, Turku University Hospital, Turku, Finland

Objectives: Patients with relapsed acute lymphoblastic leukemia (ALL) are more susceptible to the adverse effects of leukemia therapy both because of the accumulation of organ specific toxicities and the intensity of the relapse treatment. In addition, a higher proportion of patients undergo stem cell transplantation (SCT) in second complete remission (CR2), where prolonged severe immunosuppression and graft-versus-host disease (GVHD) further increase the risk of life threatening events. The aims of this study were to investigate the incidence and risk factors for treatment related deaths (TRDs) in patients with relapsed childhood ALL.
Methods: In this retrospective population-based study we analyzed data on all children that relapsed after common upfront treatment according to the Nordic Society of Paediatric Haematology and Oncology (NOPHO) ALL-92 and ALL-2000 protocols. All patients had pre-B or T-cell immunophenotype and were >1 years and <15 years at diagnosis but those undergoing SCT in first complete remission were excluded from the study. Patient data was exported from the NOPHO ALL registry but in case of incomplete registration requests were sent to treating clinics,
Results: We identified 50 patients with TRDs among the 485 patients that were included in the study (10.3%). Eleven patients died before reaching CR2, 15 in CR2 treated with chemotherapy only and 24 patients after undergoing SCT in CR2. Infections were the most common cause of death, 35 of 50 (70%). Independent risk factors for TRDs were high risk clinical profile at relapse and unfavorable cytogenetics but we did not find any significant gender or age differences.
Conclusions: Treatment related deaths are approximately three times as common during relapse treatment than during primary treatment. Infections are the most common reason for TRDs. Patients stratified as high risk at relapse and patients with unfavorable cytogenetics should be monitored closely and treated promptly for suspected infections.

EP-046

ENDOCRINE SIDE EFFECTS AFTER CHEMOTHERAPY IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

B. Uysal[1], Y. Oymak[1], K. Demir[2], T. Hilkay Karapinar[1], Y. Ay[1], S. Gozmen[1], B. Demirag[1], O. Carti[1], G. Ozek[1], B. Tatli Gunes[1], E. Albudak Ozcan[1], E. Toret[1], D. Ince[1], C. Vergin[1]

[1]Pediatric Hematology and Oncology, Dr. Behcet Uz Chidren's Hospital, Izmir, Turkey; [2]Pediatric Endocrinology, Dr. Behcet Uz Chidren's Hospital, Izmir, Turkey

Objectives: Focus on long-term side-effects after cancer therapy in childhood has become of the crucial importance. The exposure of chemotherapy at young ages has increased vulnerability to long-term treatment induced sequelae. Also contribution of radiation may increase adverse sequelae.
Methods: We aimed to evaluate endocrine side effects in 41 patients (M/F = 20/21) with acute lymphoblastic leukemia (ALL) being followed-up 1-5 years after treatment. Patients were screened for endocrine side effects, growth, blood glucose metabolism, lipid metabolism abnormalities, sexual development, thyroid metabolism, bone mineral density and adrenal insufficiency.
Results: Mean age of the patients were 10 ± 3.1 years. In 35 of 41 (85.3%) patients at least one endocrine complication was detected. One patient's (2.4%) height was under 3 percentile, 12 (29.3%) patients were obese. Forteen (34.1%) patients had insuline resistance. Three (7.3%) patients had IGF levels under -2 SDS, two (4.9%) patients had high FSH-LH levels. One (2.4%) patient had subclinical hypothyroidy, one (2.4%) patient had positive thyroid antibodies. Twenty (48.9%) patients had low levels of cortisol. Six (14.6%) patients had subclinical D vitamine deficiency, two (4.9%) patients had subclinical hyperparathyroidy, three (7.3%) patients had isolated hypercalcemia. Only insulin resistance rate was higher in patient who were apllied RT than those who weren't apllied RT.
Conclusions: In this study endocrine side effects were seen in the two years after therapy. The patients who were applied chemotherapy and RT for ALL treatment, should be followed-up closely for endocrinological side effects, and early diagnosis and treatment should be performed for endocrinological disases which may develop later in life.

EP-047

INTERACTION MODEL BETWEEN NATURAL KILLES CELLS AND LEUKEMIC CELLS: FIRTS GOALS AND PRELIMINARIES DATA

J.F. Pascual Gázquez[1], M.V. Martínez Sánchez[2], A.M. Galera Miñarro[1], M. Blanquer Blanquer[3], A. Minguela Puras[2], M.M. Bermúdez Cortés[1], A. Sánchez Salinas[3], T. Escámez Martínez[4], J.L. Fuster Soler[1], J.M. Moraleda Jiménez[3]

[1]Paediatrics Oncology and Haematology Service., Hospital Universitario Virgen de la Arrixaca, Murcia, Spain; [2]Immunology service, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain; [3]Haematology cell therapy and transplant unit., Hospital Universitario Virgen de la Arrixaca, Murcia, Spain; [4]Biobank and IMIB service., Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Objectives: Acute Leukaemia is the most common malignant pathology. Contemporary chemotherapy protocols achieve 75% overall survival; this results did not improve during the last several years. A new treatment approach is represented by the anti-tumor immune mediated inherent alloreactivity of NK cells (NKc). We need to know more about the role of the interaction between NKc and leukemic cells; about this we started a prospective trial in October of 2012 to clarify it. The trial's goals are: describe the match or mismatch NKc receptors (KIR) with leukemic cells, the cytotoxicity, the role of serum cytokines and the progress in transplant patients.
Methods: Preliminaries results are presented in this review. We included 20 acute lymphoblastic or mieloblastic leukaemia from October 2012 till January 2014, and One patient was excluded because refused to sing the consents. We collected data from 13 males and eight females, the median was 6 years old (age range from 1 to 13 years old). At the same time we stored sera and leukemic cells previous treatment.
Results: We got a 78.9% of free event survival and only a 10.5% of mortality. The sample has three children with ALM M7, thirteen B ALL and three T ALL. We transplanted six of them, watching disparities around 0 to 8 in KIR receptors.
Conclusions: In conclusion, We show that the AB genotype was the most common genotype in relapsed patients. The next steps in the study are: test the cytotoxicity in the complete remission patient at the end of treatments and link these results with KIR and HLA genotype.

EP-048

GENE EXPRESSION OF MULTI DRUG RESISTANCE PROTEIN (MDR-1), MULTI DRUG RELATED PROTEIN (MRP) AND LUNG RESISTANCE PROTEIN (LRP) IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA CASES

B. Prateek[1], S. Masih[2], S. Rani[2], N. Varma[3], J. Binota[3], D. Bansal[4], R.K. Marwaha[4]

[1]PEDIATRICS, PGIMER, Chandigarh, India; [2]Molecular diagnsotic laboratory, MDR Laboratories, Chandigarh, India; [3]Hematology, pgimer, Chandigarh, India; [4]Pediatrics, pgimer, Chandigarh, India

Introduction
Approximately 25% of ALL children present with disease recurrence. Treatment failure is due to either pharmacokinetic resistance or cell resistance to antineoplastic drugs.
Aims & Objectives
To study gene expression of Multi drug resistance protein (MDR-1), Multi drug related protein (MRP) and Lung resistance protein (LRP) in pediatric ALL and to correlate it with early response to chemotherapy and other clinical and laboratory variables.
Methods: Prospective study (2013-2014), in which 45 pediatric ALL cases were enrolled. Relative quantification of mRNA of MDR-1, MRP and LRP was done by Real Time PCR assay using SYBR-G dye. A high expression was defined as > 0.5 fold than in control cells.
Results: Of 45 cases, 33 male and 12 female (M:F-2.75:1). Mean age was 5.2 years. Based on TLC and age, 26/45 (58%) were in standard risk, 17/45 (38%) intermediate and 2/45 (4%) in high risk category. Only 3/45 (7%) were T-ALL and rest (93%) B-ALL cases. Abnormal cytogenetics was noted in 5/45 (11.0%). Day 14 check marrow status was M1 in 38/45 (84%), M2 4/45 (9%) and M3 3/45 (7%) cases. High expression of MDR-1 and LRP was noted in 10/45 (22%) cases each and MRP in 18/45 (40%) cases. A significant association was noted between slow early response (M2 & M3 status at D14) and four fold or higher LRP gene expression ($p < 0.05$). Only one case had disease relapse and it also had 4 fold high LRP expression.
Conclusions: There were 6 post induction deaths, all sepsis related. In three of them, high expression of LRP gene was noted. A study by ET Valera et al also found a positive association between increased LRP expression and poor event free survival. Larger prospective studies are needed to correlate drug related gene expressions with overall survival/outcome to better understand their clinical relevance.

EP-049

PLATELET MICROPARTICLES IN PEDIATRIC PATIENTS WITH LEUKEMIA AND SOLID TUMORS

G. Mokhtar[1], A. Tantawy[1], I. Ragab[1], I. Abdel-Rahman[2], R. Radwan[1]

[1]Pediatrics Department, Ain-shams university, Cairo, Egypt; [2]Clinical Pathology Department, Ain-shams university, Cairo, Egypt

Objectives: The contribution of platelets to the progression of cancer is an emerging area of research interest. Study aim: to assess the level of platelets microparticles (PMPs) in childhood malignancies and its relation to response to therapy.
Methods: A prospective case control study including 25 newly diagnosed patients with malignancy; acute lymphoblastic leukemia (ALL, n = 10), acute myeloid leukemia (AML, n = 10) and stage IV neuroblastoma (n = 5). PMPs were assessed by flow-cytometry at diagnosis and after complete remission/or good partial response and were compared to 25 healthy matched controls.
Results: No significant difference was found in levels of PMPs between patients and control group at diagnosis. No significant difference in median initial or post-induction PMPs between patients with ALL (1.48 (0.62 – 1.87); 2.6 (1.84 – 4.11), AML 1.48 (0.88 – 2.25), 1.84 (1.03 – 2.90)) neuroblastoma (1.77 (0.75 – 1.77); 1.76 (1.75 – 2.89)), P = 0.595 and 0.232 respectively. There was no significant difference between pre and post induction PMPs in patients with ALL (P = 0.401), AML (P = 0.482); and a significant rise in PMP was found in patients with neuroblastoma post-induction phase (P = 0.026). In ALL group, there was no significant correlation was found between platelets count and in PMPs before (r = .0.443, P = 0.2) or after chemotherapy (r = 0.236, P = 0.511); a significant positive correlation was found between platelets count and PMPs after chemotherapy (r = 0.818, P = 0.013) in AML group. In neuroblastoma group, both mean platelet count and PMPs level significantly increased after chemotherapy, and significant correlation was found between platelets count and PMPs after chemotherapy (r = 0.9, P = 0.037). Higher PMPs level at diagnosis was found in the patients who died during the induction phase.
Conclusions: We conclude that platelets microparticles rose after induction phase in children with ALL, AML and neuroblastoma; we suggest interpreting the absolute PMP count with caution in patients with thrombocytopenia and rather use a PMP/platelet count ratio; yet conclusions need to be cautiously interpreted because of the small sample size.

EP-050

ESTABLISHING CLINICAL RESEARCH IN A LIMITED RESOURCE SETTING, "ACUTE LYMPHOBLASTIC LEUKEMIA MODEL"

W. Rashed[1], S. Ezzat[1]

[1]Research, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt

Objectives: Establishing research team on Childhood Acute Lymphoblastic Leukemia (ALL) in a limited resource country like Egypt was a challenge. This challenge was increasing with the increase the number of ALL patients it receives every year (average 250 cases).
Methods: Research Department was established in November-2008. I was the first time in Egypt to introduce the concept of forming team for each disease. A multidisplenary team of ALL was formed.
Results: The above mentioned steps had a marvelous impact on childhood ALL. Initially, a genetic epidemiology grant in ALL funded by US-NIH was obtained. Based on the results of this grant we applied to another grant on ' Genome wide Association Study (GWAS) in ALL' to get fund and complete our research to identify the cause of ALL in Egyptian population and successfully obtained 10 million Egyptian pounds. The presence of ALL database and statistical analysis of the survival, allow them to 1- hold collaboration with St Jude Research Hospital in special risk protocol that allow both check quality of flow cytometry results, cytogentics results so enhance the quality and allow rapid consultation on complicated cases, 2- the presence of hospital based-cancer registry for ALL, 3- Supplying biobank with samples that will help in future research, 4- rapid statistics of the number of relapsed patients and died during induction and in relapse. In addition to Production of patient education booklet as an educational material for their treatment protocol. The future plan to make strategy becomes mandatory: 1- Identifying the genetic causes of relapse, 2- Route-cause analysis for patient died during induction and in complete remission, 3- The plan to make translational research and how to individualize treatment. 4- educate illiterate families and their kids via simple audio-visual materials.
Conclusions: The presence of clinical research has an impact on the childhood ALL patients, staff and the institution.

EP-051

SIGNIFICANCE OF DAY 29 BONE MARROW IN ACUTE LYMPHOBLASTIC LEUKEMIA WITH M 1 BONE MARROW AT DAY 8/15 IN ABSENCE OF MRD

N. Bukhari[1], S. Riaz[1], M. Ahmed[1]

[1]Pediatric Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Objectives: Acute lymphoblastic leukemia (ALL) is most common hematological malignancy among pediatric population. Different protocols like UKALL and COG are used for management and all protocols suggest bone marrow biopsy at day 8 or 15 and then at day 29 during induction phase. On day 29 Minimum residual disease (MDR) status is usually advised. Developing countries where facility of MDR is not available patients of ALL are being treated according to these protocols and bone marrow biopsies are advised on both day 8/15 and day 29. Our hypothesis is "if day 8/15 bone marrow is in remission there is no significance of day 29 bone marrow in absence of MRD facility"
Methods: All patients of ALL admitted form jan 2008 to dec 2013 and survived during induction were included. Induction therapy according to standard arm of UKALL 2003 was given. Bone marrow biopsy was done on day 8 or 15 depending upon regimen and day 29 in all patients. MDR was not available.
Results: Total 282 patients were included. Male to female ratio was 2:1. Age range from 7 month to 17 year. Seventeen (6%) patients were >10 yrs and 265 (94%) were < 10 year.30 (10.6%) patients had T cell ALL and 252 (89.4) had Pre B ALL. Seventeen (6%) patients had M2 bone marrow and 13 (4.6%) had M3 bone marrow on day 8/15 but none of them had residual leukemia on day 29. 252 (89.3%) patients had bone marrow in remission on day 8/15 and none of them had evidence of residual leukemia on day 29 bone marrow.
Conclusions: In absence of MRD facility there is no significance of day 29 bone marrow if day 8/15 bone marrow is in remission.

EP-052

SURVIVAL ANALYSIS OF CHILDREN AND ADOLESCENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED IN A ONCO HEMATOLOGIC CENTER OF CHILDHOOD - CETOHI FROM BRAZIL

M. S Souza[1], A. Mnayarji[1], R. Basegio[1]

[1]Departamento de Oncologia, Centro de Tratamento Onco Hematologico Infantil - CETOHI - do Hospital Regional, Campo Grande, Brazil

Background: In a public institution children with de novo acute lymphoblastic leukemia were treated from January 2000 to December 2012, according to Brazilian Childhood Cooperative Group-Protocol (GBTLI) ALL-99 and Berlin-Frankfurt-Munich (BFM) protocol ALL-95/02.
Aim: Evaluate the experience with teses protocols and the treatment results according to the risk groups.
Methods: Children aged 0 to 18 years old were stratified into 2 risk groups: low and high-risk group.
Results: One hundred seventh nine children entered the study (male-female ratio was 1.48:1, the average age was 7 years and 7 months and the median age was 6 years and 4 months). 111 (62,92%) children were in the low risk, 68 (37,07%) in the high-risk group. The overall complete remission rate was 88,26%. Twenty-one (12,35%) children died in induction and 04 were non-responders. The 5-year overall survival for all patients was 61,5%, in the low risk group 70,10% and in the high-risk group 52,7% the average age of follow was 6 years and 2 months. The median of follow-up was 6 years and 5 months. From the 179 patients 110 (61,5%) are still in their first complete clinical remission and other 07 children are alive after relapse. In 22,3% of the patients have relapsed. The 5-year disease-free survival for all patients was 51,5%, in the low risk group 73,1% and in the high-risk group 55,5%.
Conclusion: The treatment outcome of children with acute lymphoblastic leukemia improved remarkably over the last decade. 61,5% of children suffering from acute lymphoblastic leukemia could be cured with the GBTLI-ALL 99 and BFM-ALL 95/02 protocol. The results of the patients of this public institution were comparable with the results achieved by other services in Brazil and other countries.

EP-053

THREE CASES OF CHILDHOOD MATURE B-ACUTE LYMPHOBLASTIC LEUKEMIA WITH NON-L3 MORPHOLOGY AND MLL-AF9

T. Sarashina[1], H. Goto[1], N. Miyagawa[1], T. Yokosuka[1], K. Fukuda[1], F. Iwasaki[1], S. Hamanoue[1], H. Iwabuchi[2], T. Takachi[2], A. Saito[2], C. Imai[2]

[1]Division of Hemato-oncology/Regeneration, Kanagawa Children's Medical Center, Yokohama, Japan; [2]Department of Pediatrics, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

Objectives: Mature B-ALL is typically associated with FAB-L3 morphology and rearrangement of the *MYC* gene. However, some reports showed that rare ALL cases with non-L3 morphology and *MLL-AF9* chimeric gene can express a mature B-cell immunophenotype and may represent a distinct subset with a mostly rapid and aggressive clinical course. We report 3 such cases of mature B-ALL, and discuss the clinical, genetic, and immunophenotypic features in the context of previously reported cases.
Methods: Patient 1 was a 4-month-old female infant. Patient 2 or 3 was a 15-month-old or a 4-year-old female, respectively. The bone marrow smears at diagnosis showed FAB-L1 morphology in all patients. Immunophenotypically, they were positive for CD10, CD19, CD20 (or CD22), HLA-DR, sIgλ, and sIgM. No evidence of *MYC* rearrangement was detected in all cases with FISH analysis. *MLL* rearrangement was detected by FISH and *MLL-AF9* was confirmed by RT-PCR.

Results: They achieved complete remission after conventional chemotherapy and underwent hematopoietic stem cell transplantation as high risk ALL; patient 1 for infantile ALL with *MLL* rearrangement and the others for ALL with *MLL* rearrangement and hyperleukocytosis (WBC at diagnosis $>50\times10^9$/L). Patient 2 received bone marrow transplantation from HLA-identical sibling and patient 1 or 3 received cord blood transplantation from 5/6 or 8/8 HLA-matched unrelated donor, respectively. Patients 1 and 2 have maintained complete remission for more than 6 years since transplantation. Patient 3 remains in complete remission at 6 months after initial diagnosis.
Conclusions: In previous reports, survival of patients with ALL characterized by mature B immunophenotype, non-L3 morphology and *MLL-AF9* is poor, especially after relapse. Accumulation of cases with such features will further clarify clinical significance of the unique phenotype in childhood ALL.

EP-054

RETROSPECTIVE ANALYSIS OF A COHORT OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) CASES FROM SINGLE TERTIARY CARE CENTER IN INDIA

R. Sharma[1], Y. Chopra[1], M. Ramzaan[1], S. Katewa[1], S.P. Yadav[1]

[1]Pediatric Hematology Oncology & BMT, Fortis Memorial Research Institute, Gurgaon, India

Objectives: Pediatric ALL is characterized by varied clinical presentation with recurrent numerical and structural chromosomal abnormalities, which are thought to be specifically associated with diagnosis, risk stratification, treatment response and prognosis.
Methods: Children (upto 18yrs) diagnosed with ALL over a period of 7yrs (Jan 2006-Dec 2013) were analyzed retrospectively.
Results: A total of 61 (53 B cell, 8 Tcell) patients were evaluated. Mean age at presentation was 7.2 yrs (1 yrs - 18 yrs).M:F was 2:1. National Cancer Institute risk stratification was standard in 35, high 23 and very high in 3patients. 35 were treated on BFM 95 protocol and 26on UK ALL XI protocol.8 were lost to follow up (LTFU) at a median of 12 months (1 to 29 months) and 1 refused treatment after relapse.
As on 31st Dec2013, 52 patients were evaluated for final outcome analysis. 12 are alive on various phases of chemotherapy after a mean follow up of 21.4 months; 38are alive and completed treatment after a mean follow up of 49 months. 10 relapsed at median of 34 months (12 - 57months). Those who relapsed 4 were very early, 2 early and 4 were late relapse. Except 1 who was standard risk, all relapses were in high or very high risk (BCR-ABL) category. All were started on relapse protocol (ALL REZ BFM 95/96). 1 refused treatment, 4 given chemotherapy, 3 underwent bone marrow transplant (allogenic) and are alive on follow up and 2 expired. For the entire cohort event free survival (EFS) was70% and overall survival (OS) was 81% at 35months mean follow up.
Conclusions: Cytogenetics studies could not be done in significant number of patients due to resource constraints. There were a significant number of LTFU patients that needs to be addressed in LMIC setting.

EP-055

SOMATIC NT5C2 MUTATIONS IN CHINESE PATIENTS WITH RELAPSED PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

S.-G. Liu[1], C. Gao[1], Z.G. Li[1], R.D. Zhang[1], W.J. Li[1], L. Cui[1], M.Y. Wu[1], H.Y. Zheng[1]

[1]Hematology Oncology Center, Beijing Children's Hospital, Beijing, China

Objectives: Children with relapsed acute lymphoblastic leukemia (ALL) carry poor prognosis owing to intrinsic drug resistance. However the biological pathways that mediate chemotherapy resistance remain unknown. Relapse-specific mutations of *NT5C2* gene have recently been identified in childhood ALL. The aim of the present study was to investigate the frequency and clinical impact of *NT5C2* mutations in Chinese pediatric patients with relapsed ALL.
Methods: This study enrolled 58 patients with relapsed ALL which included 15 T cell ALL and 43 B-precursor ALL. We sequenced the exon 9, 13, 15, and 16 of the *NT5C2* gene.
Results: The R367Q mutation was detected in 2/15 (7.5%) relapsed T cell ALL patients. A novel mutation (H352D) which mapped to the active site of the NT5C2 enzyme was detected in 1/43 (2.3%) relapsed B–precursor ALL patient. All the mutations were heterozygous and located in exon 13. Clinically, all patients carrying *NT5C2* mutations relapsed early, within 36 months after initial diagnosis, although the difference was not significant ($P = 0.150$).
Conclusions: These findings suggest that *NT5C2* mutation is a recurrent event in ALL. The novel H352D mutation expands the mutation spectrum of *NT5C2*.
A*cknowledgments
This work was partially supported by National Natural Science Foundation of China (No.81300434), the Key Scientific and Technological Projects of Beijing Municipal Education Commission (No. KZ201210025031), and National Science & Technology Major Project of the 12th 5-Year Plan (No. 2011ZX09302-007-01).

EP-056

UNUSUAL MANIFESTATIONS OF NON SINOPULMONARY FUNGAL INFECTIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

S. siddaiahgari[1], B. jillela[2]

[1]Pediatric Hematology- Oncology, Rainbow Childrens Hospital, Hyderabad, India; [2]Pediatric Hematology- Oncology, Rainbow Childrens Hospital, Hyderabad, India

Objectives: Fungal infections causes significant morbidity & moratlity, increasing economic and Pscychological burden in acute lymphoblastic Leukemia children.
we described different types of non sinopulmonary fungal infections and their outcome in ALL children
Methods: Identified 4 interesting cases of ALL children with different types of fungal infection manifesting in different forms.
Results: A 10 years male with CALLA positive B cell ALL, in week 4 of Induction presented with 3 cm hyperpigmented lesion over medial aspect of Right foot. He had pancytopenia. Lesion was not responding to antibiotics and antifungals, requiring debridement and been identified as Exserohilum Rostratum in fungal culture.
Lesion resolved after 4 weeks of Iv amphotericin B and Debridement.
Case 2: Unusal Fungal infections in well child should raised the suspicion of malignancy. A 3.5 years male presented with fever of 7 days, was initially managed as Enteric fever with iV antibiotics. An abscess at cannula site noticed, culture grew Rhizopus Aerhizus. CBP revealed hb of 8.5 gm% and WBC 3800, Lyphocytes of 74%, platelets were 1.8 lakhs. Bone marrow Aspiration confirmed CALLA Positive B ALL. He responded to Amphotericin B.
Case 3: A 5 year old male with standard risk, CALLA positive ALL, on Induction presented with history of right eye swelling and chemosis. Even by week 4 of induction had neutropenia of 544 cells. Right eye Vitreous biopsy done, had endophthalmitis. Intravitreal amphotericin given. Culture of Vitreal fluid Isolated Aspergillus fumigatus. Antifungals given for 8 weeks to control fungal infection.
Case 4: 13 years female with CALLA positive, CNS negative standard count and genetics ALL, on consolidation developed skin fungal infection in axilla which has been identified as mucormycsis, She required debridement of skin lesion along with 6 weeks of Iv liposomal amphotericin B.
Conclusions: Awareness & early recognition of different fungal infections in ALL children is important to prevent mortality and morbidity.

EP-057

PEG ASPARGINASE INDUCED SUPERIOR SAGITAL SINUS THROMBOSIS: IN ACUTE LYMPHOBLASTIC LEUKEMIA CHILDREN - A REPORT OF 2 CASES

S. Siddaiahgari[1], D. Makadia[1], L. Lingappa[2]

[1]Pediatric Hematology-Oncology, Rainbow Childrens Hospital, Hyderabad, India; [2]Pediatric Neurology, Rainbow Childrens Hospital, Hyderabad, India

Objectives: To identify the cause of cerebral sinovenous thrombosis (CSVT) in 2 children on induction therapy for acute leukemia
Methods: Two children identified to have CSVT out of 178 ALL's treated from October 2008 to December 2013. Eighteen received pegasparginase and remaining L asparginase.
Results: Case 1:a 2.6 year old male with standard risk ALL developed left focal tonic-colonic seizure evolving into status epilepticus & left hemiparesis, 3 days in to consolidation, 2 weeks post second dose of pegasparginase. Induction given using dexamethasone, vincristine, peg-asparaginase and intrathecal methotrexate. He had CVST, predominantly on right side in MRI brain. Started on low-molecular weight heparin (LMWH) and levetriacetam. Left hemiparesis improved and was fully ambulatory within 1 week. Consolidation chemotherapy continued smoothly with the concomitant use of LMWH. Intrathecal methotrexate has been omitted temporarily, which was subsequently restarted. He was continued on LMWH for 6 months until post reinduction where pegasparginase is part of shedule. His repeat MR angiogram revealed partial recanalization. His thrombophilia work up initially showed low protein S and antithrombin III which became normal 6 months post CVST. Procoagulant work up on parents was completely normal. Case 2: 3.4 year old female presented with status epilepticus with left hemiparesis in week 4 of induction, 2 weeks after first dose of pegasparginase. Had siimilar course as case 1 except requiring 2 antiepileptics to control seizures. And also normal thrombophilia work up even at the time of episode. Low molecular weight heparin continued in similar fashion till reinduction. Both of them showed good response to therapy without any residual neurological disability.
Conclusions: Both cases illustrates strong correlation between rare thrombotic complication, CVST and hypercoagulable status secondary to combination of asparaginase and corticosteroid. Early and vigilant recognition and prompt anticoagulation prevents further neurological damage.

EP-058

LIPID PROFILE BEFORE AND AFTER INDUCTION CHEMOTHERAPY IN BANGLADESHI CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

R. Siddique[1], C.Y. Jamal[1], M.A. Karim[1], F. Yasmin[1], S.M.R. Rahman[1], B. Yamin[1], A. Islam[1]

[1]Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Objectives: To evaluate the changes in lipid profile after L- asparaginase and after completion of induction chemotherapy.
Methods: This was an observational analytic study carried out from March to November 2013 in the department of Pediatric Hematology and Oncology, BSMMU, with a view to evaluate the changes in lipid profile due to induction chemotherapy (Protocol UKALL 2003 modified). 35 newly diagnosed children with ALL age range 3-15 years were included in the study. Fasting (8-12 hours) serum total cholesterol, TG, HDL, LDL, fasting blood glucose, ALT, creatinine were done before treatment, after completion of asparaginase and after induction completed. Risk stratification of the patients was done by age, report of CBC and bone marrow examination.
Results: The mean ($\pm$ SD) age of 30 children of this study was 6.07 ± 2.95 years, 66.7% were in the age group $\leq$6 years and 66.7% were male. In the current study before treatment mean total cholesterol, TG, HDL and LDL values were 158.40 ± 42.70, 184.47 ± 65.32, 19.93 ± 10.85, 101.20 ± 35.01 mg/dl. After completion of L-asparaginase, TG, LDL declined significantly and HDL increased significantly. After completion of induction chemotherapy the mean values of total cholesterol, HDL LDL level increased to 195.43 ± 36.58 ($P = 0.003$), 50.20 ± 19.59 ($P = 0.001$) and 116.70 ± 27.59 ($P = 0.186$) respectively, but TG decreased to 140.93 ± 62.80 ($P = 0.060$). It was also observed that those patients who received dexamethasone 10mg/m^2 had significantly increased cholesterol level in comparison to those received it 6mg/m^2.
Conclusions: After induction chemotherapy total cholesterol, HDL and LDL level increased and TG level decreased. Increased cholesterol value was probably due to steroid rather than L-asparaginase.

EP-059

RHINOCEREBRAL MUCORMYCOSES IN CHILD WITH ACUTE LYMPHOBLASTIC LEUKEMIA

D. Skoric[1], G. Milosevic[1], S. Laban[2]

[1]Department of Hematology and Oncology, Children's University Hospital, Belgrade, Serbia; [2]Department of Microbiology, Children's University Hospital, Belgrade, Serbia

Objectives: Mucormycosis is rare fungal disease, affecting immunocompromised patients. Rhinocerebral mucormycosis is most common form and has very high mortality rate.
Methods: Here, we present a case of rhinocerebral mucormycosis in pediatric acute lymphoblastic leukemia patient (ALL).
Results: A 2.5-year-old female diagnosed with ALL presented with febrile neutropenia for the third time during induction phase. First and second line antibiotics were introduced without success. Dark discoloration of hard palate and periorbital edema were noted. Caspofungin was administered due to suspicion of aspergillosis (positive serum galactomannan assay). Due to aggravation of general condition, patient was transferred to PICU. Two days later, dark discoloration of skin was noted at the base of nose. Endocranial CT revealed hyperdense fluid in paranasal sinuses and in nasal cavity. Endoscopic examination of nasal cavity reveled perforation of nasal septum and necrosis of maxillary and ethmoidal sinuses. On 9th day of infection colloid dispersion of amphothericin B was introduced to therapy due to suspicion of mucormycosis. Tissue samples that were taken for histopathology and cultures confirmed diagnosis. Progression of local findings and deterioration of general condition continued and lead to respiratory failure. Local surgical intervention was consider but was not performed due to progression of process on cerebral parenchyma as seen on MRI. Patient developed pulmonary hemorrhage and ARDS which lead to fatal outcome on 17th day of infection.
Conclusions: Late recognition, aggressiveness of infection and inability to perform radical surgical debridement has led to fatal outcome. This was the first case of mucormycosis at our institution. Rhinocerebral mucormycosis is rare, rapidly progressing disease with high mortality rate. Early diagnosis, resolution of predisposing factors, aggressive surgical intervention and timely use of adequate antifungal agents are cornerstones of successful treatment. Nevertheless, mortality is still high and further efforts must be made to improve outcome of mucormycosis.

EP-060

METHYLENETETRAHYDROFOLATEREDUCTASE AND GLUTATHIONE S TRANFERASE GENE POLYMORPHISMS IN SECONDARY LEUKEMIA

D. Skoric[1], I. Joksic[2], T. Radic[3], T. Simic[3], G. Milosevic[1]

[1]Department of Hematology and Oncology, Children's University Hospital, Belgrade, Serbia; [2]Department of Genetics, Clinic of Gynecology and Obstetrics "Narodni front", Belgrade, Serbia; [3]Institute of Medical and Clinical Biochemistry, Faculty of Medicine University of Belgrade, Belgrade, Serbia

Objectives: Therapy-induced leukemia is well-known clinical syndrome occurring as a late complication in patients treated with cytotoxic therapy. We herein present results of analysis of common gene polymorphisms in methylenetetrahydrofolatereductase (MTHFR) and gluthatoin s transferase (GST) genes in a 10-year-old male who developed rare type of cancer, acute biphenotypic leukemia, six years after treatment of acute lymphoblastic leukemia.
Methods: We studied *MTHFR* C677T and A1298C and *GSTA1, GSTM1*, *GSTT1*, *GSTP1* and *GSTO2* gene polymorphisms to assess role of heritable factors in development of this rare type of childhood secondary leukemia.
Results: Analysis of *MTHFR* gene polymorphisms showed that the patient is homozygous for 677TT and heterozygous for A1298C, which results in lower enzyme activity. Among GST genotypes tested, lower expression *GSTA1*B* gene variant together with homozigous deletion of *GSTM1* was found. Absence of GSTM1 protein as well as down-regulated GSTA1 expression and activity could result in lower detoxification potential towards anticancer drugs.
Conclusions: Analysis of *MTHFR* gene polymorphisms showed that the patient is homozygous for 677TT and heterozygous for A1298C, which results in lower enzyme activity. This could confer to increased risk for development of secondary malignancy in several ways. Our results are in accordance with higher frequency of *GSTM1 null* genotype in secondary hematologic malignancies of patients after treatment with cyclophosphamide. It seems reasonable to asumme that *GSTM1 null* and lower activity *GSTA1*B/*A* genotype resulted in enhanced chemotherapy induced oxidative DNA damage, which could lead to mutations and secondary leukemia.

EP-061

EXPRESSION OF BID, BAK AND BCL-XL IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

M. Panagouli[1], G. Martimianaki[1], M. Pesmatzoglou[1], E. Athanassopoulos[1], E. Stiakaki[1]

[1]Pediatric Hematology-Oncology, University Hospital of Heraklion, Heraklion Crete, Greece

Objectives: The quantitative determination of the expression levels of anti-apoptotic BCL-XL, and pro-apoptotic molecules BAK and BID in bone marrow (BM) of children with acute lymphoblastic leukemia (ALL) at diagnosis and in remission and of children with Solid Tumours (ST) without bone marrow involvement.
Methods: Twenty eight children (15 males, median age 7.68 ± 1.06 years) with ALL (23 B-ALL, 5 T ALL), 25 children at diagnosis (ALLd), 23 after remission was achieved (ALLr), and 38 with Solid Tumors at diagnosis without bone marrow involvement, were studied. Total RNA was isolated from bone marrow mononuclear cells. The mRNA levels corresponding to BCL-XL, BAK, and BID were quantified by real-time polymerase chain reaction (PCR) analysis using GAPDH as normaliser. All reactions were performed in duplicates. For quantification of the genes a standard curve was made by serial dilutions of a reference line cDNA (Tanoue).
Results: The expression levels of anti-apoptotic BCL-XL were determined significant higher in ALL blasts at diagnosis compared with remission (ALLdvsALLr:3.16vs0.97, $p = 0.00001$), as well as with ST (ALLdvsST:3.16vs0.64, $p = 0.000000013$). The expression levels of BID were determined low at diagnosis of ALL and high enough in remission with statistically significant difference (ALLdvsALLr:4.57vs18.07, $p = 0.000001$), result which is in accordance with its apoptotic role. High levels were also observed in ST without BM involvement (ALLdvsST:4.57vs10.329, $p = 0.003$). Concerning the expression of apoptotic BAK gene, the levels were found statistically significant higher at ALLd compared with ALL in remission (ALLdvsALLr:4.73vs1.84, $p = 0.001$). Similar high levels were determined in Solid Tumors with statistically significant differences compared with ALLr (STvsALLr:5.44vs1.844, $p = 0.011$).
Conclusions: The over-expression of BCL-XL at ALL diagnosis seems to be suppressed by the induction treatment and remission achievement. The expression of BID is amplified in remission as a pro-apoptotic molecule stimulating apoptosis. The role of BAK levels at diagnosis and remission in respect to its pro-apoptotic function warrants further investigation.

EP-062

DO TRAUMATIC LUMBAR PUNCTURES LEAD TO GREATER RELAPSES IN ACUTE LYMPHOBLASTIC LEUKEMIA? OUTCOME FOR A SINGLE CENTER IN INDIA

S. Totadri[1], A. Trehan[1], R. Srinivasan[2], D. Bansal[1], R.K. Marwaha[1]

[1]Pediatric Hematology and Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [2]Cytology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objectives: The thorn in the success story of treatment in acute lymphoblastic leukemia (ALL) remains relapse. 10-15% patients relapse despite risk adapted therapy. This study was done to address whether traumatic lumbar punctures (TLP) contribute to relapse.
Methods: All children treated for ALL between January 2010 and December 2012 were analyzed. TLP's at diagnosis and subsequently during therapy were evaluated with outcome.
Results: 310 children were treated as per UKALL 2003 protocol. Median age: 5 years (1-13). First diagnostic lumbar puncture results- 274: CNS1; 8: CNS3; 28: TLP. TLP patients got 2 extra intrathecal (IT) methotrexate during induction. Overall, 28 (9.0%) have relapsed, with 12 (3.9%) having CNS relapse. 4 patients with a TLP relapsed (2: CNS). A TLP at diagnosis did not correlate with an increased incidence of overall relapse [$p = 0.966$] or CNS relapse [$p = 0.296$]. There was no significant difference in overall Survival (OS) and event free survival (EFS) in children with CNS1 & TLP (OS: 80.2% & 75%; EFS: 70.3% and 64.3%). A total of 3823 IT's were administered. The rate of traumatic LP was 10% (383/3823). Average

number of TLP per child was 1.2 (0-7). A receiver operator characteristic curve was generated for prediction of relapse based on TLPs during entire treatment. This offered poor sensitivity [AUC CI: 0.48-0.71]. There were 12 CNS relapses, 6 being asymptomatic and detected on routine CSF examination. These were confirmed by cell count and flow cytometry.
Conclusions: Traumatic LP at diagnosis is not associated with an increased risk of relapse. Possibly, the extra intrathecals ameliorated the effect of TLP. Having more than one traumatic LP during treatment does not increase the risk of a relapse. However, routine CSF malignant cytology surveillance has a role in detecting CNS relapse before the onset of symptoms.

EP-063

CLINICO-HAEMATOLOGICAL PROFILE AND OUTCOME OF ACUTE LYMPHOBLASTIC LEUKEMIA: DEVELOPING COUNTRY EXPERIENCE

S. Udgire[1], K. Jain[1], B. Agarwal[1], S. Mudaliar[1], A. Swami[1], N. Shah[1], M. Desai[1]

[1]Pediatric Hematology and Oncology, B.J. Wadia Hospital Parel Mumbai, Mumbai, India

Objectives: Acute lymphoblastic leukemia (ALL) is the most common hematolymphoid malignancy in children. With the advent of new chemotherapeutic protocols and good supportive care, it is highly curable. Aim of this study is to give a comprehensive overview of clinical, haematological presentation, events during therapy, outcome and other significant problems occurred in patients with ALL, as data is lacking from developing country.
Methods: Retrospective data analysis of 174 patients of ALL over a period of 3years (2009-2012), treated and followed at our centre. Infants were treated with interinfant ALL2006 protocol and others with HongKong Singapore (HKSG) 1997 prtotocol.
Results: There were 174 children of age group 3months to 15years analysed. Median age was 5years.5 (2.8%) children were infants. There was male preponderance (66.6%). Majority of them (89.6%) were of Bcell type. Clinically,168 (96.5%) patients had fever,54 (31%) joint pain,26 (14.9%) bleeding manifestations,17 (9.7%) pallor and 7 (4%) abdominal distension. At diagnosis 60 (34%) patients had high WBC count >50,000/mm^3,144 (82%) Hemoglobin <7gm/dl and 107 (61.4%) platelet count <50,000/mm^3.12/156 (7.6%) patients had CNS disease at diagnosis. Cytogenetic and molecular analysis showed 22-diploidy,23-ETV6/RUNX1,14-tetrasomy21,13-trisomy (12,4,10,17), 11-t (1,19), 7-hyperdiploidy,6-trisomy-tetrasomy (4,10,11), 4-t (9,11), 4-t (4,11), 3-TCR(translocation,3-9p21 del,1-BCR/ABL,1-monosomy9,30-normal cytogenetics.14/174 children received steroids for few days just prior to diagnosis. According to risk stratification 48 (28%) fall in Standard risk,117 (67%) Intermediate risk, and 9 (5%) High risk. Out of 174children,132 achieved complete remission (CR), 2 had resistant disease. Of remaining 40 patients;9-self referral to other hospital,8-loss to follow up,9-refused treatment,14-expired in induction. CNS events occur in 21/148 (14%) patients;4-PRES,3-stroke,6-convulsion,1-vitreous hemorrhage,2-CNSgranuloma,3-superior sagittal sinus thrombosis,2-methotrexate toxicity.21/132 (16%) patients relapsed among 132 patients of ALL who achieved CR.17 (80%) were Bcell type and 4 (20%) were Tcell type.72% had very early,14% had early and late relapse each. Nature of relapse was isolated BM in 10 (47.6%), BM & CNS in 10 (47.6%), CNS & orbit in 1 (4.7%).
Conclusions: Most common type of ALL was preB type. Most patients who receivied steroid prior to diagnosis, resulted in delay in diagnosis and impaired prognostication, therefore it requires better awareness among doctors regarding use of steroids. Cytological analysis reveals that tetrasomy21 and trisomies are most common followed by ETV6/RUNX1. CNS complications are frequent events during ALL therapy and require rapid detection and prompt treatment to limit permanent damage.

EP-064

THE OUTCOME OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA IN PATIENTS WHO PRESENTED WITH HYPERLEUKOCYTOSIS

S. Unal[1], Y. Ozsurekci[2], S. Aytac[1], B. Kuskonmaz[1], B. Tavil[1], M. Tuncer[1], S. Yetgin[1], A. Gurgey[1], F. Gumruk[1], M. Cetin[1]

[1]Division of Pediatric Hematology, Hacettepe University Medical School, Ankara, Turkey; [2]Division of Pediatrics, Hacettepe University Medical School, Ankara, Turkey

Objectives: The patients who have hyperleukocytosis at diagnosis of pediatric acute lymphoblastic leukemia (ALL) constitute 5-22% of patients. Our knowledge about the management of these patients is limited.
Methods: In our retrospective study, 101 patients between 1986-2013, who presented with hyperleukocytosis at diagnosis of ALL were included.
Results: Of the cohort, 40 received St Jude Total XI (Group 1), 46 received Total XIII (Group 2) and 15 received Total XV protocols (Group 3). The median age at diagnosis was 84 months (2-192). All patients received iv alkaline hydration, at least twice of the daily fluid maintenance. Patients were initiated methylprednisolone (MPZ, 0.5-1 mg/kg/day), and if no decrease in WBC in 12-24 hours, vincristine was administered. Cytoreductive treatments such as, leukopheresis and exchange transfusions were applied to symptomatic patients in Group 1 and 2. Cytoreductive treatments were applied in 2 patients (5%) in Group 1, 3 of (6.5%) Group 2. In Group 3, all patients except one who were unresponsive to MPZ and vincristine doses were treated with lekopheresis. In Group 3, leukopheresis was applied in 4 (26.6%) of the patients. Eight patients from Group 3 received rasburicase. Of the patients in Group 1 and 2, 9 (%10.4) developed either ICB or pulmonary leukostasis. Five-year EFS in Group 1 and 2 $46.2 \pm 9.3\%$ and $65 \pm 9.8\%$, respectively ($p = 0.03$). Five-year OS in Group 1 and 2 are $36.6 \pm 8\%$ and $65 \pm 8\%$ ($p = 0.05$). Four patients from Group 1 (10%) and 6 (13%) from Group 2 deceased during induction treatment. No death during induction observed in Group 3.
Conclusions: Initiation of lower dose and sequential chemotherapy seems to be rational instead of initiation of all treatment protocol at the same time. In our current practice, we apply cytoreductive treatments more oftenly and early mortalities and morbidities are lesser in this type of approach.

EP-065

L-ASPARAGINASE INDIVIDUALIZED DOSING AND SWITCHING IN ACUTE LYMPHOBLASTIC LEUKEMIA: A NUMBER NEEEDED TO TREAT ANALYSIS

K.F. Villa[1], F. Di Trapani[2], B. Nejadnik[3]

[1]Biostatistics, Jazz Pharmaceuticals Inc, Palo Alto CA, USA; [2]Medical Information and Communication Medical Affairs, Jazz Pharmaceuticals Inc, Palo Alto CA, USA; [3]Oncology, Jazz Pharmaceuticals Inc, Palo Alto CA, USA

Objectives: L-asparaginase is an important component of chemotherapy for pediatric acute lymphoblastic leukemia (ALL). Five-year event-free survival (EFS) in a recent published study (Vrooman 2013 JCO) was significantly higher with newly-diagnosed ALL patients randomized to individualized dosing (ID) – initial dose of 12,500 IU/m^2, with adjustments to maintain nadir serum asparaginase activity (NSAA) within 0.1–0.14 IU/mL – vs fixed-dose (FD) (25,000 IU/m^2) *Escherichia coli* L-asparaginase (EC-Asnase). Our objective was to compare the number needed to treat (NNT) associated with ID vs FD treatment strategies.
Methods: NNT was calculated as the reciprocal of the absolute risk reduction (1/ARR), where ARR equals control minus experimental event rates. We compared the NNT to prevent one event (relapse or death) with ID vs FD. We also calculated the NNT for switching asparaginase preparations because of silent inactivation (SI), defined as ID patients with NSAA <0.1 IU/mL on successive determinations despite dose adjustment or when coupled with EC-Asnase antibody positivity. NNTs were compared with those for other pediatric oncology interventions by conducting a literature search to identify randomized controlled trials (RCTs) of other interventions in pediatric hematologic and solid malignancies reported in the past 10 years.
Results: Five-year EFS for FD and ID groups was 82% and 90%, respectively (NNT = 13 for ID vs FD). FD patients with levels <0.1 IU/mL who never switched preparations had a 5-year EFS of 76% vs 95% for ID patients who switched preparation for SI (NNT = 5 for ID with switch for SI vs FD with no switch). Five RCTs in ALL and other pediatric cancers had outcome measures with NNTs ranging from 4 to 50.
Conclusions: These NNT values for ID and for switching asparaginase preparations based on evidence of SI resemble those for well-accepted oncology treatments, highlighting the value of monitoring to prospectively identify suboptimal asparaginase activity and SI.
Analysis funded by Jazz Pharmaceuticals plc or its subsidiaries.

EP-066

A NEW TRANSCRIPT OF GNAO1 IN CHILDHOOD ALL

X.W. Wang[1], H.H. Liang[1], L.X. Ding[1], B.S. Li[1], J.Y. Tang[1]

[1]Hematology&Oncology, Shanghai Children's Medical Center, Shanghai, China

Objectives: To Research the transcription methods of GNAO1 in Childhood ALL tumor cells.
Methods: GNAO1 mutations were found in 16 cases of childhood ALL tumor cells in whole exome sequencing, but in the course of the experiment transcripts that had been reported couldn't be cloned, so there might be a new GNAO1 transcript variant in childhood ALL tumor cells. Designed the gene-specific primers (GSP) of GNAO1, used RNA of TEL-AML1-positive children to reverse transcription and PCR by SMARTer RACE cDNA amplification kit, then obtained the complete sequence of the new GNAO1 transcript by sequencing.
Results: Used SMARTer RACE cDNA amplification kit and obtained the first strand reaction product according to experimental corresponding steps. After prepared Master Mix, added the first strand reaction product and the mixture of RACE universal primers (UPM), GSP1, GSP2, and GSP1 and GSP2 of relevant control samples in 0.5ml PCR tubes, after PCR amplification specific bands were obtained. The PCR product were processed by gel extraction, cloning and transformation in plasmid, then delivery the plasmid genome sequence for sequencing, the complete sequence of the new GNAO1 transcript was obtained. There were complete UPM sequence at 5'-end, complete UPM sequence and poly A at 3'-end. The new GNAO1 transcript had 7 exons, exon1 and exon2 were not reported yet. The new exon1 located between exon2 and exon3 from GNAO1-001 and GNAO1-002 transcript, the new exon2 located between exon3 and exon4 from GNAO1-001 and GNAO1-002 transcript, new exon3∼exon7 were corresponding to exon4∼exon8 from GNAO1-002 transcript.
Conclusions: A new transcription method of GNAO1 exists in Childhood ALL tumor cells.

EP-067

THE ANALYSIS OF THERAPEUTIC EFFECT OF HIGH DOSE OF CYTARABINE PLUS L-ASPARAGINASE IN CHILDREN OF ACUTE LYMPHOBLASTIC LEUKEMIA WITH MRD

J. Yang[1]

[1]Hemotology/Oncology, Shanghai Children's Hospital, Shanghai, China

Objectives: To analyze the therapeutic effect and safety of high dose of Cytarabine combined with L-Asparaginase in minimal residual disease (MRD) of childhood acute lymphoblastic leukemia (ALL).
Methods: Four color fluorescence antibody labeling method was used to monitor the dynamic changes of the MRD in children with ALL. Total 21 cases of patients (17 cases of high risk, 1 case of moderate risk, 3 cases of low rise) were considered MRD positive after remission, including 13 male cases and 8 female cases with average age 81.38 months, ranging from 9-156 months. All patients were treated with combination chemotherapy (Cytarabine 2g/m^2, d1-2, etoposide100mg/m^2, d3-5, L-Asparaginasum 25000u/$m^{2,}$ d6, dexamethasone 10mg/m^2, d1-6). The efficacy, survival time and adverse events of all patients were statistically analyzed using SPSS 19.0.
Results: The levels of MRD of 21 patients were tested after one month chemotherapy, while 17 of which turned negative and 4 of which decreased yet still positive. The patients were followed up to Dec 2013, 5 of who relapsed and 3 died. The recurrence rate was 23.80%, and the 4 years probability of an event-free survival and the overall survival were 77.6% and 80.4% respectively.
The dose-limiting toxicity includes grade 0 to 3 diarrhea and nausea; grade 2-4 neutropenia associated with fever, 2 cases with grade 2 liver function damage. There were not treatment-related deaths.
Conclusions: It is showed that high dose of Cytarabine combined with L-Asparaginase can effectively improve the prognosis of childhood ALL with positive MRD. The adverse events could be well tolerated.

EP-068

A RARE COMPLICATION OF DASANITIB IN A REFRACTORY-IMITANIB-RESISTANT ACUTE LYMPHOBLASTIC LEUKEMIA CASE: HEMORRHAGIC CYSTITIS AND COLITIS

G. Tanyildiz[1], M.O. Candir[1], S. Yesil[1], C. Bozkurt[1], G. Sahin[1]

[1]Pediatric Oncology, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey

Objectives: Dasanitib is a new generation tyrosine kinase inhibitor used in high risk childhood acute lymphoblastic leukemia (ALL) cases having Philadelphia chromosome with BCR-ABL fusion gene. In literature side effects associated with Dasanitib treatment commonly reported in adults. In this case report, a 7 year-old child diagnosed with refractory-imitanib-resistant acute lymphoblastic leukemia presented with hemorrhagic cystitis and colitis after Dasanitib treatment.
Methods: 7 year old child diagnosed with ALL resistant to imitanib treatment was enrolled to Dasanitib therapy.
Results: Forty-eight hours after initiating Dasanitib therapy hemorrhagic diarrhea was started. Stool culture result was negative in terms of pathogen agents. Hemoglobin levels were detected as 6 gr/dl, Dasanitib therapy was stopped and steroid treatment was started. Hematological parameters and clinical status were improved 48 hours after cessation of Dasanitib therapy therefore low dose Dasanitib was restarted. During the follow up period blastic white cell counts were decreased progressively and dosage of Dasanitib was increased. Dysuria presented with massive haematuria was developed after adjustment of dosage. Renal functions was normal and thrombocytopenia or coagulopathy were not defined. Urinary system ultrasonography and urine sample results were normal. Patency of urinary system tract was ensured by cathaterization of bladder and haematuria was improved completely after 2 days discontinuation of Dasanitib treatment.
Conclusions: Dasanitib is a new tyrosine kinase inhibitor and useful in cases resistant to imitanib treatment for acute lymphoblastic leukemia. Gastrointestinal system side effects associated with Dasanitib treatment are related with infiltration of T cells on epithelial surfaces. The beneficial effects of steroid treatment against to side effects of Dasanitib maybe considered as a result of T cell activation. Although imitanib is a substrate of p glycoprotein dasanitib is not, so this property of Dasanitib is an important factor about development of drug resistance in terms of kinases family. Clinicians should be keep in mind the potential side effects of Dasanitib when its usage is essential.

EP-069

THE EXPRESSION AND SIGNIFICANCE OF TLR-4 AND BCL-XL IN CHILDREN WITH ACUTE LEUKEMIA

L.I.U. Miao[1], S.H.I. Qingzhao[1], T.A.N.G. Rong[1], J. Yi[1]

[1]Paediatrics, Renmin Hospital of Wuhan University, Wuhan, China

Objectives: To examine the expressions of TLR-4 and Bcl-xL in bone marrow cells in children with acute leukemia (AL) and to detect a relationship with the classification, clinical features, therapeutic effects and prognosis of AL.
Methods: Using the SABC method of immunohistochemical staining, expressions of TLR-4 and Bcl-xLin the bone marrow cells of 76 cases with AL were detected.
Results: The expressions of TLR-4 and Bcl-xL in the initial treatment, refractory relapse and relief groups were obviously higher than that in the control group ($P < 0.05$).
There was no significant difference in the expression of TLR-4 and Bcl-xL between the acute lymphoblastic leukemia (ALL) and acute nonlymphoblastic leukemia (ANLL) groups ($t = 1.023$, $t = 1.037$;$P>0.05$). The expressions of TLR-4 and Bcl-xL in the complete remission (CR) group were lower than that in the initial treatment group ($t = 3.577$, $t = 3.895$; $P < 0.05$). The expression of TLR-4 in the refractory relapse group was higher than that in the initial treatment group ($t = 3.921$, $P < 0.05$). However, high expression of Bcl-xL occurred both in the initial treatment group and the refractory relapse group, and there was no significant difference ($t = 0.916$, $P>0.05$). Pearson rank correlation analysis indicated that there was a positive correlation between the expression of TLR-4 and Bcl-xL ($r = 0.653$, $P < 0.05$). Statistical analysis showed that the CR rates in patients with negative expression of TLR-4 and Bcl-xL were remarkably higher than that with positive TLR-4 and Bcl-xL expression ($P < 0.05$).
Conclusions: Expressions of both TLR-4 and Bcl-xL play a role in onset, progression and prognosis of AL, and the two may act synergistically in the onset and development of AL.

EP-070

OUTCOME OF RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA WITH MODIFIED ALL-REZ BFM 96 PROTOCOL IN CHINA

X. Zhai[1], H. Wang[1], J.U.N. Li[1], H.U.I. Miao[1], X. Qian[1]

[1]Hematology Department, Children's Hospital of Fudan University, Shanghai, China

Objectives: Acute lymphoblastic leukemia (ALL) is the commonest childhood malignancy and modern treatment has achieved steady improvement with long-term survival up to 80%. Nevertheless, approximately 20% of patients would experience relapse of the disease which remains the major cause of treatment failure.
Methods: We started a new relapsed acute lymphoblasticleukemia (ALL) treatment protocol based on modified ALL-REZ BFM 96 protocol aiming at improving the treatment outcome in Chinese children. All patients with first relapse of childhood ALL from 2003 to 2012 were included. Patients were stratified into four risk groups (S1, S2, S3, and S4) and the treatment consisted of intensive chemotherapy followed by allogeneic hematopoietic stem cell transplantation (HSCT) if indicated.
Results: Thirty-nine patients were recruited and median age at diagnosis of ALL was 6.2 (range 4.5–14) years. The median time from initial diagnosis to relapse was 2.5 (range, 0.6–5.2) years. The risk group (standard risk group, intermediate group and high risk) rates with initial diagnosed patients were 28.2%,35.9% and 35.9%. Nineteen patients (48.7%) achieved second complete remission (CR2). CR2 rates for S1, S2, S3, and S4 groups were 100%, 81.2%, 33%, and 15.4%, respectively. Five-year overall survival (OS) was 30.8%. OS for S1, S2, S3 and S4 patients were respectively 100%, 56%, 11%, and 7.7%.
Conclusions: We should be alert on the standard risk group patients with initial diagnosis. The relapse of children with relapsed ALL of S1 and S2 risk groups could be well treated with intensified treatment protocol. HSCT could improve the survival rates with S2 group. The S3 and S4 group needs more innovative approach to improve treatment outcome.

BONE TUMOURS

EP-071

SURVIVAL IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA: RESULTS FROM THE PEDIATRIC HEMATOLOGY AND ONCOLOGY GROUP OF TOLUCA VALLEY MÉXICO

L. Araceli[1], I. Tejocote[2], M. Laffont[2]

[1]Pediatric Oncology, Hospital Materno Infantil Issemym, Toluca, Mexico; [2]Pediatric Oncology, Hospital Para El Niño Del Imiem, Toluca, Mexico

Objectives: The objective of this study was to assess the survival of pediatric patients with osteosarcoma treated at two hospitals in the Toluca Valley, Mexico, as well as the factors relating to this
Methods: Is a study of course clinical and prognosis of patients with diagnosis of osteosarcoma, evaluating characteristics demographic clinical, paraclinical of disease, and factors of risk, as well as clinical features time survival, medical treatment and surgical as well as possible factors related to this type. We used Kaplan-Meier analysis
Results: In the period from March 1999 to March 2014 diagnostic oseosarcoma in 30 patients, with age from 3 to 16 years, 60% male, the most frequent site was followed by proximal humerus distal femur 85% with metastatic disease at diagnosis, being only 4 patients candidates for preservation of limb. Five patients died early. Survival in patients with metastatic disease was 25% at 12 months and disease not metastatic from 45% to 36 months. All patients received neoadjuvant chemotherapy with doxorubicin and cyclophosphamide and etoposide adjuvant cisplatino. Only one patient with disease not metastatic to the diagnosis was also mifamurtida.
Conclusions: Advances in chemotherapy treatment as well as the use of biological therapies have achieved a significant increase in survival in pediatric patients with osteosarcoma, however in developing countries, the late diagnostic decrease exponentially the survival, due mainly to high tumor burden in the diagnosis limiting access to the limb preservation surgery

as well as the use of biological therapies. We are carrying out training to staff of first contact for the early detection of cancer in childhood, whose impact on survival will be measurable in some years.

EP-072

ICE REGIMEN FOR RELAPSED/REFRACTORY BONE AND SOFT TISSUE SARCOMAS

B. Aydin[1], H. Susam Sen[1], T. Kutluk[1], A. Varan[1], B. Yalcin[1], C. Akyuz[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: Patients with recurrent or refractory sarcoma have dismal prognosis. In this study response to treatment and outcome of children with recurrent/refractory sarcoma who were treated with ICE regimen were retrospectively evaluated.
Methods: Patients with relapsed/recurrent bone and soft tissue sarcoma treated with ICE regimen were selected and their demographic and clinical characteristics and treatment results were analyzed. ICE regimen was given as ifosfamide (3gr/m2/day on day 1-2), carboplatin (450 mg/m2/day on day 1) and etoposide (100mg/m2/day on day 1-3).
Results: Sixty-six patients (45 males and 21 females) were evaluable for response to treatment. Median age at diagnosis was 8,3 (ranged 0.5-17.2). Tumor types were rhabdomyosarcoma (n = 26), Ewing sarcoma (n = 21), osteosarcoma (n = 11), pPNET (n = 7) and undifferentiated sarcoma (n = 1). Total 44% of patients had metastatic disease at diagnosis. ICE regimen was given median 6.3 months after diagnosis due to relapsed/refractory disease. Patients received median 5 cycles (ranged 1-9). The ORR was 58% (complete response: 28%, very good partial response: 3%, partial response: 12% and stable disease: 15%). Median duration of response and OS after ICE were 8.2 months and 25.8 months. Two-year EFS and OS rates were 27% and 63%. OS rates were significantly increased in responders (97% vs. 67%, $p < 0.0001$). 1-yr EFS rates for rhabdomyosarcoma, Ewing sarcoma, osteosarcoma and pPNET were 54%, 17%, 43% and 27% ($p = 0.04$).
Conclusions: The treatment of relapsed or refractory sarcomas remains challenging. The ORR and OS rates were significantly improved in patients with response to treatment or rhabdomyosarcoma after ICE regimen. The results showed ICE is valuable therapeutic option for relapsed/refractory sarcomas.

EP-073

SYSTEMIC AND REGIONAL HEMODYNAMICS IN CHILDREN AND ADOLESCENTS WITH BONE SARCOMAS

I. Begun[1], R. Tarasevich[1]

[1]Functional diagnostics, Belarusian Research Center for Pediatric Oncology Hematology and Immunolog, Minsk region, Belarus

Objectives: To study the hemodynamic of lower extremities taking into account of cardiac output and volume of tumors in patients with bones sarcomas.
Methods: Analysis of data obtained during of the initial ultrasound examination of the 49 patients aged 8-18 years with morphologically proven bone sarcomas lower extremities was performed. Were estimated: cardiac output (CO), volume of blood flow in main femoral artery (Q ml/min), indices - resistance and pulsation (RI, PI), as well as size of their percentage deviations for the affected limb compared with the contralateral (%Q,%RI,%PI).
Results: In system 'organism-tumor' were noted the change in cardiac output with increasing tumor volume ($r = 0.41$; $p < 0.05$), so-called 'systemic effects of the tumor' on the background of the interdependence of volume blood flow in the main artery of the affected and healthy limbs ($r = 0.68$; $p < 0.05$). Herewith a negative correlation between index value of%Q and blood flow to the healthy limb - Q ($r = -0.42$; $p < 0.05$), is confirmation, that one of component of hemodynamic changes there is redistributive blood flow. Was established the correlation volume of malignancies and%RI,%PI ($r = 0.35$-0.38; $p < 0.05$) too. That is, there has been a decrease in regional vascular tone in affected limbs.
Conclusions: Pathological mechanisms of hemodynamic support of affected limb may include systemic increase in CO, regional changes in vascular tone and against this background - the redistribution of certain volumes of blood from healthy to affected limb.

EP-074

IS THERE A ROLE FOR THROMBOPROPHYLAXIS IN PEDIATRIC SARCOMA PATIENTS? A LITERATURE REVIEW FOCUSING ON EPIDEMIOLOGY, RISK FACTORS AND OUTCOMES OF THROMBOEMBOLISM IN SARCOMA PATIENTS

M.D. Bhatt[1], U. Athale[1], A.K. Chan[1]

[1]Pediatric Hematology/Oncology, McMaster Children's Hospital, Hamilton, Canada

Objectives: Thromboembolism (TE) is a common complication of cancer in children, including those with sarcoma. TE causes significant morbidity and mortality in this patient population. Currently thromboprophylaxis is not recommended for pediatric sarcoma patients (PSP). We reviewed literature to describe epidemiology, risk factors and outcomes of TE in PSP and to evaluate thromboprophylaxis practices in PSP.
Methods: English language articles were searched on PUBMED using terms "sarcoma & thrombosis " and "sarcoma & thromboembolism " for time period between 1995 and 2013. Studies describing epidemiology, risk factors, outcomes and/or thromboprophylaxis in PSP or adult sarcoma patients (ASP) and TE were reviewed. Case reports were excluded.
Results: Among four reviewed studies, the average incidence of TE in PSP was 14% (7-16%), which is 3.5 fold higher than described in adults (4%). Audino (2013) described lower incidence (3%) in PSP, however it was limited to inpatients. Central venous catheter (CVC) dysfunction is the only statistically significant risk factor described for PSP (Athale, 2007), while trend towards clinical significance has been described for metastatic disease (Paz-Priel, 2007). Important adult risk factor of hip/thigh disease has not been studied in PSP. TE-related mortality, though infrequent, is reported. Significant morbidities include CVC removal, recurrent TE, post-thrombotic syndrome and delay in cancer treatment. Nowak-Gottl (1999) used 6-12 weeks of low molecular weight heparin thromboprophylaxis in children with bone sarcomas (n = 75); none developed TE. However, this study lacked a control group. A recent survey of oncologists, including medical and surgical, was published by Crocco (2013) describing use of mechanical and/or chemical prophylaxis by 43% of respondents.
Conclusions: Incidence of TE in PSP is higher than ASP, despite age and lifestyle related risk factors. Yet, thromboprophylaxis is recommended for ASP post-definitive surgery. Evidence for thromboprophylaxis in PSP is very limited, hence larger studies are urgently required to define the role and timing thromboprophylaxis in select PSP.

EP-075

SKIP METASTASES IN OSTEOSARCOMA: THE ST. JUDE CHILDREN'S RESEARCH HOSPITAL EXPERIENCE

M.W. Bishop[1], A.H. Loh[2], A. Bahrami[3], M.B. McCarville[4], S. Mao[5], J. Wu[5], M.D. Neel[2], A.S. Pappo[1], B.N. Rao[2]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Surgery, St. Jude Children's Research Hospital, Memphis, USA; [3]Pathology, St. Jude Children's Research Hospital, Memphis, USA; [4]Radiological Sciences, St. Jude Children's Research Hospital, Memphis, USA; [5]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA

Objectives: The presence of synchronous regional bone metastases (known as "skip" metastases) in osteosarcoma has historically been associated with poor clinical outcome. This study describes our experience with osteosarcoma and skip metastases over a 27-year period.
Methods: A retrospective review was conducted of patients treated at St. Jude Children's Research Hospital with newly diagnosed osteosarcoma between January 1986 and December 2013, with radiographic and/or histopathological evidence of skip metastasis. Data evaluated included clinical characteristics, surgical and medical treatments, histologic response, and clinical outcomes. Event-free survival (EFS) and overall survival (OS) were estimated, and clinical and pathologic factors were correlated with outcome.
Results: Skip metastases were identified in 12/382 patients (3.1%). Median age was 13.3 years (range 6.2–19 years). 6 patients presented with additional metastatic sites (5 with pulmonary nodules, 1 with a locoregional lymph node). Of 11 patients that received neoadjuvant chemotherapy and were evaluable for histologic response, 6 patients (54.5%) had a good response of greater than 90% necrosis. 7 (56.3%) developed recurrences (6 with lung nodules, 1 with local/lung disease). The one with local relapse had positive margins at the site of the skip metastasis. 6 patients were alive with median follow-up time of 58.7 months (range 4-132 months), 2 with active disease. 5 year EFS was 36.7% (SE 14.6%) and OS was 50% (SE 15.8%). Tumor necrosis greater than 90% approached significance for OS ($p = 0.06$). 4 patients without other metastatic sites at diagnosis were alive, compared to 2 who presented with pulmonary nodules; sample size was not large enough to determine a difference between these groups.
Conclusions: Skip metastases occur rarely in osteosarcoma. Outcomes may be suboptimal compared to localized osteosarcoma without skip lesions, even in the absence of other disease sites. Histologic response to chemotherapy may still predict likelihood of survival in this unique subset of patients.

EP-076

PROPOSAL FOR FUNCTIONAL REHABILITATION PHYSICAL THERAPY IN A PATIENT UNDERGOING TOTAL INTERNAL HEMIPELVECTOMY TYPE IV

D. Bonatelli[1], A.L.S. Stellet[2], E. Boldrini[1], A.S. Sarri[3], G.E. Martins[1], L.F. Lopes[4], E.A. Toller[2]

[1]Pediatric, Cancer Center Barretos, Barretos, Brazil; [2]Orthopaedic, Cancer Center Barretos, Barretos, Brazil; [3]Physioterapy, Cancer Center Barretos, Barretos, Brazil; [4]PHD Medical Director, Cancer Center Barretos, Barretos, Brazil

Objectives: Malignant primary bone tumors are rare. It mainly affects children and young adults, and may occur anywhere in the body. With the emergence of more effective drugs in the treatment and technical improvement of surgeons, internal hemipelvectomies (IH) with surgical removal of the hemipelvis or part of it, preserving more of the limb were conducted generating a challenge rehabilitation of patients. IH consists of resection of bone and affected

tissues of the pelvic girdle with limb salvage, as Enneking classification. Demonstrate the functional outcome after rehabilitation for total IH type IV.
Methods: On the first postoperative physical therapy evaluation is performed considering muscular strength, range motion, lung capacity, sitting balance, and posture in bed vascularity. Directed global cinesioterapia, changing positions, balance training in the sitting position, kinetic respiratory maneuvers and positioning of the affected limb. After discharge the patient is referred for outpatient physiotherapy where the following aspects are evaluated: muscular strength, range of motion, balance, proprioception, gait. After an evaluation is performed global cinesioterapia, stretching, strengthening, Russian current, gait training with or without support, partial and full weight bearing, workout static and dynamic balance with and without support, partial and full weight bearing, balance training static on a limb.
Results: On average after 8 months of physical therapy patient ambulation with support of crutches and has excellent balance without support any type of prosthesis or arthrodesis to reconstruct the pelvis, the extensive fibrosis, allows the patient do weight bearing on the affected limb, despite the shortening.
Conclusions: The functional outcome in patients with total internal hemipelvectomy through a specific and intense physical therapy rehabilitation can positively influence the quality of life.

EP-077

RESULTS WITH AN INTENSIVE CHEMOTHERAPY REGIMEN WITHOUT METHOTREXATE FOR THE TREATMENT OF PEDIATRIC HIGH-GRADE OSTEOSARCOMA. EXPERIENCE AT THE INSTITUTO NACIONAL DE PEDIATRÍA, MÉXICO

A. Castellanos-Toledo[1], M. Zapata-Tarres[1], H. Peña-Del-Castillo[2], J. Figueroa-Carbajal[3]

[1]Oncología Pediátrica, Instituto Nacional de Pediatría, Mexico City, Mexico; [2]División de Pediatría, Instituto Nacional de Pediatría, Mexico City, Mexico; [3]División de Pediatría, Instituto Mexicano del Seguro Social, Mexico City, Mexico

Objectives: In Mexico, pediatric high-grade osteosarcoma (HGO) occupies the fifth place of all pediatric cancers, representing the 4.4%. It presents with a high incidence of metastatic pulmonary disease and large primary tumor volume at diagnosis resulting in poor survival. We described the results from a recent cohort treated with a systemic chemotherapy regimen without methotrexate at the Instituto Nacional de Pediatria, Mexico City.
Methods: A retrospective, longitudinal and clinical study was performed from January 2005 to January 2012. Fifty-five patients younger than 18 years with extremity HGO and no prior chemotherapy treatment were included. All patients received a chemotherapy regimen without methotrexate based on a 10-week neoadjuvant chemotherapy regimen (6-courses) with cisplatin 120mg/m^2 plus doxorubicin 75mg/m^2, and a 15-week adjuvant treatment (5-courses) of cyclophosphamide 1800mg/m^2 by course given in two therapeutic arms, with a 9,000 mg/m^2 total dose for non metastatic patients, and a gradually climbed doses by course up to 12,000 mg/m2 for metastatic or bad responders patients, both arms plus etoposide 900mg/m^2 by course.
Results: Pulmonary metastases presented in 58.2% at diagnosis. Osteoblastic histology prevailed; 36.4% underwent amputation procedure and 15 (27%) limb disarticulation; 22% had limb-sparing surgery. Only 18.2% were good responder patients to neoadjuvant-chemotherapy. Five-year overall survival (OS) for non-metastatic patients was 70% and 35% for metastatic patients ($p = 0.016$). Five-year event-free survival (EFS) for non-metastatic was 65% and 30% for metastatic patients ($p = 0.032$). Five-year OS for good responders was 80% and 50% for bad responders ($p = 0.009$). No important toxicity and no second malignancies were reported at this point of the follow up.
Conclusions: This intensive and short chemotherapy regimen without methotrexate, with relatively few adverse events, improved outcome in OS mainly, and was able to achieve similar outcomes in EFS as the most current series reporting 3-year EFS from 60% to 70% for patients with localized, extremity osteosarcoma.

EP-078

LONG TERM FOLLOW UP OF EWING SARCOMA PATIENTS: THE MEMORIAL SLOAN KETTERING EXPERIENCE

K. Chastain[1], J. Chou[2], R. Adsuar[3], C. Moskowitz[2], J. Candela[3], P. Meyers[4], L. Wexler[4], A. Chou[4], S. Wolden[5], K. Oeffinger[6]

[1]Pediatrics, University of Missouri-Kansas City, Kansas City, USA; [2]Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, USA; [3]Medicine, Memorial Sloan Kettering Cancer Center, New York, USA; [4]Pediatrics, Memorial Sloan Kettering Cancer Center, New York, USA; [5]Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, USA; [6]Medicine and Pediatrics, Memorial Sloan Kettering Cancer Center, New York, USA

Objectives: We aimed to determine long-term overall survival (OS) and characterize second malignant neoplasms (SMN) for a cohort of 305 patients diagnosed with Ewing Sarcoma (ES) and treated at a single institution from 1974 through 2012.
Methods: We preformed a retrospective chart review on eligible ES patients. IRB approval was obtained prior to review. Individuals were excluded if they were not at least 6 months off therapy at time of review, or if they had not received >70% of their chemotherapy at MSKCC. Overall survival with 95% confidence intervals (CI) was assessed with Kaplan-Meier estimates and Cox proportional hazards regression. Cause-specific mortality was evaluated with the cumulative incidence function accounting for competing risks.
Results: We assessed outcomes in 305 patients (40.3% female; 12% racial/ethnic minorities) treated consecutively from 1974 to 2012. Primary site was bone in 78.4%, soft tissue in 21.6%. Median age at diagnosis was 16 years (range, 0.3 to 40); median interval from cancer diagnosis to last contact was 7.8 years (range, 1.3 to 37.2). Relapses occurred in 110 patients (36%); 93% occurred within 5 years of diagnosis. There were a total of 23 SMNs (9 MDS-AML, 6 solid tumors, 3 melanomas, and 3 non-melanoma skin cancers). Five-year OS was 65% (95% CI: 60%-70%). There were 80 deaths related to relapsed/progressed ES and the cumulative incidence of death due to ES at 5 years was 25%; 32 deaths were due to other causes. In multivariable model, racial/ethnic minority ES patients were 2.3-times more likely to have poor OS than white non-Hispanic patients (95% CI: 1.1-1.7). Older age at diagnosis was also associated with poor OS (for every 10 years increase in age, hazard ratio = 1.4; 95% CI: 1.1-1.7).
Conclusions: Overall survival and SMN risk remains suboptimal for patients with Ewing Sarcoma, highlighting the need for new targeted therapeutics.

EP-079

ZOLEDRONIC ACID FOR THE TREATMENT OF CHILDREN WITH REFACTORY GIANT CELL TUMOR OF THE JAW

M. Chien[1], L. Mascarenhas[2], R. Venkatramani[2]

[1]Department of Pediatrics, Keck School of Medicine University of Southern California, Los Angeles, USA; [2]Division of Hematology Oncology & BMT, Children's Hospital Los Angeles, Los Angeles, USA

Objectives: No approved systemic therapies currently exist for the treatment of pediatric giant cell tumor of the jaw (GCT)/central giant cell granuloma. Although the bisphosphonate zoledronic acid (ZA) has been used with success in adults, its use in pediatrics has been limited due to concern for effects on bone health and growth arrest. We review the outcome of pediatric GCT treated with ZA at our institution.
Methods: Data were collected by retrospective chart review of patients with GCT treated with ZA at Children's Hospital Los Angeles between January 2006 and December 2013. 4 mg/m^2 (4 mg max dose) ZA was administered intravenously every 4 weeks.
Results: Four patients (3 females, 1 male) between the ages of 3 months and 15 years were treated with ZA. Patient A was a 3 month old female with incompletely resected maxillary GCT. She received ZA as primary treatment due to unacceptable risk of interferon treatment, and achieved tumor remission after 4 courses. She is in remission one year following therapy. Patient B and C received ZA as second-line therapy for recurrence after surgical resection and interferon therapy. The recurrent lesion was surgically resected followed by 3 courses of ZA. While Patient B is disease free for four years, Patient C developed a local tumor recurrence two years after treatment, which was successfully resected. Patient D had an underlying diagnosis of osteoglophosis dwarfism and had refractory GCT resulting in administration of multiple regimens, including ZA. She experienced disease progression following 6 courses. Side effects of ZA included flu-like symptoms, electrolyte abnormalities including hypocalcemia and hypophosphotemia which were mild and asymptomatic. No effect on projected anthropometric growth parameters was noted.
Conclusions: Our results demonstrate that therapy with ZA is a reasonable and well-tolerated option for children with relapsed or refractory GCT, though larger studies are needed to demonstrate efficacy.

EP-080

PREDICTORS OF INFECTION IN PROXIMAL TIBIA ALLOGRAFT AND ALLOGRAFT-PROSTHESIS COMPOSITE RECONSTRUCTIONS

S.A. Lozano-Calderon[1], S.O. Swaim[1], A. Federico[2], C. Sampson[3], M.E. Anderson[1], M.C. Gebhardt[1]

[1]Orthopedic Surgery, Boston Children's Hospital, Boston, USA; [2]Oncology, Boston Children's Hospital, Boston, USA; [3]Plastic Surgery, Boston Children's Hospital, Boston, USA

Objectives: Reconstruction of the proximal tibia after wide resection is challenging. Advocates argue advantages to include bone preservation, biological reconstruction that facilitates reattachment of the extensor mechanism and other soft-tissue structures, metallic prosthesis use delay, and distal femoral growth plate preservation. Complications are numerous, infection being the most common. It is believed that infection correlates with the poor soft-tissue coverage seen in this area. This investigation evaluates our experience with 32 patients, analyzing incidence and management of infection.
Methods: 32 patients (17 males, 15 females), average age 13 years old (2-18) who underwent 33 allograft proximal tibia reconstructions were evaluated for occurrence of infection. Potential predictors of infection categorized as pre and perioperative factors were analyzed in terms of risk for developing allograft infection.
Results: Twenty-three patients had Osteosarcoma and the the remaining 9 patients had Ewings sarcoma. Most reconstructions (21) were osteoarticular allografts. Fifty percent of patients had flap coverage at the index procedure. Allograft survival rate was 73% at 4.6 years.

Allograft infection rate was 15%. Two patients were converted to a metallic endoprosthesis, 2 to a new allograft, and 1 to a knee disarticulation. Most common complications were wound dehiscence (48%), non-unions (33%) and allograft fractures (24%). No predictors of infection could be identified. A trend of lower WBC was noted in patients who developed infections; however not statistically significant. All patients who developed infections had a previous wound dehiscence. 56% of wound dehiscences had a positive bacterial culture. However, only 30% progressed to allograft infection.
Conclusions: Despite being unable to identify predictors of infection, we recommend nutritional and immunological optimization of patients before surgery and a low threshold for flap coverage at the index surgery. Wound dehiscence is a common complication for which aggressive surgical treatment is recommended to avoid progression to allograft infection. Allograft infection reduction rate as high as 25% can be attained with this approach.

EP-081

USE OF MIFAMURTIDE AND STEROID IN A PATIENT WITH OSTEOSARCOMA AND CHRONIC RENAL FAILURE SECONDARY TO CISPLATIN

A. Garcia-Espinoza[1], J. Figueroa-Carbajal[2]

[1]Pediatric Oncology, CEcan Chihuahua, Chihuahua, Mexico; [2]Pediatrics, Instituto Mexicano del Seguro Social, Mexico City, Mexico

Objectives: A case report of 13-year-old male with non-metastasic osteoblastic osteosarcoma is presented.
Methods: Patient presented May 2011 referring pain at right leg, secondary to contusion, not responding to analgesics, increased extremity volume and claudication. Tumoral lesion at right tibia on X-ray; Computed Tomography (CT) and Magnetic Resonance Image (MRI) showed an 11 × 5 × 6 cm lesion, involving adipose tissue and adjacent muscles, thoracic CT was negative for metastasis. Bone scan showed a single focal well delimitated concentrate augmentation at proximal metaphysic area. Chemotherapy with cisplatin 120mg/m2 plus doxorrubicin 25mg/m2 for 3 days, alternating with cisplatin 120mg/m2.
Results: After 5th cycle presents severe emesis, dehydration and acute renal failure (ARF), creatinine 8.8mg/dl, BUN 114, urea 243.9mg/dl, oliguria; uremic encephalopathy. Partial improvement: creatinine 13.3mg/dl, BUN 92, urea 196mg/dl. Steroid pulses initiated continuing with prednisone as maintenance. Renal ultrasound showed bilateral glomerulonephritis. Bilateral renal scan reveals deficient renographic curves in 3 phases, mainly excretory, high depth activity suggesting chronic renal failure (CRF): right kidney 47% function and effective renal plasma flow (ERPF) 54.63 while left kidney 53% function and ERPF 51.46. After 3 months creatinine 5.3mg/dl. Chemotherapy continued without cisplatin and with steroids. CT showed tumor 6 × 4 × 4 cm, limb salvage November 2011. Adjuvant cycles with cyclophosphamide-escalated from 300mg/m2 up to 650mg/m2 and etoposide 200mg/m2, for 8 cicles. Mifamurtide 2mg/m2 initiated one month after surgery, total 48 doses, 15 doses while steroid treatment. Vigilance started February 2013. Last thoracic CT and bone scan negatives with a follow up of 14 months.
Conclusions: Cisplatin is a highly effective chemotherapeutic agent. One of its limiting side effects is nephrotoxicity that may lead to CRF. As reported by Venkatakrishnan et al, mild-moderate renal impairment does not alter the clinical pharmacokinetics or pharmacodynamics of mifamurtide; no dose modifications appear necessary for these patients, in this case the steroids also seem not interact with mifamurtide.

EP-082

A NEW META-ANALYSIS IN MDM2 SHOWS NO ASSOCIATION BETWEEN RS2279744 AND RS1690916 AND RISK OF OSTEOSARCOMA: CRITICAL STUDY

I. Martin-Guerrero[1], N. Bilbao-Aldaiturriaga[1], Z. Ascaiturrieta[1], I. Granado[1], A. Patiño-Garcia[2], M. Zalacain-Diez[2], K. Goricar[3], V. Dolzan[3], A. Garcia-Orad[1]

[1]Genetics Physical Anthropology and Animal Physiology, University of the Basque Country, Leioa, Spain; [2]Laboratory of Pediatrics, University Clinic of Navarra, Pamplona, Spain; [3]Faculty of Medicine, Institute of Biochemistry, Ljubljana, Slovenia

Objectives: A recent systematic review on osteosarcoma concluded that two murine double minute 2 (*MDM2*) polymorphisms, rs2279744 and rs1690916, had an impact on disease risk. However, we and other authors have detected several weaknesses in the study such as inaccuracies in the analyses performed.
Therefore, the aim of the present study was to analyze whether *MDM2* polymorphisms increased the risk of osteosarcoma.
Methods: First, we studied the effect of rs2279744 and rs1690916 on two different osteosarcoma populations from Spain (n = 113) and Slovenia (n = 58) and their corresponding controls (n = 166 and n = 91; respectively). Second, we performed a meta-analysis with all the studies performed so far, including the two previous populations.
Results: The results in the two populations analyzed and the meta-analysis allowed to conclude that the two *MDM2* polymorphims analyzed do not statistically increase the risk of osteosarcoma, in contrast to the previous meta-analyses. Data about the discussion of our results compared to the previous meta-analysis will be also shown.
Conclusions: The *MDM2* polymorphismsrs2279744 and rs1690916 do not increase the risk of osteosarcoma.

This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13).

EP-083

NON CODING RNAS AS NEW MARKERS OF SUSCEPTIBILITY TO OSTEOSARCOMA

N. Bilbao-Aldaiturriaga[1], I. Martin-Guerrero[1], E. Lopez-Lopez[1], A. Gutierrez-Camino[1], A. Patiño-Garcia[2], M. Zalacain-Diez[2], V. Dolzan[3], A. Garcia-Orad[1]

[1]Genetics Physical Anthropology and Animal Physiology, University of the Basque Country, Leioa, Spain; [2]Laboratory of Pediatrics, University Clinic of Navarra, Pamplona, Spain; [3]Faculty of Medicine, Institute of Biochemistry, Ljubljana, Slovenia

Objectives: Osteosarcoma is the most common primary malignant bone cancer in children and young adults. Susceptibility to osteosarcoma is due to complex and multiple genetic factors. Non coding RNAs (ncRNAs), specifically long non coding RNAs (lncRNAs) and microRNAs (miRNAs), have been shown to be deregulated in diverse kinds of cancers, including osteosarcoma, showing their importance in the disease. Alterations in the ncRNA expression levels or in their function can be attributed to genetic polymorphisms. In fact, a recent study has found association between a polymorphism in miR-34b and osteosarcoma risk. The aim of this study was to evaluate the role of ncRNAs-related SNPs in susceptibility to osteosarcoma.
Methods: We analyzed blood samples from 122 osteosarcoma patients from two different populations, Spain (n = 77) and Slovenia (n = 45) and their corresponding controls (n = 321 and n = 96, respectively). In total, 235 SNPs in 222 miRNAs and 127 SNPs in 16 lncRNAs were genotyped by using the VeraCode GoldenGate Genotyping Assay from Illumina.
Results: Previous results from our group showed that SNPs in processing genes and miRNAs were associated with the risk of osteosarcoma. Therefore we decided to extend the study analyzing two different populations and increasing the number of samples and polymorphisms. Our preliminary results show that polymorphisms in ncRNAs are associated with osteosarcoma. These results are being confirmed.
Conclusions: Our results suggest that SNPs in non coding RNAs may affect osteosarcoma susceptibility.
This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13).

EP-084

RADIOFREQUENCY ABLATION FOR EPIPHYSEAL CHONDROBLASTOMAS IN CHILDREN – EMERGENCE OF A NEW MODALITY OF TREATMENT

A. Gulia[1], A. Puri[1], S. Kulkarni[2]

[1]Orthopedic Oncology Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [2]Department of Radiology, Tata Memorial Hospital, Mumbai, India

Objectives: Chondroblastoma are treated by curettage and bone grafting with risk of injury to articular surface or growth plate. Minimally invasive technique like percutaneous radiofrequency ablation (RFA) has been attempted as an alternative to surgical interventions. Present study was done to demonstrate the safety and efficacy of RFA as an novel alternative to surgery in chondroblastomas. We also evaluated the functional and Oncological outcomes.
Methods: Between January 2010 and January 2014, we treated 8 cases of chondroblastomas with RFA. All were males with a mean age of 17.5 years (range 13-21 years). All cases were primary with involvement of proximal femur in 3 cases, proximal tibia in 3 and proximal humerus & distal femur in 1 case each. The procedure was done with computed tomography guidance. Lesion was biopsied, confirmed on frozen and then treated with RFA in the same setting. The Clinical symptoms, range of movements, radiographs and MSTS score were assessed before, 24 hours, 6 weeks and then every 3 months after the procedure
Results: Significant relief of symptoms was noted on the immediate post procedure day in all patients after a single session of RFA. No patient required a repeat procedure or surgical curettage. All the patients had complete relief of symptoms with no need of any medical assistance at first follow up (6 weeks). All patients are available for final evaluation with a median follow up of 28 months (range, 3 to 50 months). There was no recurrence or treatment related complications. All patients returned to the pre disease activity level with average MSTS Score of 29 at last follow-up.
Conclusions: Percutaneous RFA is safe, effective, less morbid and minimally invasive alternative to surgery for the management of epiphyseal chondroblastoma of the extremity.

EP-085

ONCOLOGICAL OUTCOME OF PEDIATRIC EXTREMITY SKELETAL CHONDROSARCOMAS AT A TERTIARY SARCOMA TREATMENT CENTRE

A. Gulia[1], A. Puri[1], V. Ramanujan[1]

[1]Orthopedic Oncology Surgical Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Chondrosarcoma is the third most common primary bone tumour with late recurrences leading to 10-year survival rates below 50%. They are uncommon in children (<10%). Present study was done to analyse the outcomes of chondrosarcoma in pediatric population
Methods: Between 2001 and 2010, 372 cases of musculoskeletal chondrosarcoma were treated. Ten of these patients (2.6%) were under 21 years and were included in this study. All patients underwent pre surgical staging. The site of disease was humerus in 4, pelvis in 3, and one each in tibia, clavicle, scapula and femur. 7 patients had primary disease and 3 secondary (enchondromatosis 1; multiple osteochondroma 2). The mean duration of follow up was 35 months (range 6 months – 84 months).
Results: Of 10 cases, 1 wasmetastatic at presentation, (lungs) and Two had pathological fracture. Nine had limb salvage and 1 had amputation. Margins were free in 8, microscopic positive in 2. The final histopathology was mesenchymal chondrosarcoma in 1, de differentiated chondrosarcoma in 2, clear cell in 1, grade II chondrosarcoma in 5 and grade III chondrosarcoma in one patient. Both patients with de differentiated chondrosarcoma received adjuvant chemotherapy. 1 patient is loss to follow up and 6 patients are alive and disease free. Three patinet developed distant metastasis and scummed to disease.
Conclusions: Chondrosarcomas are rare in pediatric population accounting for 2.6% of all chondrosarcomas in our hospital. Surgical resection with wide margins is the treatment of choice. De differentiated and mesenchymal subtypes are associated with poorer prognosis.

EP-086

NON OPERATIVE MANAGEMENT OF ANEURYSMAL BONE CYST WITH PERCUTANEOUS SCLEROSANT INJECTIONS IN CHILDREN – EARLY RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

A. Gulia[1], A. Puri[1], V. Ramanujan[1]

[1]Orthopedic Oncology Surgical Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: To evaluate the results of treating primary aneurysmal bone cysts (ABC) with intralesional sclerosant injections.
Methods: Between February 2010 and November 2013 we treated all primary aneurysmal bone cysts with serial intralesional sclerosant injections. 25 such lesions were treated (femur/2, tibia/6, pelvis/7, fibula/3, humerus/2, hand/2 and ulna, scapula and clavicle/1 each. The median follow up was 16.3 months. All cases had a diagnostic biopsy. There were 12 females and 13 males. Age ranged from 1 – 17 years (median 11.2 years). Polidocanol was injected percutaneously into the lesion under image guidance as an outpatient procedure. Healing was assessed by serial radiographs and symptomatic improvement as observed by the patient. Opacification of the lesion with an increase in cortical thickening was taken as evidence of healing. Injections were repeated (maximum 4) at an interval of 6 to 8 weeks if the lesion did not show evidence of healing.
Results: All but 2 of the lesions showed evidence of healing. One lesion in the periacetabular area showed no evidence of healing after 3 injections and was operated with curretage and bone grafting. Another proximal humerus leision failed to heal with injection and subsequently underwent surgery. A 1 year old child needed surgery subsequently because of a progressive varus deformity developing at the site of the lesion. 14 cases healed with a single injection, 2 had 2 injections, 4 had 3 injections and 1 had 4 injections and 1 required 4 injections and a session of angioembolistaion. The first evidence of radiologic healing was seen from 6 to 24 weeks (median 12 weeks). There were no complications.
Conclusions: Though a longer follow up is mandated to rule out development of recurrence, early results for this inexpensive, non invasive method of managing aneurysmal bone cysts are promising.

EP-087

MIFAMURTIDE (L-MTP-PE) IN CHILDREN WITH OSTEOSARCOMA: THE TURKISH EXPERIENCE

R. Kebudi[1], I. Ilhan[2], M. Kantar[3], F.B. Cakir[4], E. Guler[5], N. Olgun[6], T. Celkan[7]

[1]Pediatric Hematology - Oncology, Istanbul University Oncology Institute, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Ankara Oncology Training and Research Hospital, Ankara, Turkey; [3]Pediatric Hematology - Oncology, Ege University School of Medicine, Izmir, Turkey; [4]Pediatric Hematology - Oncology, Bezmi Alem Vakif University, Istanbul, Turkey; [5]Pediatric Hematology - Oncology, Antalya University Medical Faculty, Antalya, Turkey; [6]Pediatric Hematology - Oncology, Dokuz Eylul University Medical Faculty, Izmir, Turkey; [7]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey

Objectives: Mifamurtide (liposomal muramyl tripeptide), activates macrophages, provides antitumor effect in lungs. Mifamurtide+chemotherapy improved survival in nonmetastatic osteosarcoma patients, in phase III study. After EMA approved mifamurtide for nonmetastatic osteosarcoma, it could be used off-label by the approval of the Ministry of Health on a patient basis, in Turkey. This multicentric study aims to evaluate the demographic characteristics, adverse effects, outcome of adding mifamurtide to chemotherapy in children with osteosarcoma in Turkey.
Methods: From September 2011-February 2014, in 40 nonmetastatic, 3 metastatic (after metastasectomy) osteosarcoma patients, mifamurtide was added to chemotherapy after surgery in 7 centers in Turkey. Chemotherapy regimens used were epirubicin/ifosfamide/cisplatin in 21 (Istanbul University Oncology Institute-IUOI) and other in 22 (MayoPilotII, EURAMOS, ICE etc.). Mifamurtide was given i.v.2 mg/m^2, twice weekly for 12 weeks, followed by once weekly for 24 weeks.
Results: Median age was 13 years (4-17 years). Total of 1296 doses of mifamurtide were administered, with no major side effects. Chills, fever initially were frequent. Median follow-up time for all was 15 months (3-57mo.). For nonmetastatic patients 2 year EFS was 76%, OS 83%. Fifteen/40 (38%) nonmetastatic patients completed mifamurtide, all have no evidence of disease (NED) at median 17,5 mo. (12-29 mo.); 4 relapsed at median 14 months (11-17), 1 died, 3 AWD; 21 continue treatment. 2/3 metastatic patients died (28, 57 months). When 20 nonmetastatic patients from center IUOI were compared with the historical control recieving same chemotherapy, the median FU was 14 mo (4-57), 2 had relapsed at present, whereas 33/94 of the historical cases had relapsed at median 9 months (1-40).
Conclusions: In this multicentric study, mifamurtide could be administered safely with no major side effects. The experience with mifamurtide in patients with nonmetastatic osteosarcoma is promising; a longer follow up is needed to make further conclusions for survival benefit.

EP-088

POLYLACTIDE BIOABSORBABLE STRUTS FOR CHEST WALL RECONSTRUCTION IN A PEDIATRIC PATIENT

T. Makarawo[1], R.A. Reynolds[2], M.L. Cullen[3]

[1]General Surgery, Providence Hospital, Southfield, USA; [2]Orthopedic Surgery, St. John Hospital and Medical Centers, Gross Point, USA; [3]Pediatric Surgery, St. John Hospital and Medical Centers, Gross Point, USA

Objectives: Chest wall reconstruction following pediatric tumor resection is challenging. Children have unique characteristics related to growth and prosthetic material for reconstruction must be chosen carefully. Poly-L-Lactide (PLA), a bioabsorbable prosthetic material, has been used in the plate form for reconstruction following tumor resection in children. Recently developed PLA struts have been successfully used to reconstruct pediatric chest wall deformities. This is the first description of the use of PLA rib struts to reconstruct chest wall defects after a pediatric chest wall tumor resection.
Methods: We present the case of a 15 year-old female that presented with right-sided back pain due to a 8 x 5 cm chest wall mass that was confirmed as Ewing Sarcoma of the eighth rib. The patient elected for a surgical resection of her tumor.
Via a right posterior thoracotomy, chest wall resection of the 7th to 9th ribs was performed. Reconstruction was performed using PLA rib replacement struts. For each resected rib, the replacement strut was sutured to the transverse process of the spine posteriorly and the bony component of the native rib anteriorly. Two additional struts were placed vertically in the posterior-lateral and antero-medial axillary lines. The five struts used (2 vertical and 3 horizontal) were not connected to each other so that the vertical struts join the normal ribs above and below the defect and allow for synchronized vertical rib movement. A 28Fr chest tube was placed in the tenth intercostal space.
Results: The patient made an uneventful recovery and was discharged home with all drains removed by the seventh post-operative day. The patient at 3 months follow-up has a stable chest wall with symmetrical appearance.
Conclusions: Poly-L-Lactide rib struts are a stable and physiologically advantageous method of reconstructing the chest wall after malignant tumor resection. Bioabsorbability is particularly advantageous to the growing pediatric chest wall.

EP-089

OSTEOSARCOMA OF THE SKULL: CASE REPORT AND REVIEW OF LITERATURE

I. Maza Medina[1], L. Vasquez Ponce[1], M. Oscanoa Gutierrez[1], G. Mejia Sanchez[1], M. Quiñonez Avila[2], J. Geronimo Meza[1]

[1]Pediatric Oncology Unit, Edgardo Rebagliati Martins Hospital, Lima, Peru; [2]Pathology, Edgardo Rebagliati Martins Hospital, Lima, Peru

Objectives: Osteosarcoma of the skull is very rare as a primary tumor and represents 1-2% of tumors of the skull. Due to the rarity of this tumor, we present a case of primary osteosarcoma of the skull and a review of cases reported in the literature to date.
Methods: We describe a young with primary osteosarcoma of the skull. Clinical presentation, histological features and clinical outcome were examined. A PubMed/Medline search was performed to collect all cases of primary osteosarcoma of the skull.
Results: A 17 year oldpatient presented with a history of 5 month historyof a painless parieto-occipitalmass, headache and nausea. Skull radiography evidenced a large lesion with sun radiating pattern. The initial MRI shows a mass of 18 x 15 cm with periosteal reaction and infiltrates adjacent brain parenchyma. The pathology evidences a osteogenic sarcoma. No distant lesion was evident. We started neoadjuvant chemotherapy (CT) with ifosfamide, vincristine, adriamycin and methotrexate, for 14 weeks, showing a poor tumor response. We performed a left parieto-temporo-occipital craniectomy and en bloc resection of bone tumor. Histopathology confirmed the finding of osteosarcoma with cerebral parenchymal infiltration and committed edges. He presented a favorable postoperative course continuing with

chemotherapy and radiotherapy. The patient had progression of disease and died after 15 months of diagnosis. There are at least 12 pediatric cases of osteosarcoma of the skull described in the literature from clinical case reports or small series. Due to the rarity of the disease there are no large prospective studies of this entity.
Conclusions: Skull osteosarcoma is a rare tumor, hard to manage and worse prognosis. The surgery with negative margins of the primary lesion is the most important prognostic. Chemotherapy (adjuvant and neoadjuvant) may increase survival. There are few reported cases of pediatric osteosarcoma of the skull, which makes the characterization of this entity and possible therapeutic strategies.

EP-090

ROLE OF FDG-PET SCANS IN THE EVALUATION OF BONE SARCOMAS IN CHILDREN AND YOUNG ADULTS

N. Mittal[1], P. Kent[2], S. Ibrahim[3]

[1]Pediatric Hematology Oncology, University Of Illinois - Rush University- Stroger Hospital Fellowship Program, Chicago, US; [2]Ppediatric Hematology Oncology, Rush University Medical Center, Chicago, US; [3]Diagnostic Radiology, Rush University Medical Center, Chicago, US

Objectives: 18-fluordeoxy-glucose positron emission tomography (PET) is recommended for initial bone sarcoma workup by the COG and the NCCN. Compared to conventional imaging (X-Ray/bone Scan/CT/MRI) PET has been shown to be superior in detecting soft tissue metastases and bone scan-negative skeletal metastases, but insensitive for small lung metastases. The detection of occult metastases or incorrect identification of metastases may change treatment decisions. Our objective was to describe our institution's experience of PET scanning in evaluation of primary and relapsed bone sarcoma in children and young adults.
Methods: We retrospectively evaluated the PET/CT and conventional imaging (MRI, CT chest, Bone scan) findings of 20 patients (12 male, age 6-30 years) with primary or relapsed bone sarcoma diagnosed over the past 5 years at our center. Lung metastases <5 mm in size were excluded. Nine patients had Osteosarcoma (5 metastatic) and 11 had Ewing sarcoma (5 metastatic). A total of 30 PET scans and 48 lesions met inclusion criteria.
Results: The sensitivity/specificity for detection of the bone primary were 100%/98%. The overall sensitivity/specificity for detection of any metastases was 71%/88%. Three confirmed lung metastases > 5mm, 1liver metastasis >1 cm and 2 bone lesions, both in the skull were PET negative (Figure 1). Four lesions (3 lung,1 bone) were infectious but PET positive. The positive/negative predictive value (PPV/NPV) for any metastatic bone tumor was 75%/87%. Sensitivity/specificity/PPV/NPV (%) was 63/92/67/91 for lung metastases > 5mm, 67/94/80/93 for all bone lesions and 100/96/80/100 for non-skull bony lesions (Figure 2).

Figure 1: Metastatic Lesions in Sarcoma *Not* Detected by PET

Patient	PET	MRI	CT	Bone Scan
1	Vertebrae, Lung	Vertebrae, Skull	Vertebrae, Lung	Vertebrae, Skull
2	Humerus	Humerus, Skull	Skull	Humerus, Skull
3	Femur	Femur	Femur, Liver	Femur
4	Humerus	Humerus	Lung	Humerus
5	femur	Femur	Lung	Femur
6	Femur	Femur	Lung	Femur

Figure 2. PET Scans in detecting metastatic lesions from bone sarcoma

Type of metastatic lesion	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Lung metastases>5mm	63	92	67	91
Bone metastases	66	94	80	93
Non skull bone metastases	100	96	80	100
Any metastases	71	88	75	87

Conclusions: In our cohort, PET was a useful adjunct but could not replace conventional imaging in the diagnosis and staging of bone sarcoma. In some cases PET alone would have missed metastases or under-staged disease influencing treatment decisions. More studies are needed to evaluate its role in diagnosis and staging of bone sarcomas in children and young adults.

EP-091

ORAL VP 16 IN RELAPSED/REFRACTORY EWING SARCOMA: THE EXPERIENCE OF FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI, MILAN

M. Podda[1], R. Luksch[1], D. Polastri[1], N. Puma[1], C. Meazza[1], M. Terenziani[1], A. Ferrari[1], M. Casanova[1], F. Spreafico[1], L. Gandola[2], V. Biassoni[1], E. Schiavello[1], M. Massimino[1]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Radiotherapy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Objectives: To evaluate the efficacy of low dose oral VP 16 in relapsed/refractory Ewing sarcoma, secondarily to evaluate its toxicity.

Methods: Records of all patients treated between 1989 and 2012 for relapsed/refractory Ewing sarcoma who received oral VP 16 in our department were analyzed. The dose was 20 mg/mqx2/day for 21 consecutive days every 28 days. The response was evaluated, whenever possible, after 2 cycles according to RECIST criteria.
Results: Forty-three/55 received at least 2 cycles, 9/55 suspended treatment before 2 cycled due to rapidly progressing disease. At diagnosis the median age was 14, 26/55 were metastatic. All patients received intensive poly-chemotherapy program including VP 16 iv in first (n = 52) or second line (n = 3). Twenty-one/55 received myeloablative regimen with PBSC rescue, 1 allogeneic transplantation. Oral VP 16 was prescribed in II, III, IV line in 18,25,12 patients respectively. Total number of cycles administered was 233, median 3, mean 4 (range 1-14). Forty-one/55 were evaluable according to RECIST criteria. 11 responses (9 PR, 1 VGPR, 1CR) and 9 stabilizations were recorded with a mean response duration of 7 months. Hematological toxicity G3/G4 (160/233 evaluable cycles) was recorded in 15%, 16%, 11% of cycles for hemoglobin, leukocyte and platelets respectively. 2 responsive patients decided voluntarily to stop the therapy due to gastritis G2. Of note are 5 cases of pneumonia and one HZV reactivation. We recorded 2 secondary leukemia in patients who received 12 and 14 cycles.
Conclusions: Low dose oral VP 16 may be suitable in a palliative setting with acceptable toxicity, further conclusion for the efficacy warrants a prospective study. The risk of secondary leukemia is line with that reported in literature.

EP-092

POOLED SHRNA SCREEN TO IDENTIFY TUMOUR CELL SPECIFIC THERAPEUTIC TARGETS IN EWING SARCOMA

C. Schaefer[1], C. Schleithoff[1], B. Lechtape[1], H. Jürgens[1], U. Dirksen[1], J. Potratz[2]

[1]Paediatric Haematology/Oncology, University Children's Hospital Münster, Münster, Germany; [2]General Paediatrics, University Children's Hospital Münster, Münster, Germany

Objectives: To improve prognosis and reduce treatment toxicity for patients with Ewing sarcoma, novel therapeutic targets and treatment approaches are needed. The Ewing sarcoma EWS-FLI fusion protein provides a unique tumour-cell specific target in principle, but effective targeting remains an unsolved challenge. An identification of proteins synthetic lethal to EWS-FLI expression may not alone present an alternative approach towards tumour-cell specific targeting, but further promote the understanding of EWS-FLI oncogenic transformation. Objective therefore is to identify such proteins.
Methods: shRNA technology provides a functional, i.e. loss-of-function, approach to the identification of survival-indispensable proteins, i.e. potential molecular targets. Recent advances in pooled screening approaches combined with next-generation sequencing facilitate large-scale screens. Applying this technology to an A673 Ewing sarcoma cell line model with stable knockdown of endogenous EWS-FLI or control (EWS-FLI off/on) we aim to identify novel tumour-cell specific targets synthetic lethal to EWS-FLI expression.
Results: Stable shRNA transduction of A673 cells was established and optimized for the GIPZ shRNAmir lentiviral system (ThermoScientific). The multiplicity-of-infection was adjusted to 0.3 to achieve integration of 1 shRNA per cell. Sufficient target knockdown by single-copy shRNA integration was confirmed at mRNA and protein levels using LaminA/C, EG5 or non-silencing-control shRNA sequences. Defined test pools of these shRNAs were utilized to confirm DNA recovery and PCR amplification of shRNA sequences. A probe-based real-time-PCR was developed to quantify shRNAs recovered from the defined pools to thereby simulate and validate the established pooled screening protocol in principle.
Conclusions: We established a pooled shRNA screening protocol in an Ewing sarcoma cell line model in presence/absence of EWS-FLI. The subsequent shRNA screen can contribute to the identification of novel tumour-cell specific targets and the understanding of EWS-FLI oncogenic function.
A*cknowledgements: A TranSaRNet project supported by the BMBF (FKZ01GM0869). The A673 cell line model is kindly provided by S. Lessnick (University of Utah).

EP-093

INTRAMEDULLARY EXTENSION IN PERIOSTEAL OSTEOSARCOMA – DOES IT PORTEND AGGRESSIVE BIOLOGY?

A. Puri[1], A. Gulia[1], S. Desai[1], S. Chorge[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: To evaluate if intramedullary extension in periosteal osteosarcoma was indicative of more aggressive biological behaviour in terms of poorer overall survival.
Methods: A retrospective analysis of 18 cases of periosteal osteosarcoma treated between January 2001 and December 2010 was carried out. There were 12 males and 6 females. The mean age at presentation was 16.3 years (range 5-26 years). Tibia and femur were the most common sites (seen in 8 patients each). Sixteen of 18 patients received chemotherapy, 16 had limb sparing resection, one had an amputation and one had rotationplasty.
Results: Surgical margins were free in all patients. On histopathology, intramedullary involvement was found in 7 patients (44%). All patients were available for follow up. The median follow up was 61 months (range 18- 130 months). Pulmonary metastasis subsequently occurred in 4 cases (22%). Intramedullary involvement was seen in 3 of these 4 cases.

Fourteen patients are currently alive and continuously disease free. The median follow up of survivors was 82 months (30-130 months). Disease free survival at 5 years was 77.8% and overall survival was 83.3%. Patients without marrow involvement had a better overall survival at 5 years as compared to patients with marrow involvement (90% vs 75%; p = 0.23).
Conclusions: Intramedullary involvement may suggest more aggressive disease biology in these intermediate grade tumors. The difference in our study was not statistically significant but this could be a reflection of the small numbers.

EP-094

CHEMOTHERAPY INDUCED NECROSIS AS A PROGNOSTIC MARKER IN OSTEOSARCOMA DO WE NEED TO RAISE THE BAR?

A. Puri[1], A. Gulia[1], S. Crasto[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Study co relation between chemotherapy induced percentage necrosis and overall survival (OS).
Methods: 192 consecutive patients of non metastatic osteosarcoma were analysed. Patients underwent appropriate surgical resection after receiving neoadjuvant chemotherapy. Excised specimen was analysed for chemotherapy induced percentage necrosis. Patients were divided based on the percentage necrosis as <90%, 90 – 99% and 100%.
Results: Necrosis was available in 184 patients. 77 had < 90% necrosis, 63 had 90 – 99% necrosis and 44 had 100% necrosis. 187 of these patients were available for follow up. Currently 85 patients are alive (follow up range 31 to 88 months, median 49 months). The OS of all patients was 47% at 5 years. There was no difference in OS in groups when traditional cut-off "< / > 90%" necrosis was used (46% and 32% for < 90% necrosis and > 90% necrosis respectively - p = 0.139). When we changed the cut-off to "</ = 100%" necrosis OS was 41% and 73% for < 100% necrosis and = 100% necrosis respectively (p = 0.001).
Conclusions: Our data suggests that the traditional cut off "< / > 90%" necrosis may not be a true representation of poor and good responders. It may be better to stratify patients as </ = 100% necrosis, both for prognosis and in trials evaluating post surgery chemotherapy change.

EP-095

CHEMOTHERAPY INDUCED NECROSIS AS A PROGNOSTIC MARKER IN EWING SARCOMA DO WE NEED TO RAISE THE BAR?

A. Puri[1], A. Gulia[1], S. Bhanupriya[1], N. Khanna[1], S. Laskar[1], G. Chinna swami[1], T. Vora[1]

[1]Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Study co relation between chemotherapy induced percentage necrosis and overall survival (OS).
Methods: 94 consecutive patients of non metastatic Ewing sarcoma were analysed. Patients underwent appropriate surgical resection after receiving neoadjuvant chemotherapy. Excised specimen was analysed for chemotherapy induced percentage necrosis. Patients were divided based on the percentage necrosis as <90%, 90 – 99% and 100%. Twenty-three patients received adjuvant radiotherapy.
Results: Necrosis was available in 80 patients. 25 had < 90% necrosis, 18 had 90 – 99% necrosis and 37 had 100% necrosis. All patients were available for follow up. Currently 62 patients are alive (follow up range 33 to 90 months, median 61 months). The OS of all patients was 68% at 5 years. There was no difference in OS in <90% and 90 – 99% groups (51% and 61% for < 90% necrosis and 90 – 99% necrosis respectively - p = 0. 641). On comparing the 90 – 99% necrosis and = 100% necrosis groups, OS was 61% and 87% for 90 – 99% necrosis and = 100% necrosis respectively (p = 0.041).
Conclusions: Our data suggests that the traditional cut off "< / > 90%" necrosis may not be a true representation of poor and good responders as the 90 – 99% necrosis group behaves similar to the < 90% necrosis group. It may be better to stratify patients as </ = 100% necrosis, both for prognosis and while evaluating for decisions related to treatment.

EP-096

OUTCOME OF CHILDHOOD EWING SARCOMA FAMILY TUMOURS TREATED WITH TWO CONSECUTIVE PROTOCOLS: A 15 YEAR EXPERIENCE AT UNIVERSITY MALAYA MEDICAL CENTRE, KUALA LUMPUR

R. Rajagopal[1], T. Yap[1], S. Lum[1], M. Azura[2], A. Vivek[2], S. Krishnan[1], A. Wan Ariffin[1], H. Ariffin[1]

[1]Paediatric, University Malaya Medical Centre, Kuala Lumpur, Malaysia; [2]Orthopaedic, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Objectives: Review of demographic data, clinical features and treatment outcome of patients with Ewing Sarcoma Family Tumours (ESFT) from 1998 till 2013 in University Malaya Medical Centre (UMMC).
Methods: Retrospective analysis of medical records of all patients diagnosed with ESFT aged less than 18 years treated on two consecutive chemotherapeutic regimens from 1998 to 2013. MKSCC P6 protocol from1998 to 2008 and subsequently Euro-Ewing99 protocol from 2009 onwards were used in the unit.
Results: Twenty-six patients (M:F = 1:1.3) were seen in the 15 years study period. Ten (35%) presented with metastatic disease (lung = 2, bone = 2, bone marrow = 3, combined = 3). The sites of primary tumour were: appendicular skeleton = 9; axial skeleton = 6; extra-osseous = 5; ribs = 3 and skull = 3. 22 patients (85%) had gross total resection (GTR) a median time of 6 months after initiation of therapy. With a median follow-up time of 4.5 years, the combined overall survival rate for both treatment arms was 46% (localized disease, 47% and metastatic disease, 44%).10 relapses occurred with median time of 11 months (range: 7-48 months) mainly in long bones and one had refractory disease. Relapse rate in our patients with ESFT was 50% in metastatic disease and 35% in those with localized disease. All relapsed patients died within 8 months (mean 4.5 months) despite of various salvage therapies. There were 2 induction toxic deaths in Euro-Ewing protocol. Most common side effects observed were septic shock and tubulopathy. 1 patient defaulted follow-up and hence, the disease status is uncertain.
Conclusions: In our cohort, overall survival rate was 46% in 26 consecutive patients treated on two multi-modal protocols. Relapse was seen in both local and metastatic patients and occurring within one year post-treatment. Relapse of Ewing sarcoma is associated with a dismal prognosis despite various salvage therapies.

EP-097

EVALUATION OF OVERALL SURVIVAL (OS) AND EVENT-FREE SURVIVAL (EFS) OF PAEDIATRIC SARCOMA PATIENTS - WEST OF SCOTLAND EXPERIENCE

M. Ronghe[1], D. Murphy[1], J. Sastry[1], P. Donnelly[1], A. Macdonald[1], F. Cowie[2], R. Jones[2], R. Duncan[3]

[1]Paediatric Oncology, Royal Hospital For Sick Children Yorkhill, Glasgow, United Kingdom; [2]Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; [3]Orthopedics, Royal Hospital For Sick Children Yorkhill, Glasgow, United Kingdom

Objectives: To evaluate OS and EFS of paediatric sarcoma patients with an interest in comparing metastatic cases with non-metastatic cases, and compiling statistics on treatment methods.
Methods: Retrospective observational study of sarcoma patients identified from unit database. These contained information about diagnosis, treatment, prognostic indicators, and outcomes for each patient.
Results: Fifty-sixpatients, 2001-2008. Osteosarcoma: 11 patients,7 males, age range: 4-16; median = 10; OS = 64%, EFS = 55%; Primary site of disease: Femur (47%), Tibia (41%), Humerus (5.5%), Scapula (5.5%), Other (1%); Metastatic Rate = 27% (OS = 0%). Ewing sarcoma: 24 patients,10 males, age range: 1-16, median = 12; OS = 71%, EFS = 58%; Primary site of disease: Pelvis (29%), Femur (22%), Paraspinal (16%), Chest Wall (10%), Tibia (10%); Metastatic Rate = 21% (OS = 40%; EFS = 40%); Alveolar rhabdomyosarcoma:10 patients; OS = 80%, EFS = 60%; Metastatic Rate = 20% (OS = 100%; EFS = 100%). Embryonal rhabdomyosarcoma: 11 patients; OS = 73%, EFS = 73%; Metastatic Rate = 0%.
Conclusions: Our results reflect access to an experienced and innovative paediatric sarcoma service with close links to a National Sarcoma Multidisciplinary Team. The data falls in line with other studies in terms of age of onset, location of primary tumour, metastatic rate, site of metastases, and prognosis for all cancer types. Limb salvage surgery is greatly favoured over amputation for both osteosarcoma and Ewing sarcoma. Females have a more favourable prognosis in osteosarcoma and a slightly poorer prognosis in Ewing sarcoma. Our overall survival rates are currently better than the UK-wide statistic for three of the four tumours examined.

EP-098

PROGNOSTIC IMPACT OF THE EXPRESSION PROFILE OF THE HYPOXIA RELATED GENES CA9, CA12, HIF1A, HIF2A, SCL2A1 AND VEGF IN OSTEOSARCOMA AND EWING SARCOMA

C.A. Scrideli[1], M. França[1], E.E. Engel[2], R.G.P. Queiróz[1], L. Neder[3], V.K. Suazo[1], B.O. Mori[1], L.G. Tone[1], C.A. Scrideli[1]

[1]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [2]Orthopedics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [3]Pathology, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil

Objectives: Osteosarcoma (OS) and Ewing sarcoma (ES) are the most common primary malignant bone tumors in children and adolescents. Hypoxia related genes had shown important prognostic markers and have been associated with radio- and chemoresistance in different human cancers, but few studies have been conducted in primary bone cancers. The aim of this study was to analyze the expression profile of hypoxia related genes in these tumors.
Methods: We analyzed the gene expression profile of hypoxia related genes *CA9, CA12, HIF1A, HIF2A, SCL2A1* and *VEGF* in consecutive microdissected samples of osteosarcoma

(n = 32) and Ewing sarcoma (n = 16) at diagnosis by RT-qPCR using TaqMan probes by the $2^{-((Ct}$ method. Mann-Whitney test was used to assess the correlation between gene expression and clinical/biological variables. Event-free survival was analyzed by Kaplan-Meier plots and log-rank test.
Results: Patients with osteosarcoma presented higher levels of *HIF1A* (+2.97-fold, P = 0.001) when compared with Ewing sarcoma. In osteosarcoma it was found a significant association between lower degrees of tumor necrosis post neoadjuvant chemotherapy (Huvos scores I/II) had higher expression levels of *VEGF* (+ 3.36-fold, P = 0.022) and *SCL2A1* (+2.97-fold, P = 0.011). In patients with Ewing sarcoma, *HIF1A* gene expression levels higher than median had a significant higher 5 years event free survival (100% versus 37.5%, P = 0.022)
Conclusions: Our data suggest a prognostic impact of the hypoxia related genes in pediatric osteosarcoma e Ewing sarcoma. Functional studies and analysis of a great number of cases is necessary to confirm these findings.

EP-099

OSTEOSARCOMA IN CHILDREN UNDER 8 YEARS OF AGE. A 28-YEAR EXPERIENCE AT A SINGLE INSTITUTION

J. Palacios[1], J. Shalkow[2], A. Leon[1], D. Hernandez[1]

[1]Surgical Oncology, National Institute of Pediatrics, Mexico City, Mexico; [2]Federal Director Pediatric Cancer Program, National Center for Pediatric and Adolescent Health, Mexico City, Mexico

Objectives: Osteosarcoma is the most common malignant bone tumor in children and adolescents. Prognosis in children under 10 years of age is dismal. We describe herein the treatment and outcome of patients under 8 years of age with osteosarcoma.
Methods: We reviewed the cases of children under 8 years of age, treated for osteosarcoma at the National Institute of Pediatrics in Mexico City, between 1985 and 2013.
Results: There were 29 patients with a median age of 7 years. Most common primary site was femur (51%), followed by humerus (20%), tibia (13%), fibula, cranium, and axial skeleton. Most common histologic type was osteoblastic. All patients received neoadjuvant chemotherapy according to national protocol at the time of diagnosis. Surgery for primary tumor included limb-salvage or wide local excision in 10 patients, and 14 amputations. Five patients did not accept radical surgery when proposed. Despite multimodal therapy and successful complete surgical resection, 13 patients remain alive, while 16 children died.
Conclusions: Patients under 8 years of age with diagnosis of osteosarcoma carry a dismal prognosis. They seem to have a higher rate of chemo-resistant tumors. Newer treatment strategies, possibly including tailored treatment are needed for this group of patients.

EP-100

PROGNOSTIC FACTORS IN CHILDHOOD OSTEOSARCOMA: A 15-YEAR SINGLE INSTITUTION EXPERIENCE IN PERU

L. Vasquez[1], J. Geronimo[1], I. Maza[1], M. Oscanoa[1], F. Tarrillo[1], J.M. Silva[2], L. Sialer[2], M. Quinonez[3]

[1]Pediatric Oncology, Rebagliati Hospital, Lima, Peru; [2]Traumatology, Rebagliati Hospital, Lima, Peru; [3]Pathology, Rebagliati Hospital, Lima, Peru

Objectives: To determine the prognostic factors that influence survival of pediatric patients with high-grade osteosarcoma of the extremities.
Methods: A retrospective analysis of all patients with osteosarcoma of the extremities treated at Rebagliati Hospital from January 1998 to December 2013 was performed. Patient's sex, age, primary tumor site, serum alkaline phosphatase and lactate dehydrogenase level, distant metastasis at onset, presence of pathological fracture, histological response and type of surgery were analyzed. Overall survival (OS) and event-free survival (EFS) was determined by Kaplan-Meier method.
Results: Seventy-three patients with high grade osteosarcoma of extremities were identified, with a median age of 14 years (range, 5-17 years). The most common site of primary tumor was distal femur (45.2%). Twenty-seven patients (37%) had metastatic disease at onset. In the localized group, 22 of 46 patients had conservative surgery (43.5%). The type of surgery (conservative vs radical) in these patients did not affect survival (p = 0.65). All patients received neoadjuvant and adjuvant chemotherapy. A raised serum alkaline phosphatase (p = 0.027) and poor histological response to chemotherapy (necrosis less than 90%) (p < 0.001) showed significant correlation with worse prognosis. Age, histological subtype, pathological fracture and site of primary tumor did not affect survival. Five-year estimates of OS and EFS were 64.5 ± 8.1% and 48.5 ± 8.7% for patients in the localized group, respectively. Five-year estimates of OS and EFS were 16.2 ± 7.9% and 14.4 ± 7.3% for patients in the metastatic group, respectively. The median of follow-up was 30 months (1.5-152).
Conclusions: A raised serum alkaline phosphatase and poor histological response to chemotherapy were associated to a worse prognosis in patients with high grade osteosarcoma. There is a need for improving stratification and intensifying treatment, especially in patients with metastatic disease.

EP-101

CLINICAL OUTCOME, TOXICITY AND SURVIVAL OF PATIENTS WITH EWING SARCOMA TREATED WITH THE NATIONAL PROTOCOL AT THE NATIONAL INSTITUTE OF PEDIATRICS IN MEXICO

L. Velasco-Hidalgo[1], R. Cárdenas-Cardós[1], M. Zapata-Tarrés[1], R. Rivera-Luna[1], L. Nevares-Juárez[1], L. Nevares-Juárez[1], M. Ramírez-Martínez[1], D. Guerra-Medrano[1]

[1]Oncology, Instituto Nacional de Pediatría, Mexico City, Mexico

Objectives: To analyze the survival of patients with Ewing Sarcoma (ES) treated with a National Treatment protocol at a single institution.
Methods: We included all consecutive patients with ES from January 2007 to January 2012. Tumor work-up consisted in evaluation of the primary site with MRI, high resolution CT lung, bone marrow biopsy and PETCT. Patients received treatment with Vincristine (2mg/m2 for 1 day), Doxorubicin (conventional 25 mg/m2 for 3 days or pegylated 50 mg/m2 for 1 day) and Cyclophosphamide (2.1gr/m2 for 2 days) alternated with Ifosfamide (2gr/m2 for 5 days) and Etoposide (100mg/m2 for 5 days). The number of courses was established according to the presence of metastases and the complete resection of the tumor.
Results: We studied 24 patients (median age 9.4 years), 62.5% were male. The mean time between onset of symptoms and start of treatment was 4.4 months. The presentation was 54% axial and 24% had metastatic disease. 50% of patients were treated with conventional doxorubicin and 50% with pegylated doxorubicin. 136 cycles of chemotherapy were administered, presenting toxicity in 58% of them. Overall survival was 70% in patients with localized and 45% for patients with metastatic disease (P = 0.05). Survival in patients with axial disease was 50% vs.75% with extra-axial location (P = 0.05). 9 patients died, 5 (55%) due to toxicity and 4 (44%) due to progression of the tumor. 4 patients with metastatic disease underwent autologous hematopoyetic stem cell transplantation with a survival of 50%.
Conclusions: The National Treatment Protocol is well tolerated in patients with ES, with a similar survival reported internationally. Despite of this the survival for patients with metastatic disease is low. There is a need to explore and/or expand other therapeutic options including stem cell transplant as a consolidation alternative proceeding chemotherapy with new agents and/or combinations of therapy including radiotherapy.

EP-102

OSTEOSARCOMAS OF THE MANDIBLE (MOS): MULTIDISCIPLINARY MANAGEMENT. A COOPERATIVE STUDY OF THE GSF-GETO, RARE CANCER NETWORK, GETTEC/REFCOR AND SFCE: FOCUSING ON PATIENTS

C. Verite[1], J. Thariat[2], A. Brouchet[3], H. Reychler[4], A. Auvrignon[5], D. Frappaz[6], P. Marec-Berard[6], P. Lutz[7], H. Pacquement[8], L. Brugiére[9]

[1]of pediatric medical oncology, children hospital, Bordeaux, France; [2]of radiation oncology, cancer center Antoine-Lacassagne, Nice, France; [3]of Pathology, Center hospitalier universitaire, Toulouse, France; [4]of Medical Oncology, Center hospitalier universitaire, Louvain, France; [5]of Pediatric Medical Oncology, Center hospitalier universitaire, Paris, France; [6]of Pediatric Medical Oncology, Cancer Center, Lyon, France; [7]of Pediatric Medical Oncology, Center hospitalier Universitaire, Strasbourg, France; [8]of Pediatric Medical Oncology, Cencer Center Curie, Paris, France; [9]of Pediatric Medical Oncology, Cancer Center IGR, Paris, France

Objectives: MOS is exceptional in children and adolescents.
Methods: Retrospective study conducted of all cases of MOS diagnosed in France between 1973 and 2010, aiming to determine the impact of chemotherapy, radiation therapy and surgery on outcomes and to identify prognostic factors. This report focusses on patients <18 years old.
Results: In 111 patients, 13 (14%), were less than 18 years old (median age 14 years-old (range 7-18)).5 were males; In 6 patients MOS was a second or even third primary malignancies; 4 with previous history of head and neck cancer treated by radiotherapy; 3 with Li Fraumeni syndrome. TNM staging was 12 T1, 1 T2 and 13 N0M0. Pathological WHO grades were 12 high and one low. Neoadjuvant chemotherapy including high-dose Methotrexate, Ifosfamide/Etoposide, Doxorubucin, Cisplatin was carried out in 12. One patient had progression during first line therapy, no surgery and died. Surgery was carried out for 12 pts. Resections were 7 R0, 4 R1 and 1R2; histological response was poor (>10% viable tumor cells in resected specimen) in 7 patients, good in 4 and not known in 1 case. Post opérative chemotherapy was performed in 10 patients andpost op radiotherapy for 2. At last follow up, 4 are alive in CR1 (1-7 yrs after) and 9 patients experienced an event:1 death from primary progression, one alive with disease, 3 relapses local and metastatique (3 alive), and 4 metachronous osteosarcomas, 3 in pts with Li Fraumeni syndrome. For the entire cohort, wide surgery with clear margins was the strongest prognostic factor. Neoadjuvant chemotherapy improved disease-free and metastatic-free survival.
Conclusions: MOS remains a rare and highly malignant tumor demanding aggressive therapy. Surgery is the mainstay of treatment, and margins are the most important factor for local control and survival.

BRAIN TUMOURS

EP-103

MEDULLOBLASTOMA BELOW THE AGE OF 3 YEARS: TREATMENT AND PROGNOSTIC FACTORS

S. Ahmed[1], E. Eldebawy[2], N. Elkhateeb[3], M. Awaad[4], M. Zaghloul[2]

[1]Radiotherapy, Children Cancer Hospital Egypt (CCHE), Giza, Egypt; [2]Radiotherapy, Children Cancer Hospital Egypt (CCHE) and National Cancer Institute Cairo University Egypt, Cairo, Egypt; [3]Statistics, Children Cancer Hospital Egypt (CCHE), Cairo, Egypt; [4]medical Oncology, Children Cancer Hospital Egypt (Cche), Cairo, Egypt

Objectives: To investigate the treatment end-results of medulloblastoma under 3 years old and determine the factors affecting its prognosis.
Methods: Twenty five childrens below the age of 3 years were treated at Children's Cancer Hospital_Egypt during the period from July 2007 and Oct 2013. Gross total resection was performed in 15 children (60%), subtotal excision in 9children (36%) and biopsy in one patient. seventeen children (68%) were non-metastatic, while 8 (32%) metastatic M_{1-3}. Eight out of the 11 (44%) children received infantile medulloblastoma chemotherapy protocol, while the other 14 (56%) received other chemotherapy protocols. All 8 metastatic children received craniospinal irradiation (CSI). Nine out of the M0 patients received posterior fossa (PF) irradiation, while the other 8 received CSI at age of 3 years.
Results: The 4 year OS for non-metastatic was $78.4 \pm 11.6\%$ and $22.9 \pm 19.7\%$ for M children. The EFS for nonmetastatic was $61.1 \pm 14.3\%$ and $15.0 \pm 13.8\%$ respectively. The infantile chemotherapy protocol in M0 patients led to 4-year OS of $63.6 \pm 17.7\%$ compared to $55.6 \pm 24.8\%$ for other protocols in. The OS for CSI was $88.9 \pm 10.5\%$ compared to $75.9 \pm 10.5\%$ for conformal PF irradiation. OS of GTR and less than GTR is $83.3 \pm 18.2\%$, $753 \pm 28.6\%$ respectively. Two patients of the CSI group developed CNS relapse and other two patients had spinal relapse. No relapse in patients who received PF irradiation. Non of the these detected differences were statistically significant. All children tolerated treatment with minimal immediate toxicity and late effects with more aggressive treatment.
Conclusions: Non metastatic status in Medulloblastoma below the age of 3 years carry out better OAS and EFS than metastatic category irrespective to the treatment protocol.

EP-104

HISTONE DEACETYLASE INHIBITOR PCI-24781 SHOWS INHIBITION OF CELL PROLIFERATION AND CLONOGENIC SURVIVAL IN PEDIATRIC GLIOBLASTOMA CELLS.

P.V. Andrade[1], A.F. Andrade[2], R.G. de Paula Queiroz[1], C.A. Scrideli[1], L.G. Tone[2], E.T. Valera[1]

[1]Department of Pediatrics, Ribeirao Preto Medical School USP, Ribeirão Preto São Paulo, Brazil; [2]Department of Genetics, Ribeirao Preto Medical School USP, Ribeirão Preto São Paulo, Brazil

Objectives: This study aimed to evaluate the therapeutic potential of HDACi PCI-24781 on pediatric GBM lines, SF188 and KNS42 by proliferation and clonogenic survival assays.
Methods: Proliferation assay with Resazurin dye was performed in 96-well plates using 2×10^3 cells per well. Cells were treated with the PCI-24781 with different drug concentrations (of 0.5-16(M) for 24-96h. For clonogenic survival assay, cells were seeded into six-well plates with 500 cells per dish. Cells were treated with increasing drug concentrations (0.5-16(M). After 72h, culture medium was replaced and the cells were cultured for an additional 10–14 days. Individual colonies (>50 cells per colony) were fixed with methanol, stained with crystal violet and subsequently counted. Statistical analysis was made by One- and Two-way ANOVA and Bonferoni post-hoc.
Results: Both cell lines were sensitive towards PCI-24781 treatment, displaying an inhibition of proliferation after treatment ($P < 0.05$). In SF188 cell line, the strongest effect was observed at the dose of 16(M at 96h, when growth inhibition was approximately 93%. The KNS42 cell line showed a time dependent inhibition of proliferation after treatment. The strongest effect was observed at 96h when growth inhibition was approximately 84%. In clonogenic assay, there was no colony formation after treatment, showing a great sensibility of GBM cells for PCI-24781 treatment.
Conclusions: This primary data demonstrates that PCI-24781 can induce inhibition of cell proliferation and clonogenic survival of GBM cells. Additionally it shows the potential of HDACi for the treatment of pediatric GBM. Further experiments will be performed to assess the ability of this HDACi in modulating the cellular response to ionizing radiation.
Financial Support: Fapesp (process no. 2013/15891-8).

EP-105

CLIVAL CHORDOMAS IN CHILDHOOD

T. Kutluk[1], B. Aydin[1], B. Bilginer[2], N. Akalan[2], F. Soylemezoglu[3], F. Zorlu[4], B. Yalcin[1], A. Varan[1], C. Akyuz[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey; [2]Neurosurgery, Hacettepe University- Faculty of Medicine, Ankara, Turkey; [3]Pathology, Hacettepe University- Faculty of Medicine, Ankara, Turkey; [4]Radiation Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: Clivus chordomas are rare locally aggressive neoplasm of bone treated primarily with surgery. Most series consist small numbers of children and there is no suggested standard treatment algorithm other than total surgery. This series of patients were reviewed for the characteristics and course of disease.
Methods: The files of patients with clivus chordoma who were diagnosed and followed-up between 1987 and 2014 were retrospectively analyzed.
Results: Seven patients were diagnosed and followed-up with the diagnosis of chordoma at clival localization. The median age of 5 females and 2 males was 11 years. Symptoms were headache in 3 patients, diplopia in 2 patients, sleep apnea, dysphagia, hemiparesis, motor dysfunction on arm and ataxia each in one patient for median 2.5 months. Patients were followed median 17 months (1-84 months). First medical intervention was surgery in all. Three of five patients, whom had subtotal resection, locally recurred and re-resections were needed. Three patients with recurrent tumors received radiotherapy. Two of them received chemotherapy also (one received VAC regimen and the other ifosfamide, etoposide and imatinib after their 2nd and 5th resections. Third patient refused chemotherapy; he is still alive with progressive brain metastases. First patient who were given VAC regimen died of progressive disease after first course.
Conclusions: Clivus chordoma can be problematic when total resection cannot be achieved. Addition of radiotherapy helps improving disease-free or overall survival. Chemotherapy with ifosfamide and etoposide might have benefit on recurrent tumor. Further research is needed to define the role of chemotherapy and targeted therapies on stabilization or regression of the chordomas.

EP-106

PEDIATRIC TECTAL PLATE GLIOMAS

H. Susam Sen[1], B. Yalcin[1], B. Bilginer[2], K. Karli Oguz[3], B. Aydin[1], A. Varan[1], T. Kutluk[1], N. Akalan[1], C. Akyuz[1]

[1]Pediatric Oncology, Hacettepe University Faculty of Medicine, Ankara, Turkey; [2]Neurosurgery, Hacettepe University Faculty of Medicine, Ankara, Turkey; [3]Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Objectives: Tectal gliomas are a distinctive form of brain stem tumor which are generally low-grade astrocytomas with an unusually benign behavior. Treatment includes observation of the lesion or shunting and diversion of cerebrospinal fluid (CSF) to relieve associated hydrocephalus. We aimed to investigate the clinical characteristics and management approaches in our patients with tectal plate gliomas.
Methods: Files of children treated at our hospital between 1990 and 2013 with the diagnoses of tectal plate gliomas were reviewed retrospectively for clinical characteristics and treatment results.
Results: We identified 5 females and a male with a tectal plate glioma whose ages ranged from 5.5 to 14.5 years (median 7.4). Most common presenting symptoms were headache, vertigo, tremor of the hands and gaze palsies. One patient had findings of neurofibromatosis type 1. Median duration of delay from onset of symptoms to definitive diagnosis was 9 months (2-36 months). In the magnetic resonance images (MRI) the sizes of the primary tumors ranged from 1.7 to 2.5 cm with contrast enhancement in 2 cases. At a median follow-up of 23 months (1.5-120 months) four patients underwent a CSF-diverting procedure in the form of a ventriculoperitoneal shunt or endoscopic third ventriculostomy; one patient underwent tumor resection due to progressive disease in 3 months and one patient was observed with no intervention. Three patients needed at least one more CSF-diverting procedure in the follow-up. Median progression-free follow-up was 7.8 months (1.5-66).
Conclusions: Since the lesions are capable of growth either with, or without, new neurologic symptoms, close follow-up and monitoring are essential to intervene prior to the development of irreversible debilitating neurologic sequelae. Tumor size >2 cm and contrast enhancement on MRI scans might be related to tumor progression. All children with findings of late-onset hydrocephalus should undergo MRI and tectal plate glioma should be considered in the differential diagnosis.

EP-107

UTILITY OF IDH 1 EXPRESSION IN CHILDHOOD AND ADOLESCENT AGE GROUP GLIOMAS ACROSS NORTHERN INDIA

S. Babu[1], A. Singhai[1], L. Gupta[1], N. Husain[2], A. Chandra[3], M. Sagar[1]

[1]Pathology, King George Medical University, Lucknow, India; [2]Pathology, RML Institute of Medical Sciences, Lucknow, India; [3]Neuro Surgery, King George Medical University, Lucknow, India

Objectives: Paediatric Gliomas are a heterogeneous group of gliomas encompassing tumors of different histologies. Clinical utility of IDH 1 expression has been well established in adulthood gliomas. However, paediatric data is quite scanty to consider IDH 1 expression as a

utility tool in management of paediatric gliomas. Present study is an attempt to reflect and answer this concern.
Methods: A total of 46 cases, with 20 of them being under 10 years, of paediatric gliomas of different histologies were enrolled over a period of 2 years. A parallel arm with 154 cases was constituted for adulthood gliomas. Age of patients ranged from 1 to 16 years (mean 8.2 years). There were 18 cases of pilocytic astrocytomas, 16 ependymomas, and 4 each mixed gliomas and oligodendrogliomas. Most common site of involvement was fronto-temporal followed by parieto-occipital and posterior fossa. Increased intracranial tension accompanied by varying degrees of motor paralysis was the most common clinical feature, with duration ranging from 1 to 15 months. All cases were looked for IDH1 expression as per protocol.
Results: Of 46 cases, IDH1 expression was present in 8 cases only, 4 oligoastrocytomas and 2 cases of diffuse astrocytoma and oligodendroglioma each. 6 of them showed WHO grade II, while 2 grade III. Regarding age distribution, 6 of the positive cases were over 10 years (75%). In the parallel arm too, involving adults, 60% positive cases were seen in early to mid adulthood (<40 years). This comparison was statistically significant. The accompanying parameters viz. site, symptoms, duration, nucleo-cytoplasmic expression were in concordance in both groups.
Conclusions: To conclude, it can be emphasized that utility of IDH 1 expression in early childhood gliomas is limited, however early adolescent age groups and beyond have shown concordant results. It can be considered as a diagnostic tool for gliomas presenting in older pediatric population.

EP-108

COMBINED MULTIPLE CHEMOTHERAPY AND POSTERIOR FOSSA RADIOTHERAPY IN INFANTS WITH NONMETASTATIC MEDULLOBLASTOMA

L. Baroni[1], F. Lubieniecki[2], F. Fiandrino[3], A. Martinez[4], D. Alderete[1]

[1]Oncology, Hospital Garrahan, Buenos Aires, Argentina; [2]Pathology, Hospital Garrahan, Buenos Aires, Argentina; [3]Radiotherapy, Hospital Garrahan, Buenos Aires, Argentina; [4]Radiotherapy, VIDT centro medico, Buenos Aires, Argentina

Objectives: New radiotherapy modalities, 3D-conformal radiation therapy (CRT) and IMRT allow to include the radiotherapy in the treatment of patient younger than 36m with medulloblastoma. The aim is to evaluate the results of a protocol with chemotherapy and 3D-CRT/IMRT in infants nonmetastatic medulloblastoma.
Methods: From October 2002 to December 2012, 25 infants patients with medulloblastoma were treated in our institution, 8 metastatic; 15 of 17 nonmetastatic patients were evaluable for this study. Median age at diagnosis was 12.3 (3,1-30,6) months. After initial surgery, children received 5 cycles of induction chemotherapy, including Vincritine (0.05mg/k/d1,8,15), Cisplatin (3.5mg/k/d1), Cyclophosphamide (30mg/k/d2,3), Etoposide (4mg/k/d2,3), followed by maintenance chemotherapy: Carboplatin (18mg/k/d1), Vincristine (0.05mg/k/d1, 28), Cyclophosphamide (50mg/k/d28), and Etoposide (1,6 mg/k/d2-14; 29-43 orally). Patient whith gross residual tumor received HD metrotexate during induction. Posterior fossa 3D-CRT or bed tumor IMRT with/without Temozolamide was indicated after induction or when achived 18 months old (54/55.8Gy)
Results: The histological subtypes were: 4p classic meduloblastoma, 10p desmoplastic/nodular, 1 extensive nodularity. Four patients had gross residual tumor. Thirteen patients received 3D-CRT/IMRT. The median time from resection to radiotherapy was 7.1m (5.4-25.3). The median age of 3D-CRT/IMRT was 30.2m (18.4-48.4). Two pt did not receive CRT, 1 died in induction and 1 was extensive nodularity. The median follow up was 52.7m (5.9-137). The 5 year event-free survival and overall survival probabilities were 70.9% and 78.7% respectively. Four pt relapsed, 1 supratentorial metastasis, 1 intraventicular relapse, 1 leptomeningeal dissemination and 1 in spinal space. Median time from diagnosis to relapse was 21m (5.1-21.5).
Conclusions: The results obtained in this particular group of patients are very encouraging, considering similar result in group of patients more 36months old with the use of craneoespinal radiotherapy.

EP-109

RESPONSE TO INTRAVENTRICULAR TOPOTECAN (ITV), ORAL TEMOZOLAMIDE AND ETOPOSIDE IN CHILDREN WITH RELAPSED MEDULLOBLASTOMA: A MONO-INSTITUTIONAL EXPERIENCE

D. Alderete[1], L. Baroni[1], F. Lubieniecki[2], F. Fiandrino[3], F. Auad[4], M.L. Gonzalez[4], W. Cardenas[4], P. Pacheco[4]

[1]Oncology, Hospital Garrahan, Buenos Aires, Argentina; [2]Pathology, Hospital Garrahan, Buenos Aires, Argentina; [3]Radiotherapy, Hospital Garrahan, Buenos Aires, Argentina; [4]Neurosurgery, Hospital Garrahan, Buenos Aires, Argentina

Objectives: Patients with relapsed medulloblastoma are unlikely to be cured. New effective treatment strategies are needed.
Methods: We retrospectively reviewed 9 cases of relapsed medulloblastoma between Jun 2011 - Oct 2013, treated with palliative care criteria with IVT 0.4mg/dose, temozolamide 160mg/m2/day orally d1-5/28d and etoposide 50mg/m2/day orally d1-14/28 d. Ommaya reservoir was implanted. IVT was administrated twice a week for 3m; weekly for others 3m and twice a month since that. Surgery was performed when only one site was affected or to improve patient symptoms. Response was assessed by MRI every 3m.
At initial diagnosis the median age was 76m (31-108). Six were standard-risk and 2p were high risk. They received Craniospinal radiotherapy 2,340/3,600cGy respectively and 5,400/5,580cGy respectively in posterior fossa. It was followed by adjuvant chemotherapy using Cisplatin, Vincristine, Lomustine and/or ciclophosphamide (adaptive COG strategy). One was younger than 36m and was treated with baby protocol including posterior fossa radiotherapy. At relapse the median age was 117m (82–131). Median time from diagnosis to relapse was 23m (18–47). Five had isolated intraventricular relapse, 2 had leptomeningeal dissemination and 2 had extra-axial supratentorial meningeal metastasis.
Results: Four underwent surgical resection (2p gross resection and 2p subtotal resection). Evaluable tumor was seen in 7p. Responses to chemotherapy were seen in all cases, 1p complete remission, 5p with partial response and 1p stable disease with a median follow up of 11m (4–27). Eight remain alive: 6 without progression. Two showed MRI progression (12m and 13m). One relapsed and died, 13m and 27m respectively. The treatment was well-tolerated. Grade 3 thrombocytopenia was observed in 2p, leading to 25% decrease of temozolamide.
Conclusions: The combination of ITV, oral Temozolamide and Etoposide produces objective responses with minimal toxicity in children with relapsed medulloblastoma. This strategy allows our pt to live as normal as possible their residual life.

EP-110

TREATMENT STRATEGY IN CHILDREN WITH SUPRATENTORIAL HIGH-GRADE GLIOMAS

Z. Bekic[1], G. Tasic[2], J. Bokun[3], I. Tufegdzic[3], M. Skender[4]

[1]Pediatric Oncology Dept, Institute of Oncology and Radiology of Serbia, Belgrade, Serbia; [2]Brain Tumours Dept, Clinic for Neurosurgery Clinical Center of Serbia, Belgrade, Serbia; [3]Pediatric Oncology Dept, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia; [4]Brain Tumours Dept, Institute of Patology Medical Faculty of Belgrade, Belgrade, Serbia

Objectives: The aim of our non-randomised study was to evaluate results of treatment and analyze prognostic factors in patients with supratentorial high-grade gliomas.
Methods: From 1991 to 2005, we treated 43 pts, median age 11 (range 3 to 18 years). Gross total resection was performed in 8 pts, subtotal in 8 pts, and partial in 27 pts. Anaplastic astrocytoma (AA) was found in 35 pts and glioblastoma multiforme (GBM) in 8 pts. After surgery, patients were treated with local radiotherapy to the primary site (range 55-60 Gy) and chemotherapy. Chemotherapy regimens were: Vcr, CCNU (Group 1) in 10 pts; 8/1 regimen (Group 2) in15 pts and Vcr, CCNU, CDDP (Group 3) in 18 pts.
Results: During the 10 to 216 months follow-up period, 5-year overall survival was 42,1%. Significant prognostic factors were: patohistological type (AA vs. GBM) and extent of surgery. There were no significant differences between chemotherapy regimens (Group 1 vs. 2 &3 and Group 2 vs. 3).
Conclusions: Patohistological type and extent of tumor resection are predictors of better prognosis. Among the chemotherapy regimens applied, there was no difference in overall survival.

EP-111

PROTEOMICS CHANGES AFTER INHIBITION OF SP1 TRANSCRIPTION FACTOR BY TETRA-METHYL NORDIHYDROGUAIARETIC ACID IN GLIOBLASTOMA CELLS

A.M. Castro-Gamero[1], A.F. Andrade[2], V.K. Suazo[1], H.J. Laure[3], C. Izumi[3], J.C. Rosa[3], L.G. Tone[1]

[1]Pediatrics, University of São Paulo, Ribeirão Preto, Brazil; [2]Genetics, University of São Paulo, Ribeirão Preto, Brazil; [3]Protein Chemistry Center – Molecular and Cell Biology, University of São Paulo, Ribeirão Preto, Brazil

Objectives: Tetra-methyl nordihydroguaiaretic acid (M4N), is a global transcriptional repressor of genes dependent on the Sp1 transcription factor that affects apoptosis, drug resistance, proliferation responsive genes, and radiation resistance. Recently, we have demonstrated the antineoplastic effects of M4N, it induced apoptosis, acted synergistically with chemo-radiotherapy and deregulated the Sp1-dependent genes *Survivin* and *Cdk1* in glioblastoma (GBM) cells. However, the global impact of Sp1 inhibition by M4N on transcriptome and proteome of these cells is unknown.
Methods: The GBM cell lines SF188, KNS-42, U87MG and T98G were treated with 20 and 40 (M of M4N for 48h. Cell proliferation was assayed using XTT® test. Protein extracts were obtained for western blot assays and labeled with isobaric tags for relative and absolute quantitation (iTRAQ) technology. An off line strong cation exchange chromatography (SCX) and on line reverse phase LC coupled to ESI-Q-TOF-MS were used to identify peptides and determinate proteins differentially expressed. Statistical analysis was performed using Scaffold software.
Results: M4N treatment reduced proliferation and deregulated the protein expression of Survivin and CDK1 in all cell lines investigated. The quantitative proteomic analysis identified about 100 proteins with at least 2 peptides identified and 95% protein identification probability in both cell lines. Thirteen and six proteins were deregulated after M4N treatment

in SF188 and U87 cells, respectively. Gene ontology analysis demonstrated that all the deregulated proteins by M4N participate of important cell metabolic processes, such as carbohydrate metabolism.
Conclusions: We found evidence that Sp-1 inhibition by M4N treatment altered significantly the expression of proteins related with metabolic processes in GBM cells. Further studies will investigate the molecular changes of M4N-treated GBM cells, mainly in transcriptomic field in order to achieve a better understanding of Sp1 inhibition and provide new insight into GBM biology.
Financial support: FAPESP Process number 2012/16889-4 and 2012/16888-8.

EP-112

CHEMOTHERAPY FOR IRRESECTABLE LOW GRADE GLIOMAS IN A UNIVERSITY-BASED COMBINED NEURO-ONCOLOGY SERVICE IN SOUTH AFRICA

A. Davidson[1], A. Figaji[2], K. Pillay[3], T. Kilborn[4], L. Padayachy[2], M. Hendricks[1], A. van Eyssen[1], J. Parkes[5]

[1]Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa; [2]Paediatric Neurosurgery, University of Cape Town, Cape Town, South Africa; [3]Paediatric Pathology, University of Cape Town, Cape Town, South Africa; [4]Paediatric Radiology, University of Cape Town, Cape Town, South Africa; [5]Radiation Oncology, University of Cape Town, Cape Town, South Africa

Objectives: To assess the role of chemotherapy in the management of low grade gliomas by the combined neuro-oncology services of the University of Cape Town.
Methods: A retrospective analysis was performed on the folders of patients diagnosed at the Red Cross Children's Hospital and Groote Schuur Hospital between 2001 and 2013.
Results: There were 60 children, aged 0.41 to 13.75 years [median 5.38]. Forty six tumours (77%) were WHO grade I, and 14 were WHO grade II, including 7 fibrillary astrocytomas, 4 pilomyxoid astrocytomas and one pleomorphic xanthoastrocytoma. The commonest sites were cerebellum (30%), hypothalamus (20%), cerebrum (15%) and optic tract (12%). Fourteen patients were managed expectantly, including 5 of the 8 with neurocutaneous syndromes. Thirty two patients underwent surgery at diagnosis in the form of debulking or gross total resection, and 11 patients required surgery for recurrence or progression. Fifteen patients (25%) received radiotherapy; 5 of them as first line treatment. Thirteen patients with irresectable disease (median age 2.67) were treated with chemotherapy; 11 of them with vincristine and carboplatin as the first line regimen. Eleven of these tumours (84.6%) involved the optic tracts or the hypothalamus; ten were juvenile pilocytic astrocytomas and 3 were pilomyxoid astrocytomas. One patient progressed, three showed stable disease and nine responded, reducing in volume by 40-93% (median 68%). Estimated 5-year Overall Survival (OS) was 89.2% for the whole group; 92.3% for WHO I tumours and 74.2% for WHO II tumours. Estimated 5-year Progression Free survival (PFS) for the whole group was 53.5%. The patients treated with chemotherapy had an OS of 100% and a PFS of 33%.
Conclusions: Chemotherapy is a vital part of the multidisciplinary management of low grade gliomas in low and middle income settings.

EP-113

GLIOBLASTOMA MULTIFORME A SINGLE INSTITUTION EXPERIENCE AT BELO HORIZONTE/BRAZIL

A.P. Dutra[1], J.C. Aguirre Neto[1], J.L. Sousa Filho[2], B. Silva Costa[2]

[1]Pediatric Oncology, Santa Casa de Belo Horizonte, Belo Horizonte, Brazil; [2]Neurosurgery, Santa Casa de Belo Horizonte, Belo Horizonte, Brazil

Objectives: The goal of this study was to determine the epidemiology, clinical presentation and treatment outcome of pediatric Glioblastoma Multiforme in a single center institution
Methods: Clinical data of 108 patients under 18 years of age with brain tumors from December 2000 to December 2012 were reviewed in Santa Casa de Belo Horizonte/Minas Gerais-Brazil.
Results: Six patients (5.5%) had the diagnosis of Glioblastoma Multiforme (5 female and 1 male), with average age of 6.2 years were analyzed (range 4-12 years). During diagnosis 4 patients had Supratentorial tumors and 2 posterior fossa tumor. The most common signs and symptoms were associated with intracranial hypertension in five patients (Headache, somnolence, vomit, papilledema). Three patients had seizures and hemiparesis. One patient presented with posterior fossa tumor (brainstem) had paralysis of multiple cranial pairs, intracranial hypertension and ataxia. Parcial resection was performed in five patients and one (brainstem) stereotatic biopsy. All patients were treated with radiotherapy and 3 associated with chemotherapy, just one patient use Temozolamide and survival seven months. Median of Overall survival was 5.2 months (range 6-12 months), all children died due to disease progression
Conclusions: Glioblastoma occurs rarely in pediatric patients (0.6-7.9% of all glioblastomas). Symptom duration is about 3-5 months prior to diagnosis with a dismal prognosis. Glioblastomas have a tendency to recur and disseminate despite treatment with surgery, chemotherapy, and radiation. The poor outcomes seen with this tumor suggest that the optimal treatment strategy has yet to be elucidated and much work needs to be done.

EP-114

BRAIN TUMORS IN A SINGLE-CENTER: EXPERIENCE DURING 12 YEARS AT BELO HORIZONTE/BRAZIL

A. Dutra[1], J.C. Aguirre Neto[1], J.L. Sousa Filho[2], B. Silva Costa[2], M.A. Dellaretti Filho[2]

[1]Pediatric Oncology, Santa Casa de Belo Horizonte, Belo Horizonte, Brazil; [2]Neurosurgery, Santa Casa de Belo Horizonte, Belo Horizonte, Brazil

Objectives: The goal of this study was to determine the epidemiology, clinical presentation, associated factors, pathological fictures, and treatment outcome of pediatric brain tumors in a single center institution.
Methods: Clinical data of 108 patients under 18 years of age with brain tumors from December 2000 to December 2012 were reviewed in Santa Casa de Belo Horizonte/Minas Gerais-Brazil.
Results: One hundred and eight children (58 female, 50 male) with the median age of 7.2 years were analyzed. During diagnosis 64 (60%) patients with intracranial hypertension and 21 (20%) with seizures. 55 (51%) patients with posterior fossa tumor (21 with medulloblastoma and 20 with brain stem tumors), Supratentorial tumors was present in 51 (47%) children with 24 (47%) were low grade gliomas. Six (5%) patients with glioblastoma multiforme, but four were supratentorial none alive. Total resection was performed in 40 (48%) patients, parcial resection in 35 (40%) and 5 (6%) stereotatic biopsy. Fifty-five (51%) patients were alive without tumor, 35 (32%) died due to tumor progression or infections and 8 (7%) lost of segment.
Conclusions: In a single center institution with limited resources, most patients died with tumor progression or infections. So it's necessary to improve the supportive care and development of new treatment strategies to increase overall survival.

EP-115

WEEKLY VINBLASTINE IN PEDIATRIC LOW GRADE GLIOMAS

F. Gachi[1], N. Zehani[1], C. Louni[1], K. Ezziane[1], A. Trabzi[1], K. Bouzid[1], S. Bakhti[2], M. Mahiou[3], C. Tayeb[4]

[1]Pediatric Oncology, Pierre & Mary Curie Center, Algiers, Algeria; [2]Neurosurgery, Mustapha Bacha Hospital, Algiers, Algeria; [3]Radiation Oncology, Pierre & Marie Curie Center, Algiers, Algeria; [4]radiation Oncology, Military Hospital, Algiers, Algeria

Objectives: To assess the efficacyand toxicity of weekly vinblastine in low grade gliomas of children.
Methods: We conducted a prospectivestudy involving children treated for incompletely resected or unresectable low-gradeglioma (LGG). Vinblastine (6 mg/m2) was administered weekly until progressive disease, unacceptable toxicity, or a maximum of 2 years of therapy.
Results: Thirty-two patients (median age, 7.5 years, sex ratio 0.73) were enrolled on to this study. the response rate was 46%, After a median follow up of 52 months (range 12-78 months), overall survival was 96% at 3 years and 93% at 5 years, progression-free survival is 82% at 3 years and 62% at 5 years. Toxicicity was 6% mostly hematologic, and manageable.
Conclusions: The low-grade gliomas are a chronic disease, treatment should be less aggressive as possible. Vinblastine is an effective therapeutic, with a good tolerability, ease of use and low cost, would be an interesting alternative in our contry and could be used as first line.

EP-116

MULTIDISCIPLINARY APPROACH AND VISUAL ACUITY IN TREATED CASES OF OPTIC PATHWAY GLIOMAS

I. Astigarraga[1], M. Garcia-Ariza[1], A. Echebarria[1], J. Echevarria-Ecenarro[2], R. Martinez-Fernandez[2], R. Adan[1], R. Lopez-Almaraz[1], M.J. Martinez-Gonzalez[3], A. Garcia-Ribes[3], A. Navajas[1]

[1]Pediatric Oncohematology Unit. Department of Pediatrics, Hospital Universitario Cruces, Barakaldo, Spain; [2]Department of Ophtalmology, Hospital Universitario Cruces, Barakaldo, Spain; [3]Pediatric Neurology Unit. Department of Pediatrics, Hospital Universitario Cruces, Barakaldo, Spain

Objectives: Within pediatric brain tumors, optic pathway gliomas (OPG) are a specific group that requires special handling. We review our experience in therapy response and visual prognosis of OPG.
Methods: Review of low grade gliomas (LGG) with involvement of visual pathway in the last 10 years (2004-2014). We analyzed epidemiological, clinical, radiological and histological data at diagnosis and follow-up, focusing in multidisciplinary approach, therapies, and visual acuity at diagnosis and evolution.
Results: Among 29 LGG patients referred to the Pediatric Oncology Unit, 10 had involvement of the optic pathway at the time of diagnosis (5 men/5 women). The average age was 5.0 years (4.5 months-9 years). In 5 cases the presence of neurofibromatosis 1 was confirmed. Only one patient had isolated unilateral optic nerve involvement and most had regional CNS extension.

Initial biopsy was performed on 3 patients and 1 after progression. MRI characteristics were analyzed. Different specialists were involved in their management (pediatric oncologist, neurologist, neuroradiologist, geneticist, radiotherapist, neurosurgeon, endocrinologist, ophthalmologist, otolaryngologist, nephrologist): 8 in 4 cases, 7 in 3, 6 in 2 and 5 in 1. Treatments administered were chemotherapy (9), radiotherapy (3) and surgery (3). Mean follow-up was 48 months. Two patients died due to tumor progression (one had oligodendroglioma with spinal dissemination). Visual acuity on follow up was highly impaired in 2, slightly impaired in 3, stable in the rest but one that improved after chemotherapy.
Conclusions: Despite advances in brain tumors, management of optic pathway gliomas remains a challenge. Although vital prognosis can be favorable nowadays, there is still lack of consensus regarding therapies. As poor visual outcomes occur in many cases, a close follow-up is important with precise visual assessments. Management in multidisciplinary teams remains essential for optimal care of these patients.

EP-117

GLIOBLASTOMA MULTIFORME: REHABILITATION OF A CASE

D.G. Gasperini[1], B.M. Mançano[1], E. Boldrini[1], N.L.G. Suarez[1], M.S. Murra[2], D. Bonatelli[3], M.G.A. Constantino[4], M.L.P.C. Lourenço[5], C.E.B. Cavalcante[6], L.F. Lopes[7]

[1]Oncology pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Nutrition pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Physiotherapy pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [4]Speech therapy pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [5]Occupation therapy pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [6]Radiology pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [7]PHD Medical Diretor, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: Glioblastoma multiforme is a grade IV astrocytoma and represents about 7% of intracranial tumors in childhood.
Methods: Patient 18 years old, female, admitted on 11/01/2013 with headache, vomiting and paralysis in the right arm 15 days ago, she developed right facial paralysis and mild dysphagia, FOIS 5 (Functional Oral Intake Scale).
The functional classification was based on KPS 80% (Karnofsky Performance Status) and Scale Independence in Activities of Daily Living Katz scoring 0 (ADL-Katz).
MRI of brain: "solid-cystic lesion with central necrosis, perilesional hematoma, measuring $6{,}4 \times 5{,}8 \times 5{,}7$ cm, the left frontal region, compressing the pre central gyrus and diverting the midline to right".
Made frontal parietal craniotomy, subtotal resection, the patient developed cerebral edema, done dural repair and cranial bone was placed in the subcutaneous tissue of the abdomen.
Results: In intensive care unit, Glasgow 3T without sedation, KPS 20 and ADL-Katz 6
The rehabilitation care were: 1. Nutrition: Enteral nutrition, pasty, bland, general support and supplements; 2. Physiotherapy: motor and respiratory cinesiotherapy, workout sitting posture, balance, orthostatic and functional neuro electrostimulation; 3. Speech Therapy: passive and active orofacial exercises, cold thermal stimulation, workout swallowing and breathing for decannulation of tracheostomy; 4. Occupational therapy: guidance for positioning, treatment adherence, encouragement of self-esteem and relationships, use of adapted recreational activities and expressive activity.
Outside hospital after 22 days with Functional Independence Measure (FIM) 28.57%. Made conformational radiotherapy (60 G) with temozolomide (75mg/m^2/day). Currently FOIS 7, KPS 80%, FIM 88.09% and ADL-Katz scoring 3.
Last MRI: stable disease. Currently, using temodal (150-200mg/m2/day, 5 days, 6 cycles). Cranioplasty scheduled for 07/04/2014.
Conclusions: Although we know that potentially all malignant gliomas will recidivate, it is clear in this case that patients may benefit from surgery, radiotherapy, chemotherapy and of a good rehabilitation work.

EP-118

ANTITUMOR ACTIVITY OF AMG900 ALONE OR IN COMBINATION WITH HISTONE DEACETYLASE INHIBITOR SAHA ON MEDULLOBLASTOMA CELL LINES

L. Geron[1], V.K. Suazo[2], A.F. Andrade[3], K.S. Borges[3], C.A. Scrideli[2], L.G. Tone[2]

[1]Genetics, School of Philosophy Sciences and Letters of Ribeirão Preto - FFCLRP/USP, Ribeirão Preto, Brazil; [2]Pediatrics, Ribeirão Preto Medical School, Ribeirão Preto, Brazil; [3]Genetics, Ribeirão Preto Medical School, Ribeirão Preto, Brazil

Objectives: Medulloblastoma (MB) is the most common malignant childhood brain tumor. Aurora kinases are essential for cell division and are primarily active during mitosis. Following their identification as potential targets for cancer chemotherapy, many Aurora kinase inhibitors have been discovered, and are currently under development. Recently, the combination of aurora kinases inhibitors (iAURK) with histone deacetylase inhibitors (iHDAC) has shown potential antitumor effects and had significant biological effects in preclinical cancer models. To evaluate the effects of the pan-aurora kinases inhibitor AMG 900 alone or in combination with the histone deacetylase inhibitor SaHa on pediatric MB cell lines UW402 and UW473.
Methods: Cell proliferation, clonogenic, apoptosis and qRT-PCR assays were performed in triplicate.
Results: AMG 900 caused the inhibition of cell proliferation, diminution of clonogenic capacity and increased the apoptosis rate in both cell lines ($p < 0.05$). The IC50 values were 183,16 nM and 242,16 nM for UW473 and UW402 cells, respectively. A synergistic effect in the AMG900-SaHa combination was evidenced on the inhibition of cell proliferation in both cell lines, especially in sequential drug treatment. Moreover, the combination of these drugs reached 100% of the inhibition in colony formation (synergistic effect). The treatment with AMG900 increased the p21 and GDF15 expression, but did not altered the TP53 one in the cell lines.
Conclusions: These results showed that the inhibition of aurora kinases by AMG 900 leads to antineoplastic effects on pediatric MB cell lines and its combination with iHDAC has promising effects in the treatment of this tumor.
Financial Support: FAPESP (process 2011/15645-1)

EP-119

THE HERBY STUDY: A PHASE II OPEN LABEL, RANDOMIZED, MULTICENTER STUDY OF BEVACIZUMAB-BASED THERAPY IN PEDIATRIC PATIENTS WITH NEWLY DIAGNOSED HIGH-GRADE GLIOMA (HGG)

J. Grill[1], P. Varlet[2], T. Jaspan[3], D.R. Hargrave[4], M. Massimino[5], E. Bouffet[6], A. Cañete[7], A.A. Azizi[8], F. Saran[9], G. Vassal[10]

[1]Pediatric Oncology, Institut Gustave Roussy, Paris, France; [2]Neuropathology, Sainte-Anne Hospital, Paris, France; [3]Division of Neuroradiology, University Hospital, Nottingham, United Kingdom; [4]Pediatric Oncology, Great Ormond Street Hospital, London, United Kingdom; [5]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [6]Neuro-Oncology, The Hospital for Sick Children, Toronto, Canada; [7]Pediatric Oncology Unit, HU La Fe, Valencia, Spain; [8]Department of Pediatrics, Universitätsklinik für Kinder und Jugendheilkunde, Vienna, Austria; [9]Pediatric Oncology, Royal Marsden NHS Trust, Sutton, United Kingdom; [10]Clinical and Translational Research Division, Institut Gustave Roussy, Villejuif, France

On behalf of the European Innovative Therapies for Children with Cancer (ITCC) Consortium, The European Society of Paediatric Oncology (SIOP-E) Brain Tumour Group, and the Australian Children's Cancer Trials Group

Objectives: Despite recent therapeutic advances, outcomes in pediatric HGG remain poor. A phase I study (Glade-Bender et al., *J Clin Oncol*. 2008) indicated that bevacizumab is well tolerated in children with refractory solid tumors and yielded pharmacokinetic data that support further studies of bevacizumab in childhood cancer.
Methods: A total of 120 eligible patients aged 3 to 18 years with newly diagnosed, localized supratentorial or infratentorial cerebellar or peduncular, histologically confirmed World Health Organization grade 3 or 4 HGG (central independent histologic confirmation) will be randomized to 6 weeks of concomitant temozolomide and local radiotherapy, followed by a 4-week temozolomide treatment break and 48 weeks of adjuvant temozolomide ± bevacizumab every other week. Children aged 6 months to 3 years are included in a young patient cohort; at relapse these patients will receive temozolomide and bevacizumab without radiotherapy. All patients/parents provided written informed consent per the local institutional review boards. The primary end point is event-free survival, defined as the time to earliest occurrence of tumor progression/recurrence (by central independent assessment per Response Assessment in Neuro-Oncology criteria), secondary malignancy, or death. Secondary end points include overall survival, response rate, safety, feasibility, and tolerability. All randomized patients will be followed for $\geq$3 years. A futility analysis will be performed after the first 60 randomized patients have been followed for 1 year; the primary analysis will be performed after all patients have been followed for 1 year. Updated analyses will be performed 3 years after the last patient has been randomized.
Results: HERBY is being conducted at 87 clinical sites in 15 countries. The first patient was randomized in October 2011. Among 118 patients screened to date, 79 have been randomized, and 1 has been enrolled in the young patient cohort.
Conclusions: Completion of the study is expected in 2016.

EP-120

PEDIATRIC MALIGNANT BRAIN TUMORS TREATED WITH BEVACIZUMAB

B. Herrero[1], I. Martinez[1], M. Villa[1], C. Rubio[2], J. Valero[2], A. Duque[3], B. Lopez-Ibor[1]

[1]Pediatric Hematology and Oncology Unit, HM Hospitales, Madrid, Spain; [2]Radiation Therapy, HM Hospitales, Madrid, Spain; [3]Neuroradiology, HM Hospitales, Madrid, Spain

Objectives: Bevacizumab is a humanized monoclonal antibody that recognizes and blocks vascular endothelial growth factor. It has been evaluated in malignant brain tumors in children. We report our experience with bevacizumab in these tumors in our pediatric oncology unit.
Methods: A retrospective study in all patients with malignant brain tumors treated with bevacizumab between May of 2010 and February of 2014 was undertaken. Bevacizumab was

administered at a dose of 10 mg/m^2 q2wk along with chemotherapy (Irinotecan) until progression.
Results: 16 patients diagnosed with malignant brain tumors and treated with bevacizumab from 2010 to 2014 are presented. 5 DIPG (5) patients were treated at diagnosis right after radiation therapy. All other patients were treated at relapse or progression: Ganglioglioma (4), Anaplastic ependymoma (2), medulloblastoma (2), PNET (1), Oligodendrogliomatosis (1) and atypical teratoid rhabdoid tumor (1). The mean age at diagnosis was 6.2 years old [0.8-18.8]. Treatment was administered for a mean time of 8.1 months [1-18]. It was quite well tolerated with minimal toxicity (bleeding or wound healing problems), leading to temporarily treatment interruption in three patients. Treatment was stopped in one patient because of parental decision. At the present time: 1 patient continues in complete remission (6.3%), 3 patients have stable disease (18.7%), 2 patients are alive with tumor progression (12.5%) and 10 died with tumor progression (62.5%). Two of them had severe complications (high blood pressure and massive stroke) which may have accelerated death within the context of tumor progression.
Conclusions: Bevacizumab is a well tolerated drug and it can be used in combination with other antineoplastics stabilizing the tumor growth. Our results are likely to be influenced by the use of this drug as a second line in patients with progression of the disease and worse basal status.

EP-121

CLINICAL EXPERIENCE WITH NIMOTUZUMAB IN CHILDREN DIAGNOSED WITH DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)

B. Herrero[1], I. Martinez[1], M. Villa[1], J. Valero[2], A. Duque[3], S. Garcia-Duque[4], J. Hinojosa[5], B. Lopez-Ibor[1]

[1]Pediatric Hematology and Oncology Unit, HM Hospitales, Madrid, Spain; [2]Radiation therapy, HM Hospitales, Madrid, Spain; [3]Neuroradiology, HM Hospitales, Madrid, Spain; [4]Neurosurgery, HM Hospitales, Madrid, Spain; [5]Neurosurgery, Hospital Quiron, Madrid, Spain

Objectives: Nimotuzumab is a humanized monoclonal antibody that targets the epidermal growth factor receptor (EGFR). It has been evaluated in malignant brain tumors in children. Our experience with nimotuzumab in DIPG is presented.
Methods: A retrospective study of patients with DIPG diagnosed and treated with Nimotuzumab between March of 2011 and March of 2014 at our unit was undertaken. Nimotuzumab was administered at a dose of 150 mg/m^2 weekly during Radiotherapy (six weeks) and q2weeks thereafter until tumor progression or toxicity.
Results: We took care of 8 patients diagnosed with DIPG and treated with nimotuzumab over three years. Five were females. The mean age was 7.6 years (range 1.9-18.8). All of them received nimotuzumab in combination with radiotherapy. Seven patients received also vinorelbine during and after of radiotherapy. Five patients were treated also with bevacizumab, and six patients received also Dexamethasone. Nimotuzumab was administered for 1.5-17 months (mean: 3 months). Nimotuzumab was well tolerated in all cases. Mean follow up was 7.5 months (5-30). Half of patients (4) have died, two have progressive disease and two of them have stable disease.
Conclusions: DIPG has a poor prognosis. Radiation Therapy (IMRT) is the standard treatment upon diagnosis. Nimotuzumab is a recombinant monoclonal IgG antibody that recognizes human EGFR, blocks the binding of its ligands and leads to the inhibition of cell proliferation and pro-apoptotic signals and a decrease in vascular endothelial growth factor (VEGF) production. Nimotuzumab represents a new tool for treating DIPG along with radiation therapy. It has proved to be no less effective than chemotherapy, it can be administered along with other drugs and it has no toxicity in this group of patients.

EP-122

NIMOTUZUMAB EXPERIENCE IN PEDIATRIC HIGH-GRADE GLIAL TUMOURS

M. Kantar[1], S. Onen[1], S. Kamer[2], S. Aksoylar[1], N. Cetingul[1], Y. Anacak[2]

[1]Pediatric Oncology, Ege University School of Medicine, Izmir, Turkey; [2]Radiation Oncology, Ege University School of Medicine, Izmir, Turkey

Objectives: Nimotuzumab (NMZ) which is a monoclonal antibody against E-GFR on tumor cells becomes widespreadly used in pediatric oncology. In this study we shared our experience with nimotuzumab in high-grade gliomas.
Methods: We used nimotuzumab (150 mg/m^2/w) in combination with vinorelbine (VNR) in 5 DIPG, one glioblastoma multiforme and one recurrent anaplastic ependymoma. In DIPG group median age was 9 years-old (3.5-17), there were 4 female and 1 male. Diagnosis of DIPG was made with MRG in 4 cases, except one who have had biopsy.
Results: All were irradiated after diagnosis. TMZ was used in 4 out 5 patients, prior to NMZ-VNR, with 2-10 courses starting at irradiation. Upon clinical or radiological progression, NMZ-VNR combination was started at median 7 (3-13) months. Median time of NMZ-VNR use was 6 months (1.5-15). One patient did not receive TMZ, but still on NMZ-VNR. She is alive for 17 months. Three out of other 4 patients died of progressive disease, but one with biopsy-proven disease is still alive for 30 months.
We have also used NMZ-VNR in a patient with GBM who have been treated with surgery and irradiation plus TMZ, but progressed at 13 months. Use of NMZ-VNR combination for 4 months unfortunetely failed to stop progression in this patient.
Last patient was an anaplastic ependymoma who relapsed 2 years after inial diagnosis. After second surgery NMZ-VNR combination was started at 27 months. During 9 month-use of this combination she stayed progression-free, however she later progressed and died of disease.
Conclusions: Nimotuzumab was very well tolerated. Nimotuzumab plus vinorelbine combination seems to have some benefit in high-grade gliomas. Our results with two patients are encouraging. In children, we need to have more clinical trials with these targeted therapies of high-grade gliomas or recurrent gliomas.

EP-123

PINEALOBLASTOMAS

R. Kebudi[1], B. Koc[2], F. Yaman Agaoglu[3], O. Gorgun[2], J. Wolff[4], S. Bay Kapu[2], A. Kebudi[5], E. Darendeliler[3]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Istanbul University Oncology Institute, Istanbul, Turkey; [3]Radiation Oncology, Istanbul University Oncology Institute, Istanbul, Turkey; [4]Pediatric Hematology - Oncology, Cleveland Clinic Childrens, Ohio, USA; [5]Oncologic Surgery, Maltepe University Medical Faculty, Istanbul, Turkey

Objectives: Pinealoblastomas (PBL) are rare tumors of the central nervous system and more common in children. The objective of this study is to evaluate the demographic data and outcome of children with PBL in a single center.
Methods: Files of children diagnosed with pinealoblastoma in the Istanbul University, Oncology Institute were evaluated retrospectively for demographic data, treatment and long term outcome.
Results: During 1990-2012, 6 children (3 male, 3 female) with a median age of 6 years (2 years- 14 years), were diagnosed with pinealoblastoma, in the Istanbul University, Oncology Institute. At the same time interval 494 patients <19 years old were diagnosed with malignant central nervous system (CNS) tumors in the same center, thus pinealoblastomas constituted 1. 2% of all CNS tumors. Three had subotal resection and three underwent a biopsy. At diagnosis, one had spinal seeding both in MRI and cerebrospinal fluid cytology. All recieved craniospinal radiotherapy and chemotherapy, the patient<3 years old recieved neoadjuvant chemotherapy first. The median follow up is 5 years (1-9.5 years). Two patients are alive for 5 and 9.5 years. One has just had a total thyroidectomy for papillary thyroid cancer as a second malignancy at 9.5 years. All others have died at a median of 2.7 years due to progressive disease.
Conclusions: In conclusion, PBL are aggressive tumors necessitating intensive treatment strategies including surgery, craniospinal radiotherapy and chemotherapy. Patients should be folowed up for long term side effects such as second malignancies.

EP-124

NEUROCOGNITIVE EVALUATION OF LONG TERM SURVIVORS WITH ATYPICAL TERATOID RHABDOID TUMOR (ATRT): THE CANADIAN REGISTRY EXPERIENCE

T. Fay-McClymont[1], D. Johnston[2], L. Janzen[3], S. Guger[3], K. Scheinemann[4], A. Fleming[5], C. Fryer[6], D. Mabbott[3], A. Huang[3], E. Bouffet[3], L. Lafay-Cousin[1]

[1]Pediatric Hematology Oncology and Bone Marrow Transplantation, Alberta Children's Hospital, Calgary, Canada; [2]Pediatric Oncology, Children's hospital of East Ontario, Ottawa, Canada; [3]Pediatric Oncology, Hospital for Sick Children, Toronto, Canada; [4]Pediatric Oncology, Mc Master University Hospital, Hamilton, Canada; [5]Pediatric Oncology, Montreal Children's Hospital, Montreal, Canada; [6]Pediatric Oncology, Bristish Columbia Women and Children's Hospital, Vancouver, Canada

Objectives: Because ATRT is a rare disease of infancy carrying grim prognosis, focus on long term outcome, especially neurocognitive remain very limited. With new era of multimodality therapy, some patients are now long term survivors.
Methods: We reviewed the neuropsychological (NP) status of the survivors from the Canadian ATRT registry.
Results: Among patients diagnosed between 1995-2012, 16/72 were survivors (22%). Formal NP assessments were available in 8 patients. Five patients could not be tested (3 too young, 1 blind significantly impaired, 1 lost to follow up). Additionally 1 patient was in special education class (grade 12), one received educational assistance (grade 8), one met academic expectation (grade 4). For the 8 patients with comprehensive NP, median age at diagnosis was 28.8 months (11.2-60.7). Four tumors were infratentorial and 3 were metastatic. Four patients underwent complete resection. All patients received post operative sequential high dose chemotherapy (Carpoplatin/Thiotepa). Five patients received intrathecal chemotherapy. Two patients underwent radiation (1focal, 1CSI). Median age at time of NP was 7.3 years (3.9-9.28). Full Scale Intellectual Quotient (FSIQ) ranged from 60 to 119 (median = 71). Simple expressive and receptive language appeared relatively preserved (low average to superior). Three most recently diagnosed patients (median time assessment post diagnosis 2.6 years (2.6-4.7)) had average to high average scores for FSIQ, academic and visual spatial skills, visual and verbal memory. Four other diagnosed earlier tested at a median time of 5.1 years

(3.3-8.3) post-diagnosis had FSIQ ranging from 60 to 71 (median = 68) and one patient with preexisting genetic syndromic condition was extremely low functioning (FSIQ<50). Approximately 50% of their scores were in the impaired range.
Conclusions: Whether these findings suggest further decline overtime or reflect improvement in overall management of these recently diagnosed patients remain unclear. Nevertheless this cohort of infants appears significantly impaired at school age despite the absence of systematic radiotherapy. Larger series focusing on neurocognition are definitely needed before embracing adjuvant radiotherapy as standard of care.

EP-125

LATE MORBIDITY IN LONG-TERM SURVIVORS OF CHILDHOOD BRAIN TUMORS:A NATIONWIDE REGISTRY- BASED STUDY IN FINLAND

P. Lähteenmäki[1], M.E. Gunn[1], T. Lähdesmäki[2], J. Matomäki[3], M.O. Arola[4], M. Grönroos[1], N. Malila[5]

[1]Pediatric Hematology and Oncology, Turku University Hospital, Turku, Finland; [2]Pediatric Neurology, Turku University Hospital, Turku, Finland; [3]Pediatrics, Turku University Hospital, Turku, Finland; [4]Pediatric Hematology and Oncology, Tampere University Hospital, Turku, Finland; [5]Cancer Epidemiology, Finnish Cancer Registry, Helsinki, Finland

Objectives: The population of long-term survivors of childhood brain tumors (BT) is growing and the follow-up of survivors should be organized in a structured way. Most of the earlier research on the morbidity of BT survivors has suffered from small sample sizes. On the other hand, larger studies are often based on self-reporting with a possibility for recall and selection bias.
Methods: All patients diagnosed with a neuroepithelial BT at age 0-15 years in Finland between 1970 and 2004 were identified from the Finnish Cancer Registry, and their new diagnoses (≥5 years after cancer diagnosis) were assessed using the Hospital Discharge Registry containing data on hospitalizations and outpatient visits in specialist health care. Siblings of the BT patients were identified as controls of the patients via Population Registry.
Results: The 5-year survivors of childhood BT had a significantly increased hazard ratio for endocrine diseases (HR 14.7), mental and behavioral disorders (HR 1.8), mental retardation/ disorders of psychological development (HR 16.6), diseases of the nervous system (HR 9.8), disorders of vision and hearing (HR 10.5), and diseases of the circulatory system (HR 2.7) compared with the sibling control group. Most of the outcomes also had an increasing prevalence up to 10 or 30 years after primary diagnosis. Irradiation treatment did not explain all the excess of morbidity, Survivors of embryonal tumors had kidney problems more than the other groups. Female survivors had higher hazard ratios for mental and circulatory problems compared with siblings than had the male survivors.
Conclusions: Systematic long term follow-up and supportive measures are essential due to numerous late effects among childhood brain tumor survivors. Even health related quality of life of survivors might improve if late sequelae were recognized and taken care of adequately.

EP-126

ENERGY EXPENDITURE IN WHITE ADIPOSE TISSUE IS ACTIVATED IN RESPONSE TO BRAIN TUMOUR GROWTH

C. Lam[1], L. Robinson[2], M.E. Symonds[2], B. Coyle[1]

[1]Children's Brain Tumour Research Centre, University of Nottingham, Nottingham, United Kingdom; [2]Academic Division of Child Health Obstetrics & Gynaecology, University of Nottingham, Nottingham, United Kingdom

Objectives: Brain tumours are the most common solid tumours in children. The PI3K pathway is frequently activated during tumourigenesis through deletion of the tumour suppressor phosphatase and tensin homolog (PTEN). In contrast, this same pathway may also be inhibited by increased PTEN expression in adipose tissue resulting in an increase in uncoupling protein (UCP) 1 expression and metabolic protection from tumourigenesis. This intrinsic protection is thought to arise from interscapular brown adipose tissue (iBAT) but may also occur through 'beiging' of inguinal white adipose tissue (iWAT). The aim of this study was to see if an association existed between UCP1 expression in adipose tissue and paediatric brain tumour growth through elevated PTEN levels.
Methods: Two types of medulloblastoma (WNT (n = 3) and group 4 (n = 5)) and ependymoma (n = 3) tumour cells were orthotopically xenografted into mice. iBAT and iWAT samples were extracted from tumour and non-tumour bearing mice (n = 5) to examine UCP1 and PTEN expression through QRT-PCR and Western blotting. Haematoxylin and eosin staining and UCP1 antibody immunohistochemistry (IHC) was also used to determine each BAT depot. Thermogenic activity of the adipose tissue was indirectly measured by thermal imaging of mice.
Results: iWAT from ependymoma tumour-bearing mice had evidence of beiging and increased UCP1 abundance through histology and IHC, while UCP1 expression in iBAT remained high in all mice. An increase in UCP1 gene expression and thermogenesis was observed in mice with spinal metastasis. PTEN expression did not relate to UCP1 expression.
Conclusions: Our data indicated mice implanted with aggressive tumours had increased UCP1 in iWAT. Though PTEN is not involved, other pathways like the β-adrenoceptor pathway should be explored due to its association with tumourigenesis and UCP1 expression in WAT. In conclusion, this pilot study suggests rapidly growing and metastatic brain tumours may stimulate metabolic protection via an increase UCP1 expression in iWAT.

EP-127

NO IMPACT OF HIGH DOSE CHEMOTHERAPY REGIMEN IN CHILDREN WITH HIGH RISK CNS TUMORS

A. Lassaletta[1], R. Robles[1], M. Garcia-Abos[1], N. Del Toro[1], L. Moreno[1], R. Urabayen[1], J. Ruiz-Pato[1], L. Madero[1], M.A. Diaz[1], M. Gonzalez-Vicent[1]

[1]Pediatric Hematology Oncology, Hospital Niño Jesús, Madrid, Spain

Objectives: It is unclear whether any specific high dose chemotherapy (HDC) regimen for autologous stem-cell rescue (ASCR) in children with high-risk or recurrent CNS tumors is superior. This study evaluates the outcome of different HDC regimens in children with CNS tumors.
Methods: Clinical characteristics, outcome and toxicity in children with high-risk CNS tumors treated from 1995 with HDC followed by ASCR were retrospectively reviewed. Primary endpoints were overall survival (OS) and event free survival (EFS). Toxicity was a secondary endpoint.
Results: Fifty-nine patients (22 males) with a median age of 5 (range, 1-18) were evaluated. Diagnoses were: medulloblastoma (34), CNS-PNET (10), high-grade glioma (6), ATRT (4), and other (5). Location was infratentorial in 71% of them. Disease status prior to HDC was: complete remission (CR) 25, non-CR 34. HDC regimen was: busulfan/melphalan (20); busulfan/thiotepa (16); carboplatin/etoposide/thiotepa (4), HD-thiotepa (3), tandem-HDC (5), and other (10). Median number of CD34 $\times$ 10^6/Kg was 5.15 (range, 0.9-48). Median days of admission were 19 (range, 10-50). Seventy-one percent of the patients developed mucositis (38% grade IV) and 31% engraftment syndrome. Transplant-related mortality was $4 \pm 2\%$. At 5 years OS and EFS were $27 \pm 8\%$ and $21 \pm 7\%$ respectively. Five-year OS was $48 \pm 11\%$, $12 \pm 11\%$, and $28 \pm 12\%$, for patients receiving busulfan/melphalan, thiotepa-containing regimens, and other HDC-regimens respectively ($p = 0.4$). Five-year EFS was $34 \pm 12\%$, $10 \pm 8\%$, and $28 \pm 12\%$, for patients receiving busulfan/melphalan, thiotepa-containing regimens, and other HDC-regimens respectively ($p = 0.6$). Patients in CR prior to HDC achieved a 5-year EFS of $44 \pm 11\%$ vs. $7 \pm 6\%$ for those not in CR ($p = 0.02$).
Conclusions: Although HDC with ASCR was well tolerated, and has been incorporated to our routine practice, overall results remain disappointing. No single HDC regimen showed superiority in children with high-risk CNS tumors. Disease status prior HDC remains the strongest predictor of survival.

EP-128

FOLLOW-UP STUDY OF INTELLECTUAL FUNCTIONING IN CHILDREN TREATED FOR A BRAIN TUMOR

J. Lemiere[1], T. Vercruysse[1], S. Jacobs[1], M. Haers[1], K. Vandenabeele[1], S. Geuens[1], V. Labarque[1], S. Van Gool[1]

[1]Paediatric Haemato-Oncology, UZLeuven, Leuven, Belgium

Objectives: Below average intellectual functioning, with performance IQ more affected then verbal IQ, is a well-known finding in children treated for a brain tumor. However, most studies are cross-sectional, making it difficult to evaluate the evolution of intellectual functioning and to disentangle tumor specific from treatment factors. In the present study we investigated the evolution of IQ performance between two time-points (at diagnosis and after treatment).
Methods: A total of 24 children diagnosed with a brain tumor at the University Hospitals Leuven were tested twice with the age-appropriate Wechsler scale. The first assessment was conducted as soon as possible after diagnosis and before initiation of chemo- and/or radiotherapy. The second assessment was performed 2-3 years after diagnosis. Mean age at diagnosis was 9.42 years. Localization was infratentorial in 63%; 25% of children were diagnosed with medulloblastoma. 21% received ventricular drainage and 71% underwent surgery before baseline testing. 67% underwent cranial irradiation during their treatment.
Results: At baseline, total IQ and performance IQ were significantly below the normative average ($t = -3.38$, $p = 0.003$ and $t = -4.18$, $p < 0.0001$). Performance IQ was significantly lower than verbal IQ ($t = -3.00$, $p = 0.006$). A similar pattern was found at the second assessment. A repeated measures analysis with tumor type as between factor and the use of radiotherapy as covariate demonstrated a significant interaction effect for the difference score ($F = 4{,}50$, $p = 0.046$). The discrepancy between verbal and performance IQ increased with 9.5 IQ points over time for children with medulloblastoma.
Conclusions: Our results demonstrated a discrepant intelligence profile already present in newly diagnosed children. This pattern remained present 2-3 years after diagnosis but the discrepancy became more pronounced in children with medulloblastoma. More specific neuropsychological testing at diagnosis is recommended to refine the cognitive profile and larger groups are needed to evaluate more potential predictors of cognitive outcome in children treated for a brain tumor.

EP-129

STAT3 SIGNALING: A CRITICAL TARGET AMONG RESVERATROL-INHIBITED SIGNAL TRANSDUCTION PATHWAYS IN HUMAN MEDULLOBLASTOMA CELLS

J. Liu[1], L.J. Yu[1], Q. Wang[1], S. Wen[1], M.L. Wu[1], X.Y. Chen[1], Q.Y. Kong[1], H. Li[1]

[1]*Liaoning Lab of Cancer Genetics and Epigenetics, Dalian Medical University, Dalian, China*

Objectives: Medulloblastoma is the most frequent brain malignancy in childhood and characterized with rapid growth, earlier intracranial dissemination and frequent recurrence. Although the combination of operation with craniospinal radiation and/or multi-agent chemotherapy have been adapted in clinical settings, the outcome of medulloblastomas remains poor due to the difficulty in removing the tumor radically and the side-effects of conventional adjuvant therapies. Several signaling pathways are activated in medulloblastomas and play pivotal roles in the tumor development and progression. Resveratrol, a non-toxic polyphenoal compound, possesses multifaceted biological activities and shows inhibitory effects on medulloblastoma cells. However, the underlying anti-medulloblastoma mechanism (s) of resveratrol remains unclear. This study aims to address this issue.
Methods: The influences of resveratrol in the statuses of cancer-associated pathways mediated by Wnt, Notch, NF-kB, Sonic hedgehog/SHH and STAT3 of medulloblastoma UW228-2 and UW228-3 cells were analyzed by multiple experimental approaches.
Results: Resveratrol suppresses Wnt, Notch, Sonic hedgehog/SHH and STAT3 activations as well as the expression of their downstream genes. NF-kB signaling is enhanced by resveratrol and its selective inhibition directly commits resveratrol-treated cells to apoptosis without induction of differentiation. Selective inhibition of Wnt, Notch or Sonic hedgehog/SHH activation has little effect on the growth of medulloblastoma cells. A single dose of AG490 effectively inhibits STAT3 activation and leads the treated cells to growth arrest and apoptosis.
Conclusions: Multiple cancer-associated signaling pathways are concurrently inhibited by resveratrol, of which STAT3 inactivation is the critical event because of the importance of this signaling in the survival of medulloblastoma cells. STAT3 signaling can be regarded as the molecular target and resveratrol as a promising agent in the management of medulloblastomas.

EP-130

OMEGA-3 FATTY ACIDS INHIBIT MEDULLOBLASTOMA GROWTH IN VITRO AND IN VIVO

L. Ljungblad[1], M. Wickström[1], J. Johnsen[1], P. Kogner[1], H. Gleissman[1]

[1]*Dept. of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden*

Objectives: Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are omega-3 fatty acids with antitumoral effects in several cancer types. DHA also protects neural cells from apoptosis and is of importance in the maintenance of normal brain development and function including cognitive functions.
Medulloblastoma, the most common malignant brain tumor of childhood is a highly invasive embryonal tumor arising in the cerebellum or brainstem. Multimodal treatment is necessary including surgery, radiotherapy and chemotherapy. However, treatment often results in significant neurological sequelae and the risk of resistant relapses is significant. The neuroprotective and antitumoral properties of omega-3 could therefore be of great benefit
Methods: Cytotoxic activity of DHA and EPA was studied in cell viability assays in a panel of medulloblastoma cell lines. The molecular mechanisms were characterized using cell- and molecular biology techniques. Mice with human medulloblastoma xenografts were treated with omega-3 fatty acids prophylactically and therapeutically while tumor growth was monitored.
Results: DHA and EPA induced medulloblastoma cell toxicity with IC_{50} values ranging from 1.9 to 68 (M in six medulloblastoma cell lines. DHA inhibited the prostaglandin E2 production, indicating a possible mechanism of action. *In vivo*, omega-3 supplementation resulted in significantly delayed establishment of xenograft tumors and significant inhibition of tumor growth when established tumors were treated. The in vivo treatment was non-toxic.
Conclusions: *Medulloblastoma* cells are highly sensitive to omega-3 induced toxicity both *in vitro* and *in vivo*. DHA/EPA are therefore good candidates for improving current therapy by acting as both "sword and shield " by killing off cancer cells while protecting healthy neurons from therapy-induced toxicity promoting cognitive function in survivors. Thus, omega-3 has the potential of a tumor growth inhibitor as well as that of reducing sequelae.

EP-131

TUMOR HISTOLOGY ACCORDING TO TUMOR LOCATION IN CHILDHOOD CENTRAL NERVOUS SYSTEM TUMORS: SINGLE CENTER STUDY

A. Mehrvar[1], A.A. Hedayati Asl[1], M. Tashvighi[1], M. Faranoush[1], N. Mehrvar[2], M. Alebouyeh[1]

[1]*Oncology, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran;* [2]*Research, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran*

Objectives: central nervous system tumors account for second most common childhood malignancies and the first cause of mortality in children with cancer. Patients received multimodality treatments according to the pathology of their tumor. In this area, improving treatment modalities can lead to increase the survival rate of patients. by this study, we examined the pathologic types of childhood brain tumors based on tumor location in patients who referred to MAHAK's Pediatric Cancer Treatment and Research Center (MPCTRC) in Tehran, Iran for treatment.
Methods: A retrospective review of all children less than 15 years old with a CNS histologically proven tumor, who presented to MPCTRC from April 2007 to April 2010, was performed. Data was analyzed by SPSS version 19.
Results: There were 198 (124 males) children eligible for the study. The majority of the tumors were infratentorial ($n = 134$), supratentorial ($n = 60$) and spinal ($n = 4$). the mean age per tumor location was 6.33 ± 4.08 years for supratentorial, 5.96 ± 3.41 years for infratentorial, and 7.75 ± 4.99 years for spinal tumors. Tumor histology according to infratentorial location was as: medulloblastoma (49.26%), low grade glioma (23.16%), high grade glioma (15.65%), ependymoma (10.43%), AT/RT and Germ cell tumor 0.75% respectively. according to supratentorial location, there were low grade glioma (34.97%), high grade glioma (31.6%), ependymoma (10.09%), PNET (13.33%), AT/RT (3.33%) and Germ Cell tumor, Craniopharyngioma, Primary CNS malignant lymphoma, histiocytosis 1.67% respectively. At the time of this analysis, there were 82 (41.4%) deaths, and 11 (5.6%) lost for follow-up.
Conclusions: In this hospital base study, the rate of commonest types of CNS tumors were similar to other reports. these data can be as a benchmark for increasing our understanding of childhood CNS tumors in Iran.

EP-132

SMALL MOLECULE TOLFENAMIC ACID INHIBITS MARKERS OF ANGIOGENESIS IN MEDULLOBLASTOMA CELLS VIA TARGETING SPECIFICITY PROTEIN TRANSCRIPTION FACTORS

J. Murray[1], U.T. Sankpal[2], L. Tabor[2], M. Felini[3], W.P. Bowman[2], R. Basha[2]

[1]*Hematology & Oncology Center, Cook Children's Health Care System, Fort Worth, USA;* [2]*Department of Pediatrics, University of North Texas Health Science Center, Fort Worth, USA;* [3]*Department of Obstetrics/Gynecology, University of North Texas Health Science Center, Fort Worth, USA*

Objectives: Medulloblastoma (MB) requires aggressive multimodality therapy. Survivors frequently suffer numerous long-term side-effects from such therapy. The objective of this study was to explore novel strategies for enhancing and optimizing the therapeutic effects of current MB treatments. Specificity protein (Sp) transcription factors (Sp1 and Sp3) are known to regulate survivin, an inhibitor of apoptosis protein associated with a poor prognosis and resistance to treatment. Sp proteins also modulate the expression of vascular epithelial growth factor (VEGF) and regulate angiogenesis. Small molecule tolfenamic acid (TA) inhibits MB cell proliferation and tumor growth in mice xenografts by targeting Sp proteins and survivin. We evaluated the effect of TA on the expression of VEGF and VEGFR1 and compared it with the changes in the key transcription factors, Sp1, Sp3, HIF-1(, and ERK1/2 phosphorylation and microRNAs, miR20a and miR27a (regulators of Sp1 repressors).
Methods: Human MB cell lines, DAOY and D283, were treated with vehicle (DMSO) or TA (10-100(M) and cell viability was monitored at 24-72 hours post-treatment using a CellTiterGlo kit. Mithramycin A (10-100nM) was used in some control experiments. The expression of Sp1, Sp3, survivin, ERK1/2, pERK1/2 and actin were determined by Western blot analysis and microRNA expression was measured using TaqMan small RNA assays.
Results: TA caused a dose and time-dependent inhibition (15 (g/ml: ~50% at 48 hours) of cell viability and decreased the expression of Sp1, Sp3, survivin, VRGF, VEGFR1 and total/phospho ERK1/2. TA (15 (g/ml: 48 hours) caused ~40% decrease in the expression of miR20a and miR27a.
Conclusions: These results demonstrate that TA targets key regulators of MB tumor growth mediated via Sp proteins-associated molecular mechanisms, including the candidates involved in angiogenesis. Further research will focus on epidemiological studies to evaluate the association of Sp proteins in MB, along with dedicated molecular profiling to better understand the underlying mechanisms.

EP-133

INTRAOPERATIVE MRI FACILITATES AGGRESSIVE BRAIN TUMOR RESECTIONS IN INFANTS, CHILDREN AND ADOLESCENTS

J. Murray[1], R. Roberts[2], D.J. Donahue[2], C. Guajardo[2], J. Honeycutt[2]

[1]*Hematology & Oncology Center, Cook Children's Health Care System, Fort Worth, USA;* [2]*Neurosciences Center, Cook Children's Health Care System, Fort Worth, USA*

Objectives: The prognosis for children with operable brain tumors correlates to the degree of resection, regardless of benign versus malignant histology. The use of adjuvant chemotherapy and/or radiation therapy is critical, but initial tumor resection remains paramount. The application of diagnostic quality intraoperative magnetic resonance imaging (iMRI) has been recently introduced to pediatric neurosurgery. We have designed and implemented a unique IMRIS iMRI operating room suite whose mobile, ceiling-mounted, 1.5 Tesla Siemens magnet glides from a diagnostic suite to the operative suite. We present our first 200+ consecutive iMRI brain tumor resections.
Methods: In February 2007, we dedicated an iMRI operating room suite housing MRI-compatible anesthesia equipment, standard operating room equipment (intraoperative neuro-

navigation and mobile operating microscopes) and robust safety protocols. The iMRI room is engaged for epilepsy and Chiari surgery, vascular malformations and brain tumor resections.
Results: We employed the iMRI operating room for 207 tumor extirpation cases over a 7 year period. Patients ranged in age from infancy to late adolescence, with a mean age of 9 years. Posterior fossa tumors accounted for 41% of the resections. Low-grade neoplasms represented 67%. There were an average of 1.2 intraoperative MRI scans per procedure, with a mean scan time of 37 minutes. Intraoperative scanning prompted additional tumor resection in 43% of cases. There were no iMRI-related complications, no increased incidence of infection (one patient) and no anesthesia problems. The next day re-operation rate (going back to neurosurgery the next day due to unseen, unresected tumor) was zero.
Conclusions: iMRI facilitates aggressive brain tumor resection in infants, children and adolescents with a low complication rate. The technology is safe and has resulted in no unanticipated 'go back' reoperations the next day as had historically occurred in our prior non-iMRI cases. iMRI during tumor resection surgery has become standard practice at our institution.

EP-134

INTRATHECAL-/INTRAVENTRICULAR-METHOTREXATE IN CHILDREN WITH CNS TUMORS: AN EXPERIENCE OF A SINGLE INSTITUTE

Y. Nakano[1], S. Nakamura[1], K. Yamasaki[1], C. Nitani[1], K. Okada[1], H. Fujisaki[1], Y. Osugi[1], J. Hara[1]

[1]Department of Pediatric Hematology and Oncology, Children's Medical Center Osaka City General Hospital, Osaka, Japan

Objectives: Intrathecal- and intraventricular-chemotherapies using methotrexate (IT-MTX and IV-MTX) are powerful tools controlling CNS leukemia and IT-MTX is standard treatment. However, as for these procedures, leukoencephalopathy is concerned about in combination with radiation therapy in CNS tumors. The aim of this study is to exam the incidence of leukoencephalopathy correlating with IT-/IV- MTX.
Methods: We retrospectively reviewed the medical records of pediatric patients with CNS tumors treated with IT-/IV-MTX in our institute since 2006 till 2012.
Results: Thirty-six patients, aged 0 to 26 years, were treated with IT-/IV-MTX. 13 patients were diagnosed with germ cell tumor, 16 medulloblastoma, 5 ependyoma and 1 AT/RT. MTX (8 to 12 mg) was given via lumber puncture (IT-MTX) in a single does and 1.5 to 3 mg of MTX was given via Ommaya reservoir (IV-MTX) for a single or three to four consecutive days. 29 newly diagnosed patients received IT-MTX in combination with systemic chemotherapy with (n = 20) or without (n = 9) radiotherapy: mainly, 24Gy local irradiation for germinoma and 50-55Gy local and 18-24Gy craniospinal irradiation for medulloblastoma. 12 patients with relapsed tumors received IT-/IV-MTX in combination with radiotherapy (n = 9). At present, 31 patients survive for 5 to 96 months. Four patients received more than 10 courses of IT-/IV-MTX and two of them developed asymptomatic leukoencephalopathy. These two patients received IT/IV MTX for recurrent diseases after 1st. line treatment with irradiation and systemic chemotherapy.
Conclusions: In this study, development of leukoencephalopathy was limited to patients with recurrent diseases. In newly diagnosed patients, IT/IV MTX seems to be the treatment that should be developed in future.

EP-135

A RETROSPECTIVE MULTICENTER ANALYSIS OF CHILDREN WITH LOW GRADE GLIOMAS - RESULTS OF THE JAPANESE PEDIATRIC BRAIN TUMOR CONSORTIUM

Y. Osugi[1], C. Kiyotani[2], H. Sakamoto[3], T. Yanagisawa[4], M. Kanno[5], H. Moritake[6], Y. Kosaka[7], J. Hirado[8], T. Takimoto[9], A. Nakazawa[10], J. Hara[11]

[1]Department of Pediatrics, National Hospital Organizaiton Osaka National Hospital, Osaka, Japan; [2]Department of Solid Tumor Oncology, Child Cancer Center National Center for Child Health and Development, Tokyo, Japan; [3]Department of Pediatric Neurosurgery, Osaka City General Hospital, Osaka, Japan; [4]Department of Neuro-Oncology, Saitama Medical University International Medical Center, Saitama, Japan; [5]Department of Pediatrics, Yamagata University Hospital, Yamagata, Japan; [6]Division of Pediatrics Department of Reproductive and Developmental Medicine, University of Miyazaki, Miyazaki, Japan; [7]Department of Hematology/Oncology, Hyogo Children's Hospital, Hyogo, Japan; [8]Clinical Department of Pathology, Gunma University Hospital, Gunma, Japan; [9]Division of Data Analysis, Child Cancer Center National Center for Child Health and Development, Tokyo, Japan; [10]Department of Pathology, Child Cancer Center National Center for Child Health and Development, Tokyo, Japan; [11]Department of Pediatric Hematology/Oncology, Osaka City General Hospital, Osaka, Japan

Objectives: We retrospectively investigated long–term history of children with low-grade gliomas (LGGs) diagnosed at 27 centers in Japan from 1998 to 2013.
Methods: There were 219 children (mean age 5.9 years (range: one month-15 years) in the study; tumor location: cerebrum 46, cerebellum 57, optic pathway/thalamus 87, midbrain 4, others 25) were assessed. In 67 patients tumors were totally removed. Histological WHO grading was grade I in 144 (pilocytic astrocytoma (A) 128), grade II in 51 (diffuse A 20, pilomixoid A 11) and LGG, NOS in 18. In six patients histological examinations were not done.
Results: Initially, 99 received chemotherapies and 24 received radiotherapy. The patients were followed for median of 35 months (one-190 months) from diagnosis. At present 93 patients have been in complete remission and 117 in stable disease, but recurrence have been observed in 83 among them. Seven patients died of diseases. In one of them, malignant transformation of the disease was observed 9 years after diagnosis. For all LGG 15-year OS and PFS were 94.5+2.6% and 43.0+5.2%. 10-year OS and PFS of PA, DA, and LGG, NOS were 95.1+3.3% and 38.2+6.4%, 70.6+20.8% and 50.7+12.9%, 100% and 72.7+17.7%, respectively. Among PA, 10-year PFS of optic pathway was inferior to that of cerebellum (18.4+7.0*vs.*60.3+9.0%). In patients with residual tumor after surgery, 10 year PFS was 33.7+6.2%, which was worse than that in patients whose tumors were totally removed (66.1+8.8%). There were no patients suffering recurrence 7.9 years after diagnosis. As the sequelae, epilepsy, hydrocephalus and lost vision were seen. 31 have some endocrinal problems (26 need therapy) and 28 need some support for living. One had second malignancy.
Conclusions: LGGs especially PA have clinically benign appearance and the incidence of malignant transformation was low. Pathologic diagnosis, tumor location and resection extent influence the outcome of the disease. We also need to follow the late effect sequel.

EP-136

MEDULLOBLASTOMA AND RISK OF PERI HIPPOCAMPAL DISEASE PROGRESSION

L. Padovani[1], A. Geoffray[2], C. Dufour[3], F. Doz[4], J. Gentet[5], S. Boll[6], C. Carrie[7], X. Muracciole[1]

[1]radiotherapy, La Timone Children's Hospital, Marseille, France; [2]radiology, Lenval Hospital, Nice, France; [3]medical oncology, gustave roussy institut, Villejuif, France; [4]medical oncology, Curie institut, Paris, France; [5]medical oncology, La Timone Children's Hospital, Marseille, France; [6]medical oncology, Gustave Roussy Institut, Villejuif, France; [7]radiotherapy, Leon Berard Center, Lyon, France

Objectives: To report the natural history of medulloblastoma (MB) with incidence of hippocampal area metastases.
Methods: Children treated for high-risk (HR) MB (majority included in PNET HR+ 5) and for metastasis at time of relapse were reviewed for distribution of metastatic location. Axial post-contrast MRIs, and central review reports were used to identify metastasis and hippocampus. Clinical and radiographic were analyzed in term of nodular or leptomeningeal infiltration and distance to peri hippocampal and hippocampal region divided in three groups of MTS: hippocampal (H-MTS), near hippocampal (1-10 mm from hippocampus; NH-MTS), at distance (AD-MTS). We divided the hippocampal area into the anterior and the posterior area.
Results: 51 patients were analyzed: 33 initially HR-MB (iMB) and 19 at time of relapse (ToR) (1 HR with spinal location at diagnosis and treated with craniospinal irradiation (CSI) at 23.4 Gy and 18 low risk at diagnosis). In iMB group, 16 (48%) had sustentorial metastases at diagnosis: 4 intra lateral ventricular nodules, 1 leptomeningitis infiltration, 2 metastasis NH-MTS, 9 AD-MTS including 4 with V3 infiltration. On the 19 patients in ToR group, 12 developped a sustentorial location: 6 with intra lateral ventricular nodules, 2 in NH-MTS (included the HR patient with leptominigitis infiltration), 1 in contact with hippocampal area and 3 in AD-MTS. In NH MTS, only 3/10 were near to anterior area.
Conclusions: These results underline that in high risk MB and in patients with relapse after low risk, 50% and 60% respectively developed sustentorial location. No metastasis underwent into hippocampal area. 12% at diagnostic and 15% after progression presented metastases near to hippocampal area. This study is still on going to define a sub- group of patients with low risk of hippocampal progression to propose partially hippocampal-avoidance CSI.

EP-137

EPENDYMOMA TREATED IN A MULTI-DISCIPLINARY CLINIC SETTING IN SOUTH AFRICA

J. Parkes[1], A. Davidson[2], A. Figaji[3], K. Pillay[4], T. Kilborn[5], L. Padaychy[3], M. Hendricks[2], A. van Eyssen[2]

[1]Radiation Oncology, University of Cape Town, Cape Town, South Africa; [2]Radiation Oncology, Groote Schuur Hospital and the University of Cape Town, Haematology-Oncology Service, Department of Paediatrics and Child Health, Red Cross Children's Hospital, Cape Town, South Africa; [3]Paediatric Neurosurgery, Red Cross Children's Hospital and the University of Cape Town, Cape Town, South Africa; [4]Paediatric Pathology, Red Cross Children's Hospital and the University of Cape Town, Cape Town, South Africa; [5]Paediatric Radiology, Red Cross Children's Hospital and the University of Cape Town, Cape Town, South Africa

Objectives: To review the demographics and outcomes of Paediatric ependymoma patients referred to the combined paediatric neuro-oncology services of the University of Cape Town.
Methods: A retrospective analysis was performed on all children aged 13 years or less diagnosed with ependymoma at the Red Cross Children's Hospital (RCCH) and Groote Schuur Hospital (GSH) between 1980 and 2013.

Results: Fifty-nine children were seen aged between 1 and 13 years with a median of 6 years. 4 patients had no data available and were excluded from the analysis.
44 patients (80%) had brain tumours, of which 32 (73%) were infratentorial, 11 (25%) were supratentorial and one was not known. 8 patients (15%) had spinal tumours. 34 (63%) patients had localised disease,10 patients (18%) had advanced or metastatic disease and 11 patients had no staging information.
25 patients (45%) had a gross total resection of tumour, 15 patients (27%) had a subtotal resection and 7 patients (13%) had biopsy only. In the remainder of patients, extent of surgery was not documented. Ten patients (18%) received chemotherapy and 42 patients (76%) received radiotherapy, of which 18 (43%) received craniospinal radiotherapy and 4 (9%) received proton therapy. Estimated relapse free survival (RFS) of all patients was 54.8% and overall survival (OS) was 65%. (n = 53) For brain tumours only (n = 43) RFS was 50%. For grade 2 tumours (n = 36) RFS was 47.25%, whereas for anaplastic tumours (n = 11) RFS was 62.5%. For infratentorial tumours (n = 28) RFS was 51.8% and for supratentorial (n = 5) tumours it was 37.9%. For patients treated between 2001 and 2010 only, 5 year OS was 75.3%.
Conclusions: Management of ependymoma is difficult and best done by a multi-disciplinary team even in a resource-constricted environment. Management strategies have evolved over the 33 years of study and outcomes have improved.

EP-138

QUALITATIVE EVALUATION OF OUR CRANIOSPINAL IRRADIATION TECHNIQUE (PLANNING AND SET UP) IN PEDIATRIC PATIENTS WITH MEDULLOBLASTOMA (MB)

M. Perez de Antueno[1], J. Barros[1], L. Rafailovici[1], L. Filomia[1], J. Chiozza[1], M. Skumanic[1], A. Martinez[1]

[1]Radiotherapy, Vidt Medical Center S.A, Buenos Aires, Argentina

Objectives: Craniospinal irradiation historically became the mainstay of therapy for MB, introduced Cooperative Groups adjuvant chemotherapy in the treatment of MB and leading to improved survival and subsequent reduction of RT dosage in irradiation treatment. To achieve a dose reduction in this kind of treatment offers better neurocognitive results and clinical outcomes in patients with average risk. This concept supports the importance of developing adequate techniques for dose delivery in RT. The purpose of this paper was to document the quality of RT delivered in pediatric patients with MB implementing our technique proposed for our task group.
Methods: We present our technique of planning and patients' set up for MB treatment. 24 pediatric patients with chemotherapy scheme were treated in our department during the period 2009-2012. The mean age was 8 years (3 – 14 yrs.) After surgery, a RT treatment was delivered with 3D conformal RT (CRT). Different devices were used for the patients immobilization. The individual set ups varied in prone or supine according to the patient clinical status. RT dose in critical structures, was recorded in plans for each patient.
Results: These technique allowed us to deliver highly reproducible treatments with a very low rate of relapse, only the 12.5%. As a secondary goal with the inmobilization devices, we improved the comfort of patients and reduced the margin of error in the set up of each field.
Conclusions: In the management of pediatric patients with MB, any strategy to reduce RT dose into the craniospinal axis, must include accurate planning verification and the dose delivered in all risk organs and any PTV for each treatment. In our experience with CRT, consistency in the set up each day of treatment is crucial and the proposed technique is a good way to achieve it.

EP-139

EVALUATING THE EFFECTS OF TREATMENT BRAIN TUMORS AND INTRACRANIAL DISEASES IN CHILDREN BY ROTATING GAMMA KNIFE (RGK) AT BACH MAI HOSPITAL, VIETNAM

P. Pham Cam[1], K.H.O.A. Mai Trong[1], H.A. Tran Dinh[1], D.A.I. Le Chinh[1]

[1]Nuclear Medicine and Oncology Center, Bach Mai Hospital, Hanoi, Vietnam

Purpose: To assess the effects of treating brain tumors as well as intracranial diseases by rotating gamma knife (RGK) at Bach Mai Hospital, Vietnam.
Methods and Materials: A prospective clinical interventions in 67 patients ($\leq$ 15 years) were diagnosed with brain tumors or intracranial diseases, treated with rotating gamma knife from July 2007 to July 2013 at Bach Mai Hospital, Vietnam.
Results: Average age is 10.5 years old. Ages at the time of radiosurgery ranged from 4 (youngest) to 15 (oldest). The male/female ratio: 1,8. In our study, 67 patients including arteriovenous malformations (AVM) 22.4%, pineal tumors 16.4%, astrocytoma 7.5%, cavernoma 6.0%; ependynoma 6,0%. Clinical symptoms: headache: 73.1%; nausea, vomiting: 53.7%; convulsions: 25.4%; hemiplegia: 20.9%; cerebellar syndrome: 6%. Tumor location: frontal - temporal sides: 56.5%; intraventricular 6.0%; brainstem 7.5%. The median tumor size was 2.13 ± 1.24 cm (range 0.6–4.1 cm). The median prescribed dose was varied (depending on nature and position of the tumor): 14.4Gy; min: 8Gy, max 20Gy. In group arteriovenous malformations and low grade astrocytoma had good response. Craniopharyngiomas had poorly response. So far, 55 patients (82.1%) improved obviously clinical symptoms: reduced headache, nausea, tumor size. 12 patients (17.9%) died due to progressive tumor after treatment.
Conclusions: Radiosurgery for treating brain tumors and intracranial diseases with Rotating Gamma Knife is safe and effective for children.

EP-140

TREATMENT OUTCOME OF CHILDREN WITH MEDULLOBLASTOMA: 20-YEAR EXPERIENCE FROM A SINGLE INSTITUTION IN MALAYSIA

R. Rajagopal[1], T. Yap[1], S. Lum[1], S. Krishnan[1], H.A.N.Y. Ariffin[1], A. Wan Ariffin[1]

[1]Paediatric, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Objectives: To review outcome of children with medulloblastoma treated at University Malaya Medical Centre (UMMC) from 1994 till 2013.
Methods: Clinical and prognostic indicators of 52 patients with medulloblastoma from 1994 to 2013 were retrospectively analyzed. Children aged more than 3 years were treated on CCG 9892 protocol and for those less than 3 years, UKCCSG CNS 9204 (1994-1996) and Headstart (from 1997 onwards) protocols were used. Risk stratification was based on Chang staging classification.
Results: There were 20 male patients. Median age of diagnosis was 3.5 years (range:0.9-15) and median duration of symptoms was 3 weeks (range:1-20). Vomiting (n = 29), headache (n = 21), unsteady gait (n = 15) and diplopia (n = 6) were common presenting symptoms.15 patients were excluded from the review; 5 refused treatment after surgery, 8 defaulted follow-up and 4 transferred to other hospitals. The remaining 37 patients were treated as per protocol based on risk stratification. 43% (n = 16) of them had metastatic disease at diagnosis. Post-operative residual tumour >1.5 cm^2 and distant metastasis at presentation were associated with high relapse rate of 71% and 75% respectively. In this cohort, age at diagnosis, gender, duration of presenting symptoms, delayed post-operative imaging and delay in radiotherapy did not significantly influence the outcome. Analysis of histopathological result was excluded due to lack of description details. Fifty-seven percent (n = 21) of patients died; 4 related to treatment associated complication and 17 due to disease recurrence or progression. Median time of recurrence was 11 months (range:1-24) and most of them died within 1 year. None of them responded to salvage chemotherapy. The 5-year overall survival rate is 39.4% with a median follow-up time of 9 years (range:6-13). Neuro-endocrine abnormalities are commonest long-term side effects.
Conclusions: Our results demonstrate dismal prognosis of medulloblastoma due to advanced stage of disease at diagnosis. High rate of treatment refusal and abandonment were observed in our centre.

EP-141

STUDY OF TERT AND MECHANISTICALLY RELATED MOLECULES IN MEDULLOBLASTOMAS

R. Reis[1], M. Viana-Pereira[2], G.C. Almeida[3], J.N. Stavale[4], S. Malheiro[4], J. Pimentel[5], C. Clara[6]

[1]Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, Brazil; [2]Life and Health Research Institure, Minho University, Braga, Portugal; [3]Department of Pathology, Barretos Cancer Hospital, Barretos, Brazil; [4]Department of Pathology, Federal University of São Paulo, S Paulo, Brazil; [5]Laboratory of Neuropathology, Santa maria Hospital, Lisbon, Portugal; [6]Department of Neurosurgery, Barretos Cancer Hospital, Lisbon, Portugal

Objectives: Hotspot activating mutations of the *TERT* promoter region were recently described in several tumor types. These mutations lead to enhanced expression of telomerase, being responsible for telomere maintenance and allowing continuous cell division. Additionally, *ATRX* mutations are an alternative telomere maintenance mechanism, associated with histone H3 mutations, responsible for disrupting the histone code and affecting regulation of transcription. Alternatively affecting histone regulation are *SETD2* inactivating mutations and SETD2 absence results in microsatellite instability (MSI). Here, we investigated the clinical relevance of these mechanistically related molecules in medulloblastoma.
Methods: A cohort of 113 formalin-fixed paraffin embedded medulloblastoma (aged 1-70 years) was used to investigate hotspot mutations of *TERT* promoter region, *H3F3A* and *HIST1H3B*, using Sanger sequencing. SETD2 deregulation was analyzed at the protein level by immunohistochemistry. MSI status and 24 MSI target genes were studied by multiplex PCR followed by genotyping
Results: We have successfully sequenced *TERT* in 68 medulloblastoma and identified a total of 18 mutated cases (26.5%). The C228T and C250T mutations were detected, respectively, in 15 and 3 samples. Similarly to previous reports, *TERT* mutations were more frequent in older patients ($p < 0.0001$), being found only in 5 patients younger than 20 years of age. In addition, *TERT* mutated tumors were more frequently recurrent ($p = 0.035$) and *TERT* mutations were significantly enriched in tumors located in the right cerebellar hemisphere ($p = 0.035$). No other clinicopathological data available was found to be statistically significant. No mutations were found on *H3F3A* or on *HIST1H3B*. MSI phenotype was seen in 10% of the analyzed samples. SETD2 expression is currently under pathological evaluation
Conclusions: *TERT* promoter mutations are frequent in medulloblastoma and associated with older patients, tumors prone for recurrence and arising in the right cerebellar hemisphere. On the other hand, MSI phenotype and Histone mutations are rare events in medulloblastoma.

EP-142

MEDULLOBLASTOMA IN CHILDHOOD:TUNISIAN EXPÉRIENCE

I. M'hamdi[1], S. Aissi[2], H. Rifi[3], N. Chraiet[2], L. Kochbati[4], A. Mezlini[2]

[1]Radiothérapy, Salah Azaiz, Tunis, Tunisia; [2]Medical Oncology, Salah Azaiz, Tunis, Tunisia; [3]Mdical Oncology, Salah Azaiz, Tunis, Tunisia; [4]Rdiotherapy, Salah Azaiz, Tunis, Tunisia

Objectives: Medulloblastoma is the most common brain embryonal tumour in children. The aim of this retrospective study is to evaluate clinical, radiological, therapeutic and prognostic features of this disease.
Methods: Seventy seven children with medulloblastoma were treated in our department between 1994 and 2010, the clinical presentation was dominated by signs of intracranial pressure (80%), gait instability (28.9%) and altered eye movement and diplopia (10.4%). The tumour were located in the fourth ventricle (35%) and vermian (30%).A ventricular shunt before resection was performed to increase intracranial pressure (7%). The resection was complete in 76.6% of patients. Four patients have leptomenegeal dissemination. Sixty eight patients (88%) had postoperative radiotherapy (RT), preceded by an initial chemotherapy (CT) in 25 cases (32.4%), exclusive in 36 cases (46.7%) and followed by CT in 5 cases (6.4%). The average dose to the craniospinal axis was 27.13 Gy (Range, 18 - 36Gy) with a boost to the posterior fossa to a total dose of of 49.76 Gy (Range, 50-56 Gy). Exclusive CT was recommended in 9 patients. CT protocols most commonly used were VP16 - carboplatin or BBSFOP.
Results: The median age was 9 years with a sex ratio of 2.2. After a median follow up of 32.7 months, 29 patients (37%) were in complete remission, 46 patients (59%) presented local recurrence that 36 required reoperation and 12 a CT alone. Two patients were lost to follow up after the initial resection.
Conclusions: Medulloblastoma is curable in a significant proportion of patients with average-risk disease at initial diagnosis. The delay in diagnosis and quality of excision remain the most important factors that influence the prognosis.

EP-143

RADIATION THERAPY IN THE TREATMENT OF BRAIN-STEM TUMORS IN CHILDREN

M. Russo[1], N. Isa[1], M. Reyes[1]

[1]Pediatric Radiotherapy, National Cancer Institute, Santiago, Chile

Introduction: Due to their location, tumors of the trunk (TT) present a high surgical risk and the diagnosis is usually made by imaging. In Chile, these cases are treated according to the PINDA Program (national treatment guide for pediatric tumors). All patients receive radiotherapy (RT) after diagnosis. The aim of this study is to evaluate the treatment results for TT at the National Cancer Institute (NCI) between 1993 and 2011.
Patients and Method: A retrospective review of patients diagnosed with TT at NCI was conducted. Patient population, symptoms, treatment received and overall survival are described. Prognostic factors were analy-zed.
Results: From November 1993 to December 2011, 70 children were referred for possible RT, 68 of them actually received it. The median age at diagnosis was 7 years old. In March 2014, out of 70 patients, 61 were de-ceased, all due to disease progression. The median survival of patients who received RT (68 patients) was 11,1 months from the end of treatment; the survival rates at 1, 2, 3 and 5 years was 48%, 16%, 15% and 15% respec-tively. Univariate analysis showed that survival was affected by the MRN high resolution imaging ($p = 0.08$, HR 1,64) and by the diffuse tumor pattern ($p = 0.025$, HR 1,14). Multivariate analysis showed survival is affected by the MRN high resolution imaging ($p = 0.011$, HR 2,56) and a higher dose of RT protector ($p = 0.017$, HR 0,87).
Conclusions: The poor re-sults obtained in the treatment of TT with RT at the INC are similar to those reported by other centers. Further explorations regarding other treatment options based on combined therapy using RT are needed.

EP-144

PRE-RADIATION CHEMOTHERAPY IMPROVES SURVIVAL IN PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMAS (DIPG)

Z. Gokce Samar[1], C. Faure Conter[1], C. Carrie[2], L. Claude[2], C. Chabert[3], D. Frappaz[4]
[1]pediatric, Institut d'Hématologie et d'Oncologie Pédiatrique, Lyon, France; [2]radiotherapy, Institut d'Hématologie et d'Oncologie Pédiatrique, Lyon, France; [3]radiology, Institut d'Hématologie et d'Oncologie Pédiatrique, Lyon, France; [4]oncology, Institut d'Hématologie et d'Oncologie Pédiatrique, Lyon, France

Objectives: The median survival rarely exceeds 9 months after standard treatment of DIPG by focal radiotherapy. The BSG 98 protocol was a prospective trial of frontline chemotherapy aimed at delaying radiation until time of clinical progression. As OS results were encouraging *(Frappaz Neuro Oncology 2008)*, this protocol was proposed as a routine in our cancer center for further DIPG patients who did not participate to another prospective study. The current abstract deals with this new cohort.
Methods: Protocol consisted of frontline chemotherapy. Each cycle included three courses delivered monthly; the first course was nitrosourea-cisplatin, and the second and third were high-dose methotrexate. Standard radiotherapy was delivered either at time of progression or electively after 12 month. A contemporary comparison cohort of 9 patients who received any experimental treatment that contained at least local radiation therapy served as controls. The initial and 3 monthly MRI were retrospectively centrally reviewed by a specialized neuro-radiologist who confirmed diagnosis of DIPG according to published criteria.
Results: From 15/09/2004 to 14/01/2013: 16 patients were treated according to BSG 98 protocol. Two patients underwent one cycle; 2 patients two cycles; one patient three cycles; nine patients four cycles and one patient was going on his third cycle (not finished yet). Three patients experienced severe iatrogenic infections, and ten patients required platelet transfusions. Median survival increased significantly in patients treated according to protocol compared to contemporary control (15 months vs 8 months $p = 0.029$), median PFS was longer (respectively 8 vs 3 months $p = 0.077$) and median radiation free survival was 7 months.
Conclusions: BSG 98 strategy is confirmed as one of the most effective current treatment of DIPG. It may serve as a control arm in randomized trial exploring innovative treatment, and may be proposed to parents and children who are reluctant for biopsy.

EP-145

SALVAGE CHEMOTHERAPY WITH BEVACIZUMAB-IRINOTECAN ASSOCIATION IN RECURRENT/REFRACTORY BRAIN TUMORS IN CHILDREN

A. Schiavetti[1], G. Varrasso[1], G. Reale[1], A. De Grazia[1], E. Ferrara[1], M. Paiano[1], A. Clerico[1]

[1]Pediatrics, Sapienza University of Rome, Rome, Italy

Objectives: To date, there is no current standard of care in the treatment of recurrent/refractory brain tumors and the majority of patients succumb to disease. A novel treatment strategy exploring the use of anti-angiogenic agents combined with cytotoxic CHT has been investigating but only few studies are reported. We report a phase II study in a series of consecutive cases with recurrent/refractory brain tumors.
Methods: Eight children (6 males and 2 females), median age at initial diagnosis 114 months, (range 17-240), affected by relapsed medulloblastoma (5pts), glioblastoma (1pt), PNET (1pt), low-grade glioma (1 pt), were treated with bevacizumab and irinotecan association. Five of these also received temozolamide. All pts had received two previous CHT lines. The median age at start of treatment was 143 months (range: 72-300). All pts received treatment as follows: bevacizumab 10 mg/kg i.v. with irinotecan 150 mg/m^2 i.v. every 2 weeks $\pm$ temozolamide 200 mg/m^2 p.o. daily for five consecutive days every 28 days. In total 117 courses were administered (median/pt:14.6, range 4-44). Two pts are still on treatment.
Results: Two pts (MB) who started treatment after radical surgical re-operation remained in CR respectively for 19 and 14 months. One of these is still on treatment, the other one progressed 6 months after therapy was stopped. Five pts (3 MB, 1 PNET, 1 GB) maintained SD (62%) for a median of 5.4 months (range 2-9). One pt (LGG) obtained a PR after 3 months and he is still on treatment. PFS at 6 months was observed in 5 pts (62%). Treatment was well tolerated with a good quality of life. Toxicity included allergy (1 pt) and grade 3 thrombocytopenia (5 pts).
Conclusions: In our small series of pts, bevacizumab-irinotecan association $\pm$ temozolamide showed encouraging results with a low-toxicity. Further studies in a larger population of pediatric pts with brain tumors are needed.

EP-146

HIF1A IS OVEREXPRESSED IN MEDULLOBLASTOMAS AND ITS INHIBITION IS ABLE IN REDUCE PROLIFERATION AND INCREASE HIF2A AND ATG16L1 METHYLATION LEVELS IN A CELL LINE MODEL

C.A. Scrideli[1], G.A.V. Cruzeiro[2], M.B.F. Reis[1], A.K. Eterovic[3], D.A. Moreno[4], L. Neder[5], R.S. Oliveira[6], S. Aguiar[7], J.A. Yunes[7], S.R. Brandalise[7], L.G. Tone[8], E.T. Valera[8]

[1]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [2]Genetics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [3]System Biology, MD Anderson Cancer Center, Houston, USA; [4]Genetics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [5]Pathology, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [6]Surgery, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [7]Pediatrics, Centro Infantil Boldrini/State University of Campinas, Campinas, Brazil; [8]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil

Objectives: Medulloblastoma (MB) is the most common malignant brain tumor in childhood. Several studies had correlated hypoxia genes to tumor progression and chemo/radioresistance in human cancers but few is known about these genes in MB. The aim of this study was to analyze the expression profile of hypoxia related genes in MB.
Methods: This study evaluated the gene expression profile of the hypoxia related genes *CA9, CA12, HIF1A, HIF2A, SCL2A1* and *VEGF* in 38 pediatric medulloblastoma in comparison to

those from 7 non-neoplastic fetal cerebellum samples by qRT-PCR using TaqMan probes. Additionally it was analyzed the effect of hypoxia and normoxia level conditions in the pediatric medulloblastoma cell line UW402 in gene expression and the effect of the *HIF1A* silencing by siRNA in cell proliferation (by XTT assay) and methylation levels of 10 genes related to hypoxia and apoptosis by pyrosequencing.
Results: A lower expression level of *CA9* (−4.21-fold, P = 0.009), *CA12* (−44.8-fold, P < 0.001) and *VEGF* (−5.24-fold, P = 0.001) and a higher *HIF1A* expression level (+1.93-fold, P = 0.022) was observed in MB samples when compared to fetal non-neoplastic cerebellum when analyzed by Mann-Whitney test. In UW402 cell line, the hypoxia condition resulted in up regulation of the genes *HIF1A, VEGF, SCL2A1* and *CA9*. After *HIF1A* knockdown (protein silencing efficiency 88% analyzed by Western blot) it was found a decrease of 30% in cell proliferation (P < 0.05, One-way ANOVA) and the reduction of the expression of the genes *VEGF, SCL2A1* and *CA9*. Inhibition of *HIF1A* caused significant increase in the pattern of methylation of genes *ATG16L1* and *HIF2A*
Conclusions: Except to *HIF1A* gene, a lower expression of hypoxia related genes was observed in MB when compared to fetal cerebellum. Silencing of *HIF1A* in pediatric MB cell line was able in decrease significantly the cell proliferation, suggesting that *HIF1A* could be a potential therapeutic target gene in MB.

EP-147

EFFECTIVENESS OF TREATMENT OF CHILD SUPRATENTORIAL PRIMITIVE NEUROECTODERMAL TUMORS

A. Shaverskyi[1], Y. Orlov[1], V. Zyabchenko[1], P. Plavskyi[1]

[1]*Paediatric, Romodanov Institute of Neurosurgery, Kiev, Ukraine*

Objectives: Supratentorial primitive neuroectodermal tumors in children are relatively rare, and are one of the most malignant brain tumors.
Methods: This work is based on results of retrospective analysis of treatment of 73 children with primitive supratentorial neuroectodermal brain tumors, that have undergone treatment in the Institute during 1995 - 2011. The patients consisted of 43 (58.9%) male and 30 (41.1%) female children, and the mean age at surgery was 5.5 years (range 1 month – 17 years). 24 (32.9%) cases were infants.
Results: Total resection was performed in 48 (65.8%) cases, subtotal in 19 (26.0%) cases and partial in 4 (5.5%) cases. Two children had a biopsy. The operative mortality was 5.5%. In 29 (39.7%) cases tumor was classified as neuroblastoma and in 4 (5.5%) cases - ganglioneuroblastoma. The presence of tumor cells in the CSF was found in 18 (24.7%) cases, metastasis to other parts of the brain diagnosed in 3 (6.8%) cases and metastases in the spinal cord in 5 (6.8%) cases. Extraneural dissemination in two cases. 57 (82.6%) patients underwent chemotherapy, and 39 (56.5%) patients had radiation therapy. Follow-up data from 1 month to 13 years is available for all patients, average survival rate 31.2 months. There was a significant worse survival in younger children, while no significant difference was found in the survival according to patient sex, tumor pathology or the stage of disease at the time of diagnosis.
Conclusions: Complexity of the surgery, application of radiation therapy and chemotherapy affect the survival rate and overall quality of life of the patient. An aggressive surgical approach is associated with postoperative low mortality and long survival. Inclusion in the complex treatment of radiation and chemotherapy prolongs survival.

EP-148

INTRACRANIAL TUMORS IN NEWBORN BABIES

A. Shaverskyi[1], Y. Orlov[1], P. Plavskyi[1]

[1]*Paediatric, Romodanov Institute of Neurosurgery, Kiev, Ukraine*

Objectives: We report a retrospective study of brain tumors diagnosed during the neonatal period and treated at the Institute of Neurosurgery, NAMS of Ukraine" from 1980 till 2012.
Methods: In 33 years, 15 cases of newborn babies with brain tumors were observed at the Institute of Neurosurgery, which makes 0.3% of all the children with brain tumors treated at the Pediatric department over the above mentioned period. Ten of them were males (66.7%), and five - females (33.3%). The histological analysis of the tumor was confirmed in13 (86.7%) observations. Benign tumors were diagnosed in 6 (46.1%) cases: plexus papilloma — 1, atypical plexus pailloma — 1, hemangiopericytoma — 1, a mature teratoma — 1, and lipomas — 2. Malignant tumors were found in 7 (53.9%) cases: anaplastic astrocytomas — 3, neuroblastoma — 1, an immature teratoma — 1, medulloblastoma — 1 and sPNET — 1. The histostructure was not identified in 2 cases.
Results: In total, 11 patients underwent 13 operations, as tumor removal was complemented by a shunting procedure in two cases. A total tumor removal was performed in 7 patients, a subtotal tumor removal – in 2 cases and a biopsy – in one case. The mortality after the tumor removal was 20%. 7 patients were followed; the average life expectancy was 3.1 years (from 1 to 12 years).
Conclusions: Modern diagnostic techniques make it possible to diagnose the congenital brain tumors at the early stages of life, or prenatally. Though the treatment outcomes and the survival rate remain poor, certain categories of children show a quite satisfactory period of outcome and the quality of life.

EP-149

LEPTIN CONCENTRATION AND NUTRITIONAL STATUS IN THE COURSE OF TREATMENT IN CHILDREN WITH BRAIN TUMOURS

G. Sobol-Milejska[1], K. Musiol[1], A. Mizia-Malarz[1], W. Stolpa[1], H. Wos[1]

[1]*Department of Pediatric Oncology Haematology and Chemotherapy, Medical University of Silesia Upper Silesia Children's Care Heatlh Centre, Katowice, Poland*

Objectives: The assessment of the nutritional status of children with malignant brain tumours in the course of treatment in correlation with the concentration of leptin
Methods: The study involved 44 children treated for CNS tumours. The body mass index and leptin value were analysed three times:before the beginning of the treatment, during the maintenance treatment and after its completion.
Results: The initial SDS BMI were similar to the control group value of this parameter. The SDS BMI decreased during therapy, but after the completion of the treatment SDS BMI value increased. During the therapy an increase in the concentration of leptin and its decrease after the completion of the therapy was observed.
Conclusions: In children with brain tumours there are quantitative disorders of the nutritional status which correlate with the period of the treatment. The correlation between the concentration of leptin and the nutritional status of children with brain tumours was not confirmed.

EP-150

INVESTIGATION OF VDR GENE POLYMORPHISM IN PEDIATRIC PATIENTS WITH BRAIN CANCER

B. Yilmaz[1], G. Tokuc[1]

[1]*Pediatric hamatology and oncology, Marmara University, Istanbul, Turkey*

Objectives: Vitamin D is a steroid in structure. Intracellularly, it bounds to special receptors and plays an important role in cell proliferation and inflammation. In recent years, it is also believed that Vitamin D may play a protective role in some cancer types. Certain regions of the VDR gene may show a genetic difference in structure. The most frequent polymorphisms in this gene are in Taq-1, Fok-1 and Bsm-1 regions. Some cancers are associated with VDR gene polymorphism like colorectal Ca, breast Ca and prostate Ca in adults. Reviewing the medical literature, there has no such a study been done on children so far.
Methods: We investigated the three most common gene polymorphisms in VDR gene in 32 childhood brain tumour and 40 healthy children.
Results: We could't find any relationship between childhood brain tumors and VDR gene polimorphism in these 3 regions.
Conclusions: In children, the relationship of VDR gene polimorphism, D vitamin status and pediatric solid tumours needs to be evaluated with larger series of patients.

EP-151

PENCIL BEAM SCANNING PROTON THERAPY WITH AND WITHOUT CONCOMITANT CHEMOTHERAPY FOR CHILDREN WITH ATYPICAL TERATOID/RHABDOID TUMOR: THE PAUL SCHERRER INSTITUTE EXPERIENCE

D.C. Weber[1], R. Malyapa[1], F. Albertini[1], U. Kliebsch[1], L. Mikroutsikos[1], P. Morach[1], C. Ares[1], R. Schneider[1]

[1]*Center for Proton Therapy, Paul Scherrer Institute, Villigen, Switzerland*

Objectives: Atypical teratoid/rhabdoid tumor (ATRT) of the CNS is a rare and extremely aggressive embryonal neoplasm of early childhood. The mean reported survivorship of these young ATRT children ranges from 6 to 11 months. Unlike conventional radiotherapy, proton therapy (PT) allows for optimal dose distributions, with the added benefit of no exit dose. We assessed the clinical results of pencil beam scanning (PBS) PT in the treatment of non-metastatic ATRT patients.
Methods: Fifteen children (male, $n = 8$, 53%) were treated with PBS PT between May 2008 and January 2013. Mean age at diagnosis was 17.4 ± 7.0 months. The localization was infratentorial (type A) and supratentorial in 9 and 6 patients, respectively. Gross total resection of the primary tumors was achieved in 7 (47%) patients. The median dose administered focally under sedation was 54 Gy (RBE). All and 7 (47%) patients received pre-PT and concomitant chemotherapy, respectively. Acute toxicity was assessed according to the CTCAE, version 4.0.
Results: After a median follow-up time of 24.5 months (range, 9.7-69.2), 3 (20%), 4 (27%) and 2 (13%) patients presented with local failure (LF), distant brain failure (DBF) and spinal failure (SF), respectively. Combined treatment failures (2 LF and DBF, $n = 2$; DBF and SF, $n = 1$) were observed in 3 (20%) patients. Six patients died, all of tumor progression. Median overall survival (OS) was not reached. The 2-year local failure, DB progression-free survival and OS rates are 22%, 76.6%, and 72.7%, respectively. Age ($p < 0.01$), localization ($p = 0.012$) and type of resection ($p = 0.067$) were prognosticators for OS. PT was well

tolerated. No grade > 2 acute toxicity was observed. One grade 4 and another grade 1 impaired motor function were observed in 2 (13%) patients.
Conclusions: PBS PT is an effective treatment for young children with ATRT. After PT, with or without concomitant chemotherapy, the median OS was not reached in this series. Acute toxicity was manageable.

EP-152

LONG-TERM SURVIVAL OF TWO YOUNG CHILDREN WITH RELAPSED ATYPICAL TERATOID/RHABDOID TUMOR

H. Yamada[1], S. Sakaguchi[1], J. Fujimura[1], H. Tamaichi[1], T. Kurimoto[1], Y. Saito[1], A. Kondo[2], M. Saito[1], T. Shimizu[1]

[1]Pediatrics, Juntendo University Faculty of Medicine, Tokyo, Japan; [2]Neurosurgery, Juntendo University Faculty of Medicine, Tokyo, Japan

Objectives: Atypical teratoid/rhabdoid tumor (ATRT) is a highly malignant embryonal central nervous system tumor that primarily occurs in children less than three years of age. Median survival is less than 10 months and approximately three-fourths of patients eventually relapsed despite of aggressive treatment. Treatment options for patients with relapsed disease are particularly limited.
Methods: We conducted a retrospective chart review of two patients treated for relapsed ATRT.
Results: Case 1: The patient was diagnosed with posterior fossa ATRT at the age of three months. The initial treatment consisted of gross total tumor resection and chemotherapy. The patient had local relapse six months after the completion of chemotherapy and underwent gross total tumor resection and four courses of intensive multidrug chemotherapy. The patient is now alive without evidence of disease 10 years after the initial diagnosis. Case 2: The patient was diagnosed with posterior fossa ATRT at the age of 19 months. The initial treatment consisted of gross total tumor resection and chemotherapy followed by craniospinal irradiation. The patient had metastatic relapse at anterior cranial fossa 12 months after the completion of the treatment. After the subtotal tumor resection, 50 weeks of multidrug chemotherapy was initiated. Stereotactic radiosurgery using Cyberknife was performed for the residual tumor during the chemotherapy. The patient is now alive 4 years after the initial diagnosis.
Conclusions: The prognosis of patients with relapsed ATRT is extremely poor. However, multimodality approach including chemotherapy, surgery and stereotactic radiotherapy may prolong survival and maintains quality of life.

EP-153

PRE-IRRADIATION CHEMOTHERAPY FOR CHILDHOOD INTRACRANIAL EPENDYMOMA

T. Yokosuka[1], N. Miyagawa[1], T. Sarashina[1], K. Fukuda[1], F. Iwasaki[1], S. Hamanoue[1], H. Goto[1], S. Ito[2], N. Aida[3], Y. Tanaka[4]

[1]Department of Hemato-oncology/Regeneration Medicine, Kanagawa Children's Medical Center, Yokohama, Japan; [2]Department of Neurosurgery, Kanagawa Children's Medical Center, Yokohama, Japan; [3]Department of Radiology, Kanagawa Children's Medical Center, Yokohama, Japan; [4]Department of Pathology, Kanagawa Children's Medical Center, Yokohama, Japan

Objectives: Standard therapy for childhood intracranial ependymoma is maximal tumor resection followed by involved-field irradiation. Although not used routinely, chemotherapy has produced objective responses in ependymoma, both at recurrence and in infants. We undertook a clinical trial of pre-irradiation chemotherapy in children with intracranial ependymoma at Kanagawa Children's Medical Center to investigate the potency of pre-irradiation chemotherapy.
Methods: Between 2003 and 2013, 18 children with newly diagnosed ependymoma were treated in our institute. All but 1 patient who could not receive chemotherapy because of severe brainstem compression by tumor were enrolled in the study. All children were with non metastatic ependymoma. The median age was 4 years (0- 10 years). The primary site was infratentorial in 10, supratentorial in 7 patients. Gross total resection (GTR) was achieved in 9 patients, subtotal resection (STR) was achieved in 8 patients. WHO grade II and grade III tumors were 6 and 11, respectively.
Results: All children received chemotherapy (vincristine 1.5 mg/m^{2,} etoposide 100 mg/m^2 x 5 days, cyclophosphamide 1.2 g/m^2 x 2 days, cisplatin 20 mg/m^2 x 5 days) following surgery and focal irradiation. Fourteen children completed 4 cycles chemotherapy. The median follow-up was 5 years (range 0.3–11 years). For the entire group, 5 year overall survival (OS) and event-free survival (EFS) was 71.8%, and 47.5%, respectively. Three patients experienced disease recurrence, and eventually died. The 5 year OS was 100% for grade II and 63.7% for grade III tumors (P = 0. 303). The 5 year OS was 60.0% for patients who underwent a STR versus 80.0% for those who underwent a GTR (P = 0.433).
Conclusions: These results suggest that primary chemotherapy strategies have an important role in the treatment of children with intracranial ependymoma. Patients with STR have inferior outcome despite responses to chemotherapy, and should be considered for second-look surgery prior to irradiation.

EP-154

PEDIATRIC EPENDYMOMA: AN ITALIAN SINGLE-INSTITUTION EXPERIENCE

A. Verrico[1], L. Quaglietta[2], R. Migliorati[2], G. Scimone[3], D. Di Gennaro[3], V. D'Onofrio[4], P. de Antonellis[5], M. Zollo[6], G. Cinalli[7]

[1]Pediatrics, University of Naples Federico II, Naples, Italy; [2]Hematology-Oncology, Santobono-Pausilipon Children's Hospital, Naples, Italy; [3]Radiotherapy, San Giovanni di Dio e Ruggi D'Aragona, Salerno, Italy; [4]Pathology, Santobono-Pausilipon Children's Hospital, Naples, Italy; [5]Centro di Ingegneria Genetica e Biotecnologia Avanzate, Ceinge, Naples, Italy; [6]Medicina Molecolare e Biotecnologie Mediche, University of Naples Federico II, Naples, Italy; [7]Neurosurgery, Santobono-Pausilipon Children's Hospital, Naples, Italy

Objectives: Ependymomas constitute 10% of all primary Central Nervous System tumors in children and have a 5 years progression-free survival (PFS), at best, of 60%. We report on our single-institutional experience.
Methods: All children who had a diagnosis of ependymoma confirmed through central neuropathology review and who attended the Neurosurgery unit at Santobono-Pausilipon Children's Hospital during 2007-2013 were enrolled.
Results: Twenty-seven consecutive children (median age, 3.1 years; range, 0.4-12.4 years) were studied. Male to female ratio was 1:2. Ninety-two percent of the tumors were intracranial, 77% occurred in the posterior fossa (PF). Supratentorial and spinal localizations were associated with age older than 3 years. On imaging ependymomas were heterogeneous containing cysts, calcification, occasional hemorrhage and irregular enhancement. There was no disseminated case at diagnosis. PF Ependymomas were infiltrating the brainstem in 13% of cases and projected to the cerebellopontine angle and upper spinal canal in 35% of cases. Eighty-four percent of children with PF ependymomas received a complete surgical resection. Histopathological variants were: cellular, clear cells, papillary and anaplastic. Following surgery, all but 4 patients received additional therapy: radiotherapy in 50% and chemotherapy in 68% of cases.5 years PFS was 41% (median PFS, 1.25 years; range, 0.25-8.75 years). PFS for children with supratentorial tumors was slightly better than that for children with PF tumors. There was a correlation between anaplastic histology and a higher rate of disease recurrence (85 vs 46%). Recurrence occurred on tumor bed and in 28% of cases was also metastatic. All patients who received only surgery had progression. Recurrence rate was significantly lower if radiotherapy paired with surgery (5 years PFS, 64%) independently of extent of resection. It seems there was no advantage in PFS in patients who received chemotherapy.
Conclusions: This tumor collection is an useful source for molecular studies aimed to identify genes relevant to recurrence.

EPIDEMIOLOGY

EP-155

EPIDEMIOLOGY OF CHILDHOOD CANCER IN WESTERN AFRICAN REGION: ASSESSING GENDER DIFFERENCES

O. Adetokunboh[1]

[1]Division of Community Health, Stellenbosch University, Cape Town, South Africa

Objectives: It is widely believed that male are more susceptible to develop cancer than their female counterparts except some types or sites of cancers. The same also applies to the childhood cancers where there is little difference between male and female globally. Knowing the gender susceptibility can give important clues to the aetiology of cancers. The study seeks to assess if there is any gender difference among children with cancers in Western African region.
Methods: Secondary data analyses were conducted using the Globocan 2012 datasets. The incidences of all childhood cancers excluding non-melanoma skin cancers were analysed. Fifteen countries of the Western African region were examined. Paired data analysis was conducted to determine the differences among male and female cancer patients. The analysis was carried out using Stata / IC 12.1.
Results: The region recorded 18455 new cases in 2012, which is 22% of Africa burden (7837/36428). Males had mean of 692 (305 – 1079 95%CI) and females mean of 538 (229 – 848 95% CI); P = 0.0000.
Nigeria had the highest number among both male and female with 1882 and 1631 respectively. Cape Verde had the lowest number of cases.
Conclusions: Western African region had significant gender difference in new cases of childhood cancers. Male are much more than the female unlike what was initially believed or as it is in other regions.

EP-156

ANALYSIS OF TOTALLY IMPLANTABLE VENOUS ACCESS PORTS IN PAEDIATRIC ONCOLOGY.

A. Favre[1], G. Santana[2], E. Machado[3], A. De Mattos Guaraldi[4], C. Martins[5], A. Moura Junior[1], S. Superti[6], F. Ferreira[7], F. Albanez Souza[1], R. Carvalho[1]

[1]Pediatric Surgery, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [2]Pediatric Oncology Nurse, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [3]Coagulation Committee, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [4]Corynebacterium and Diphtherium Laboratory, Universidade Estado do Rio de Janeiro - PGCM, Rio de Janeiro, Brazil; [5]Infection Control Committee, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [6]Laboratory of Microbiology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [7]Nurse Research, Instituto Nacional de Câncer, Rio de Janeiro, Brazil

Objectives: Venous access is a challenge in pediatric oncology. In order to overcome this barrier, venous tunneled catheters were created, which is widely used in pediatric and adult patients undergoing chemotherapy. The objective of this study was to evaluate the complications of the totally implantable venous access ports (TIVAP) in pediatric oncology patients.
Methods: We have retrospectively analyzed 71 patients under 16 years old, treated with chemotherapy between January 2009 to December 2010, submitted to TIVAP insertion. We followed a Catheter Protocol, in which contemplated an operation room insertion, manipulation care and control in a specific catheter ambulatory by expert surgeons and nurses. The cases of infection were supervised by the Hospital Infection Control Committee. The patients with suspicion of thrombosis were submitted to a Doppler scan, and in the confirmed cases, the catheter was removed and initiated a thrombolytic therapy.
Results: In 259 pediatric patients with catheter 71 patients had TIVAP. There is no statistically gender difference (35males:36females). Of these, 70 were followed in the catheter ambulatory. Most of them were non-hematological tumors 61 (87.1%), only 9 (12.9%) hematological patients. In 50 patients (71.43%) there were no complications, and the catheter are still in use; 7 (10%) were removed after completed chemotherapy protocol. The complications that caused catheter removal were infection in 6 (8.57%) (bacterial infection in 5 and fungal infection in 1); thrombosis in 2 (2.86%); thrombosis and infection in 1 (1.43%). Four patients (5.71%) died during the treatment with no catheter related complications.
Conclusions: The use of long term catheter, in pediatric oncology, is safe and provide a good adhesion to the treatment. Our results showed a infection rate compared with the literature. It is important o follow up the patients with TIVAP by a specialized team and a catheter ambulatory.

EP-157

DELAY IN DIAGNOSIS OF CHILDREN TO A THIRD CARE CENTER SPECIALIZED IN PEDIATRIC ONCOLOGY IN MEXICO CITY, A LOW INCOME COUNTRY

F. Arreguin[1], Y. Paredes[1], M. Zapata[2], B. Almazan[3], S. Paez[3], J. Figueroa[4]

[1]Pediatric Oncology, Centro Medico Nacional "20 de Noviembre " ISSSTE, Mexico City, Mexico; [2]Pediatric Oncology, Instituto Nacional de Pediatria, Mexico City, Mexico; [3]Pediatric Oncology, Centro Medico Nacional 20 de Noviembre ISSSTE, Mexico City, Mexico; [4]Pediatric Oncology, Mexican Institute of Social Security, Mexico City, Mexico

Objectives: In developing countries there is a delay in the referral of patients to specialized medical centers in pediatric cancer treatment thus worsening the prognosis. Aim: To describe the time between the beginning of symptoms and signs of illness and the final definitive diagnosis of cancer.
Methods: Medical records of 456 pediatric patients with cancer treated in the last ten years at the Department of Oncology of Centro Medico Nacional 20 de Noviembre ISSSTE in Mexico city were reviewed.
Results: Diagnosis distribution was similar to the one reported in the literature. 26.5% consulted a medical doctor within the first five days of the first symptom. The average referral from the first doctor to the cancer unit was 105 days, while the delay in the cancer unit to the final diagnosistook 9 more days. The average number of doctors that the patients consulted before the pediatric oncologist was 4.
Conclusions: There is an important delay in the referral of sick children to a cancer center. We must consider a better education of medical and administrative people in order to improve survival.

EP-158

THE INCIDENCE AND SURVIVAL AMONG ADOLESCENTS WITH CARCINOMA IN ISRAEL DURING THE YEARS 1998 TO 2009

L. Berkun[1], R. Rabinovicz[2], M. Barchana[3], I. Liphshiz[4], S. Linn[3], B. Futerman[5], M. Ben Arush[1]

[1]Pediatric Hematology Oncology, Rambam Health Care Campus, Haifa, Israel; [2]Pediatric Department, Shneider children's hospital, Tel Aviv, Israel; [3]Epidemiology, University of Haifa, Haifa, Israel; [4]Epidemiology, Ministry of Health, Jerusalem, Israel; [5]Epidemiology, Rambam Health Care Campus, Haifa, Israel

Objectives: Our goal was to describe adolescent carcinoma incidence and survival in Israel, and to identify demographic and epidemiologic variations among adolescents with carcinoma.
Methods: We used data from the Israel National Cancer Registry in order to examine the incidence and survival of adolescent cancer in Israeli adolescents aged 15-19 years, diagnosed during the years 1998-2009. Cases were analyzed according to sex, ethnicity and compared to the population of children diagnosed before the age of 15 years old. We estimated the survival probability updated to December 2009, and calculated the 5-year survival for new cases until the end of 2004.
Results: Among the 1532 new cases of cancer children between the ages of 15 to 19 years old, 143 adolescents with carcinoma were diagnosed, median age was 17.83 for the Jewish children and 17.32 for the Arab children. Incidence rate was 24.95 per million, 24.6 for the Jewish children and 25.9 for the Arab children. The incidence of children diagnosed before the age of 15 was 5.72 per million. Carcinoma was located to the thyroid gland in 78 cases, testis in 15 cases, nasopharynx in 14 cases, bladder in 9 cases, parotid gland in 8 cases, colon in 6 cases, ovary in 5 cases, unknown primary site in 8 cases. The overall survival at 5 years for the Jewish children was 90.7%, 76.9% for the Arabic population ($P < 0.001$). In comparison with the SEER data the incidence of adolescents with carcinoma was higher in Israel.
Conclusions: This study may add more information for further investigation of the genetic and environmental factors that cause adolescent cancer in Israel. As well as delineate the genetic basis for ethnic origin disparities in survival.

EP-159

PSYCHOLOGICAL FACTORS MEDIATE THE RELATION BETWEEN PHYSICAL FITNESS AND QUALITY OF LIFE IN CHILDREN WITH CANCER

K. Braam[1], E.M. Van Dijk-Lokkart[2], L.M. Buffart[3], E. Van Dulmen- den Broeder[1], T. Takken[4], J. Huisman[5], J.H.M. Merks[6], M.M. Van den Heuvel- Eibrink[7], G.J.L. Kaspers[8], M.A. Veening[8]

[1]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands; [2]Medical Psychology, VU University Medical Center, Amsterdam, Netherlands; [3]Epidemiologyand biostatistics, VU University Medical Center and EMGO Institute for Health and Care Research, Amsterdam, Netherlands; [4]Child Development and Exercise Center, Wilhelmina Children's Hospital UMC Utrecht, Utrecht, Netherlands; [5]Medical Psychology, Wilhelmina Children's Hospital UMC Utrecht, Utrecht, Netherlands; [6]Pediatric Oncology, Emma Children's Hospital Academic medical Center, Amsterdam, Netherlands; [7]Pediatric Oncology/Hematology, Erasmus MC Sophia Children's Hospital, Rotterdam, Netherlands; [8]Pediatric Oncology/Hematology, VU University Medical Center, Amsterdam, Netherlands

Objectives: Children with cancer have a decreased physical fitness and QOL. This study aimed to investigate the relation between physical fitness and QOL, and whether this was mediated by psychological factors.
Methods: These cross-sectional analyses are based on the baseline QLIM (Quality of Life in Motion) study data; a randomized controlled trial evaluating the effects of physical exercise and psychosocial intervention on physical function and fitness among children aged 8-18 years old, during, or no longer than one year post cancer treatment. Data of 68 children (54% males) aged 12.8 (SD 3.1) years were analysed, of whom 68% were treated for a haematological malignancy. Cardiorespiratory fitness (CRF) was assessed by a maximum cardiopulmonary exercise test. Psychological functioning was assessed by questionnaires (PedsQoL for QOL physical functioning and fatigue; Child Depression Inventory for depressive symptoms and Youth Self Report for behavior problems). Series of linear regression analyses were conducted to examine the association between CRF and QOL, CRF and the mediator variable, and the mediator variable and QOL, controlling for age and sex. The mediation effect was examined using the product of coefficients method, and bootstrapping to calculate 95% confidence intervals.
Results: CRF was positively associated with QOL ($b = 1.33$ 95% CI: 0.88 – 1.77). The association was mediated by fatigue (mediation effect (M): 0.36; 95% CI: 0.11 – 0.79), depressive symptoms (M: 0.22; 95%CI: 0.01 – 0.56) and internalizing behavior problems (M: 0.47; 95% CI: 0.07 – 1.28). The mediation effects accounted for 27%, 26%, and 38%, respectively.
Conclusions: CRF scores are significantly associated with QOL and this association is mediated by fatigue, depression and internalizing behaviour problems. In order to increase QOL in childhood cancer patients, interventions should focus on improving CRF, since this may reduce fatigue, and distress, and improve the QOL. Future longitudinal studies should confirm this finding.

EP-160

BEYOND BURKITT LYMPHOMA: A WIDE SPECTRUM OF PEDIATRIC MALIGNANCIES ARE CURABLE DESPITE RESOURCE LIMITATIONS IN A PUBLIC TERTIARY HOSPITAL IN LILONGWE, MALAWI

N. El-Mallawany[1], I. Mtete[2], M. Mutai[2], R. Mlotha[2], H. Joerg-Lang[2], G. Liomba[3], R. Krysiak[4], G. Fedoriw[5], S. Gopal[4], M. Kim[6], P. Mehta[7], P. Kazembe[6]

[1]Pediatrics, New York Medical College, Valhalla, USA; [2]Paediatrics, Kamuzu Central Hospital, Lilongwe, Malawi; [3]Pathology, Kamuzu Central Hospital, Lilongwe, Malawi; [4]Medicine, University of North Carolina Project-Malawi, Lilongwe, Malawi; [5]Pathology, University of North Carolina, Chapel Hill, USA; [6]Pediatrics, Baylor College of Medicine Children's Foundation-Malawi, Lilongwe, Malawi; [7]Pediatrics, Baylor College of Medicine, Houston, USA

Objectives: While Burkitt lymphoma (BL) is the most common pediatric malignancy in sub-Saharan Africa, we herein describe our experience treating a variety of childhood cancers in Lilongwe, Malawi.
Methods: We retrospectively analyzed records of pediatric oncology patients between 12/2011 – 6/2013. Diagnosis was usually clinical, however fine needle aspiration +/- biopsy was performed routinely starting in 1/2013. Patients received transport reimbursement plus extensive follow-up counseling.
Results: There were 254 children diagnosed with cancer: 142 males, 112 females. Diagnoses included: 45% lymphoma, 21% Kaposi sarcoma (KS), 18% solid tumors of the abdomen (majority Wilm's tumor), 8% sarcomas, 4% leukemias, and 5% other. There were 21 Hodgkin (17 biopsy-confirmed) and 94 non-Hodgkin lymphomas (NHL). In NHL, 39 had jaw involvement—23 jaw +/- nodes, 7 jaw and abdominal masses, 9 jaw and CNS+ (cranial nerve palsies and/or spinal cord compression). These 39 were probable BL diagnoses; there were also 32 possible BL and 23 other NHL (lymphoblastic lymphoma or diffuse large B-cell lymphoma) based upon pathology and/or clinical characteristics. Seven NHL patients had primary mediastinal mass (probable lymphoblastic lymphoma). Altogether, 97 children presented with an abdominal mass—52 had lymphoma. Pediatric NHL Murphy staging revealed: 27 stage I/II, 49 stage III, and 18 stage IV (CNS+ or presumed bone marrow involvement). 47 patients were HIV+: 43 KS/4 NHL. There were 10 endemic (HIV-negative) KS patients. Overall, 48% completed their treatment regimen and 15% were lost to follow-up. 78 children (31%) achieved 12-month overall survival. Three patients with CNS+ BL achieved 12-month complete remission with dose-modified CHOP chemotherapy plus intrathecals.
Conclusions: BL accounted for 28% of childhood cancers; lymphoma altogether accounted for 45%. The majority of lymphomas (>70%) presented stage III/IV, with abdominal mass as the most common primary site. Prompt diagnosis with careful, but intensive chemotherapy, can result in curative outcomes despite significant resource limitations.

EP-161

EPIDEMIOLOGY AND SURVIVAL ANALYSIS OF EGYPTIAN CHILDREN WITH SOLID TUMORS (SINGLE CENTER EXPERIENCE)

N. Elsherif[1], M. Altawil[1], I. El Desouki[2], A. Ahmed Mohamed Refaat[3]

[1]Pediatric, Ain Sham University, Cairo, Egypt; [2]Epidemiology And Biostatistics, National Cancer Institute, Cairo, Egypt; [3]Pediatrics, Ain Shams University, Cairo, Egypt

Objectives: The total incidence of solid tumors among children is 65.3/million. The overall survival for solid tumors at 5, 10 and 20 years follow-up reaches 80, 79 and 76%, respectively as result of continuing improvement and increasing efficacy of treatment. This study evaluates the clinico-epidemiological aspects and survival analysis of solid tumors among children treated in a single pediatric oncology center over the last 10 years.
Methods: This is a retrospective data analysis of all children with solid tumors who were diagnosed during the period from January 2003 to January 2013 in the Pediatric Oncology Unit, Children's Hospital, Ain Shams University, Cairo, Egypt.
Results: There were 123 patients diagnosed with solid tumors (15% of total patients diagnosed with cancer during same period). They included 56 (45.5%) males and 67 (54.4%) females. The frequency distribution of newly diagnosed patients with solid tumor were heterogenous over period of 10 years being highest in year 2011 and lowest in year 2010. Throughout the 10 years period, excluding CNS tumors, Neuroblastoma was the most common (34.9%), Wilm 's tumor (22.7%) came next in frequency, then retinoblastoma (13.8%), followed by Germ cell tumor (8.9%), hepatoblastoma (6.5%), Osteosarcoma (4%), Ewing sarcoma (3.2%), and Rhabdomyosarcoma (4%). The 1, 5, 7-years overall survival (OS) of patients with solid tumor was 90.3%, 59.7, 55.4%. Male patients, patients without family history of malignancy, those who were operated upon had significantly higher 1, 5, 7 years OS. The 3 years OS of patients with retinoblastoma was the highest (87%), while those with osteosarcoma had the lowest OS (53.3%).
Conclusions: In our center, the incidence of pediatric solid tumors is rising, and the frequency of the different types varies from year to year; in the past 10 years, the OS rates were improving as a result of implementation of internationally approved optimal treatment regimen based on risk factors and molecular markers.

EP-162

FACTORS INFLUENCING PARENTAL CONSENT FOR PARTICIPATION IN CLINICAL RESEARCH INVOLVING THEIR CHILDREN IN EGYPT

A. Fouda[1], N. Nasef[1]

[1]Pediatrics, Mansoura University Children Hospital, Mansoura, Egypt

Objectives: Factors affecting parents' decision to involve their children in clinical research have not been studied
in all cultural backgrounds. We aimed to explore the attitudes and beliefs influencing parents' decision to involve their children in clinical research in Mansoura, Egypt.
Methods: Study design and sample Parents or legally authorized representatives
of children admitted to the inpatient departments of Mansoura University Children's Hospital, Mansoura, Egypt, between January 2009 and December 2011 were eligible for the study. Parents or guardians were approached within 48 hours of the child's admission and were asked to complete a questionnaire exploring factors that would influence their decision to involve their child in clinical research.
Results: Of 523 families approached, 357 flled the questionnaire. Only 98 (27.5%) parents consented to involve their child in clinical research. The children of consenters were significantly older than refusers: 8.6 (SD 7.2) versus 2.6 (SD 1.2) years. Factors favouring consent were: research of bene?t to child (84.7%), enough explanation about the benefits (40.8%) and to learn more about child's condition (29.6%). Factors favouring refusal were: use of new drugs or vaccines (89.6%) and invasive procedures (84.2%). Parents' rate of consent was positively correlated with the research being non-invasive and the belief that research was of benefit to their child and negatively correlated with belief that refusal may negatively affect the care provided to their child.
Conclusions: In this hospital in Egypt, minimally invasive research of clear benefit to the child and with a clear explanation of the research process by staff were the most important motives for parental consent to involve their children in clinical research.

EP-163

PEDIATRIC OSTEOSARCOMA IN NIAMEY: FIRST RESULTS FROM THE NIGER CANCER REGISTRY

S. Mamoudou Garba[1], H. Hami[1], H. Mahamadou Zaki[2], A. Soulaymani[1], H. Nouhou[2], A. Quyou[1]

[1]Laboratory of Genetics and Biometry, Faculty of Science Ibn Tofaïl University, Kenitra, Morocco; [2]Laboratory of Pathological Anatomy and Cytology, Faculty of Health Sciences Abdou Moumouni University, Niamey, Niger

Objectives: Worldwide, an estimated 160 000 children are diagnosed with cancer each year, with an incidence of about 14.9 cases per 100 000 children less than 20 years of age. More than 80% of children with cancer live in developing countries where access to information, early detection and effective treatment and care is often poor. This study aims to investigate the epidemiological characteristics of osteosarcoma in pediatric patients during the past 18 years in Niamey.
Methods: This is a descriptive retrospective study of pediatric osteosarcoma cases, reported between 1992 and 2009 to the Niger Cancer Registry, established in 1992, in the Faculty of Health Sciences at the Abdou Moumouni University in Niamey.
Results: During the study period, 15 children under the age of 15 years were diagnosed with osteosarcoma in Niamey, accounting for 4.5% of all pediatric malignancies collected during this period. Nearly three-quarters of the cases (73.3%) were males with a male-female ratio of 2.75. The average age of diagnosis was 11.7 ± 2.5 years (range 5-14 years). Nearly 87% of these cases were diagnosed in children aged 10-14 years. The most common sites of osteosarcoma at initial diagnosis were the long bones of the lower limbs. The most prevalent ethnic group was the Djerma-Sonrai.
Conclusions: The most recent estimates of childhood cancer incidence and mortality in the world reveal sharp differences between developed and developingcountries possibly related to missed opportunities for early diagnosis and incomplete reporting of childhood cancer in Africa.

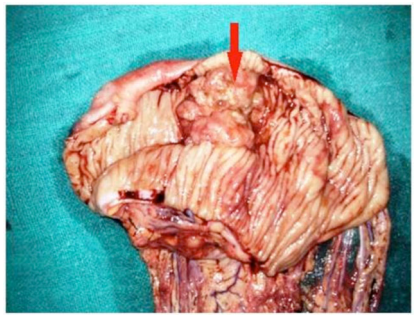
EP-165

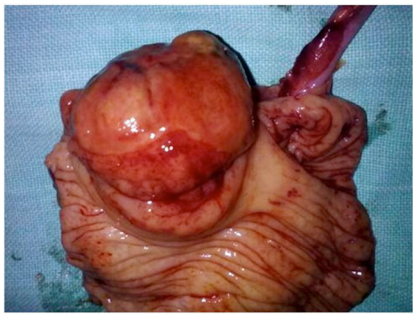
COLORECTAL CARCINOMA IN PEDIATRIC AGE GROUP- EPIDEMIOLOGICAL PARADIGM

D. Jain[1], R. Mathur[2], B. Lahoti[2], S. Sharma[2]

[1]Department of Surgical Oncology Division of Pediatric Oncology, Tata Memorial Centre, Mumbai, India; [2]Department of Surgery Division of Pedaitric Surgery, M.G.M. Medical College M.Y. Hospital & Govt. Cancer Hospital, Indore, India

Objectives: Colorectal cancer is a rare disease in pediatric age group with an annual incidence of 1.3 cases per million children. Spectrum of colorectal cancer includes the pediatric population also, which usually presents at advanced stage, unfavorable histology and ultimately poor prognosis. Difficult differential diagnosis, delay in presentation and aggressive biological behavior leads to poor outcome.
Methods: Retrospective analysis of all pediatric colorectal cancer patients presented to Division of Pediatric Surgery between June 2006 to June 2012 were included in the study. A specifically designed audit form was devised to capture all relevant information regarding clinical presentation, pathologic factors, treatment outcome, prognostic factors and follow up.
Results:





During the study period of 6 years from June 2006 to June 2012 only 7 cases of pediatric colorectal cancer were reported. Median age was 11.8 years [range, 5-16years]. Five patients presented with features of intestinal obstruction and diagnosed during emergency laparotomy. The most common site of involvement was rectum (59%) & transverse colon being the next most common site (26%). Adenocarcinoma was histological type in all patients. 3 patients died within 2 years of follow-up. Rest 4 patients are receiving treatment and under follow-up.
Conclusions: Colorectal cancer is a rare disease in pediatric age group. Diagnostic dilemma, difficult differential diagnosis, delayed presentation & treatment, advanced stage and poor histological features contributes to the poor prognosis of the disease in pediatric age group as compared to adults. As in adult colorectal cancer; early detection, stage stratification, multidisciplinary treatment plan and participation in prospective clinical trials will help in improving the prognosis and outcome in pediatric patients.

EP-166

DEMOGRAPHIC, CLINICAL AND SURVIVAL FEATURES OF CHILDHOOD CANCERS IN ISTANBUL UNIVERSITY, ONCOLOGY INSTITUTE (1990-2012)

R. Kebudi[1], D. Uludag[2], I.U. for the[3]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [3]Pediatric Hematology - Oncology and Radiation Oncology Divisions, Istanbul University Oncology Institute, Istanbul, Turkey

Objectives: The aim of this study is to identify demographic, clinical and survival features of childhood cancers admitted to Istanbul University, Oncology Institute, Pediatric Hematology-Oncology in 22 years.
Methods: Charts of patients <19 years admitted (1990-2012) were evaluated retrospectively for age, gender, birth date, date of diagnosis, place of birth/residence, family history, concominant diseases, primary diagnosis, primary site, stage, presenting symptom and duration, date of the last examination/death. (Istanbul University Cerrahpasa Medical Faculty Clinical Trials, Ethics Committee no. 83045809-3507)
Results: There were 2,413 children with cancer enrolled. Median age was 7 years (3 days-19 yrs). Male:female 1,26. Distrubution in age groups were 0-1 years 7.9%; 1-4 years 31.9%; 5-9 years 24.9%; 10-14 years 26.1%;15-19 years 9.2%. Five year survival of all patients 74.4%. Distrubution in disease groups were [5 year survival]: Central nervous system (CNS) tumors (n = 494) 20.5% [61.0%]; Malign bone tumors (n = 367) 15.2% [60.9%]; Lymphoma (n = 360) 14.9% [90.7%]; Soft tissue sarcomas (n = 317) 13.1% [68.9%]; Retinoblastoma (n = 207) 8.6% [94.3%]; Neuroblastoma (n = 164) 6.8% [64.6%]; Leukemias (n = 133) 5.5% [82.0%]; Germ cell tumors (n = 130) 5.4% [89.8%]; Carcinomas (n = 129) 5.3% [83.8%]; Renal tumors (n = 88) 3.6% [81.9%]; Hepatic tumors (n = 24) 1.0% [44.7%]. After 2005, number of patients diagnosed at early stage has increased ($p = 0.001$). In the whole group, the 5 year survival rate was 85.2% in patients diagnosed at an early stage, while the 5 year survival rate in patients with advanced stage disease was 57.0% ($p < 0.001$)
Conclusions: The most common solid tumor, similar to developed countries, was CNS tumors. The frequency of retinoblastoma and bone tumors were high (reference center). Survival in patients diagnosed at early stage were significantly higher than those with advanced stage, which is promising for the future. Cancer registry in our country has developed in recent years, registries in major centes help to obtain more detailed data on the epidemiology and clinical characterictics of cancer patients which may help organizing health care programs.

EP-167

THE CURRENT STATUS OF FOLLOW-UP SERVICES FOR CHILDHOOD CANCER SURVIVORS IN TURKISH PEDIATRIC ONCOLOGY CENTERS

K. Mutafoglu[1], D. Ince[1], T. Kutluk[2]

[1]Dept. of Pediatric Oncology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [2]Dept. of Pediatric Oncology, Hacettepe University Cancer Institute, Ankara, Turkey

Objectives: We aimed to describe survivorship services provided by the Turkish Pediatric Oncology Centers including the extent of services provided, resources and barriers to service development.
Methods: All 31 institutions in Turkey which have a pediatric oncology program were invited to participate this survey in order to define the pediatric cancer survivor services. Participation rate was 100%.
Results: The number of new cancer cases were 50-100 in 52%, and >100 at%13 of the centers. Seventy-one percent of centers were treating leukemias and solid tumors, others were treating all cancers except for leukemias. Majority (90%) of the institutions reported providing survivorship care. However, survivor follow up services were given within the routine pediatric oncology outpatient clinic practice by the attending pediatric oncology doctors at 96.4% of the centers. Only one centre reported a survivor clinic with a multidisciplinary team. Pediatric oncology clinics were staffed by: pediatric oncologist (31/31), pediatrician (3/31), oncology fellow (16/31), nurse (6/31), oncology nurse (15/31), social worker (1/31), psychologist (7/31); dietitian (6/31). Nine institutions keep survivors until the age of 18 at the treating institution, 7 centers until they feel ready for transition, and 5 keep them indefinitely. Nine centers reported having a standard follow up guideline, 5 centers reported having a standard clinical assessment form. A copy of care plans were given to survivors in only 5 centers. When a sub-specialists evaluation was needed, this service was provided through consultations at 28 centers (at the same day in 13, with an appointment at another day in 15). The most prevalent barriers were insufficient qualified staff (83%), the lack of dedicated time for program development (72%), lack of physical space (70%), and lack of funding (63%).
Conclusions: Survivorship services needs to be improved in Turkey. Governmental attempts are required to overcome the defined barriers to developing survivorship programs by the institutions.

EP-168

ENVIRONMENTAL HEALTH INDICATORS AND INCIDENCE OF CHILDHOOD CANCER IN PERNAMBUCO, NORTHEASTERN OF BRAZIL: THE ROLE OF URBANIZATION

L.N.V. Bastos[1], J.C. Silveira Jr[1], C.F. Luna[1], N. Lucena-Silva[2]

[1]Saúde Pública, Centro de Pesquisas Aggeu Magalhães-FIOCRUZ, Recife, Brazil; [2]Imunologia, Centro de Pesquisas Aggeu Magalhães-FIOCRUZ, Recife, Brazil

Objectives: To evaluate the impact of environmental health indicators on the incidence of childhood cancer in Pernambuco state, Northeastern of Brazil.
Methods: Based on the autorization reports for chemotherapy and radiotherapy authorization for 2009 until 2012 provided by the State Health Secretary of Pernambuco, new cases of childhood cancer (aged under 20 years) were analyzed in terms of gender, age, diagnosis and municipality of origin. Population for 2009 to 2012 was estimated by the whole period based on the official population counting. Health environmental indicators of Driving Force (Gini Index, Population growth rate, Urbanization rate, Human Development Index); Pressure (Number of vehicles, agricultural establishments, extractive and manufacturing industries per capita), and Situational (Basic Health Unit per capita) were provided by official sources. Empirical Bayesian estimator, Moran's global and local index were estimated and multiple regression was used to evaluate association of health indicators and cancer incidence.
Results: We analyzed 1261 new cases of cancer from 19 years and 11 months diagnosed in Pernambuco from 2009 to 2012. The average crude incidence rate was 113 cases per million people, with an increasing rate of 0.44%. The ratio male:female was 1.20, except in children under 1 year. Leukemia/lymphoma predominated with 45.28% of cases, central nervous system tumors corresponded to 16.6%, and the remaining solid tumors accounted for 38.12% of cases. The mean average incidence rate of municipalities grouped in the upper quartile by Bayesian method was 126.11 cases/million, while for counties in the bottom quartile was 65.31 cases/million ($P < 0.000$). Moran's local index identified 14 municipalities with spatial autocorrelation. Bivariate analysis identified positive correlation between cancer and urbanization ($P = 0.018$), confirmed by multiple regression model ($P = 0.010$).
Conclusions: The adjusted average incidence rates of cancer showed grouping of municipalities with high rates in the eastern of state. Habit change due to urbanization might increase exposure to cancer promoting agents; the casual relation, though, is more complex.

EP-169

EFFECTS OF E-WASTE EXPOSURE ON THE SYNTHESIS OF HEMOGLOBIN IN PRESCHOOL CHILDREN

L. Ma[1]

[1]Pediatrics, The Second Affiliated Hospital of Shantou University Medical College, Shantou, China

Objectives: Guiyu is the major electronic-waste (e-waste) recycling town in China. The primary purpose of this study was to measure the effect of e-waste exposure on the synthesis of hemoglobin (Hb) in preschool children.
Methods: Two hundred and twenty-two children (aged from 3 to 7, exposure group) lived at Guiyu town and 204 children (aged from 3 to 7, control group) lived in a no e-waste polluted

town were chosen to test their blood lead, Hb, ferritin, folate, vitamin B_{12} levels and hemoglobinopathy, then fill the self-questionnaires by their parents.
Results: In order to better access the effect of environmental toxicants on the synthesis of hemoglobin, there were no significant differences in the levels of ferritin, folate, vitamin B_{12} between exposure and control groups, and all children had been excluded thalassemia. The blood lead levels (BLLs) and rate of BLLs $\geq$10ug/dL in exposure group were signifcantly higher than that in control group (all $P < 0.01$). Three groups were divided according to BLLs (Group A: <5.0ug/dL, Group B: 5.0-9.9ug/dL, Group C: $\geq$10.0ug/dL). It can be seen that the levels of Hb were decreased along with elevated BLLs significantly in exposure group ($F = 3.52$, $P = 0.03$), however, not shown in control group ($F = 1.98$, $P = 0.14$). Furthermore, the prevalence rate of anemia along with BLLs $\geq$10ug/dL in exposure group was significant higher than that in control group (4.0% versus 0.5%, $P < 0.05$), and the prevalence rate of anemia without BLLs $\geq$10ug/dL and iron deficiency in exposure group was significant higher than that in control group (6.5% versus 2.0%, $P < 0.05$).
Conclusions: Different from the general environment, the lead exposure in e-waste area might aggravate the inhibition of synthesis of Hb, and other potential e-waste toxicants might also have a responsibility for it.

EP-170

COMPARISON OF RETINOBLASTOMA INCIDENCE AMONG CHILDREN IN THE REPUBLICS OF KYRGYZSTAN AND KAZAKHSTAN

E. Makimbetov[1], G. Abdualieva[2]

[1]Surgery, Kyrgyz-Russian Slavonic University, Bishkek, Kyrgyz Republic; [2]Epidemiology, Kazakh Institute of oncology radiology, Almaty, Kazakhstan

Objectives: To study descriptive epidemiology of retinoblastoma among children in the Central Asian republics of Kyrgyzstan andKazakhstan.
Methods: This study covers the period 1997-2006. The data on all registered cases of retinoblastoma were provided by specialized and non-specialized hospitals in both countries. We calculated retinoblastoma incidence rates by age group (0-4, 5-9, 10-14), geographic regions, gender, and ethnicity. We report crude, and age-standardized rates (ASRs), calculated using the world reference population.
Results: On average, annual all types of childhood cancer incidence was 71.8 per one million in Kyrgyzstan and 73.8 in Kazakhstan. During the study period, a total of 106 children under 15 with malignant tumors of the eye were registered in Kazakhstan. This corresponds to 3.6% of registered childhood malignancies in this country. A total of 74 new cases (6.1% of all pediatric malignant tumors) were registered in Kyrgyzstan. Among all childhood cancers, retinoblastoma was the eighth most common malignancy. The average annual crude incidence rates were 2.6 per one million in Kazakhstan (male: 2.8; female: 2.4) and 3.9 (male: 4.1; female: 3.6) in Kyrgyzstan. Incidence rates ranged from 1.8 in 1998 to 4.1 in 1999 and 2005 (Kazakhstan). ASR was higher (8.3) in Kyrgyzstan than in Kazakhstan (7.6) for the age group 0-4years. High incidence rate of retinoblastoma (5.6) was found among those of Uzbek ethnicity compared with other ethnic groups (Kyrgyz: 4.8; Russian: 2.7) in Kyrgyzstan. Incidence rate was slightly higher among those from rural regions then urban regions (RR = 0.9, 95% CI 2.7-7.4). No significant difference in retinoblastoma incidence was found for ethnicities in Kazakhstan.
Conclusions: The incidence rates of retinoblastoma in these Central Asian countries are relatively low and comparable to levels of disease in some countries of Asia, Africa, and South America. Our findings support the idea that there is need for population based childhood eye cancer surveillance and etiologic research.

EP-171

A STUDY ON CANCER INCIDENCE FROM SEVEN MAJOR HOSPITALS IN NEPAL (2003 -2010)

K. Pradhananga[1]

[1]Cancer Prevention Control & Research, B P Koirala Memorial Cancer Hospital, Bharatpur, Nepal

Objectives: This study gives overview to reliable information of the cancer incidence in Nepal for 8 years period from 2003-2010. It helps to make some prevention, control plan and policies to the clinicians, policies makers to give priorities for the cancer prevention and control activities.
Methods: This was descriptive type of study and all cases were collected from medical record section of seven collaborative hospitals for data analysis. A breakdown of the incidence by year, age and gender has been analysed. Age standard incidence of common cancers and age specific rate has been tabulated.
Results: The total 41,713 cases were included in this study to know the burden of cancer patients in 7 major hospitals of Nepal where cancer diagnosed and treated from 2003-2010. In this study Female (53.3%) cases were diagnosed more than males (46.7%). Overall, the most common cancer sites in Males were lung, stomach and leukemia but in Females Cancer of cervix uterus, breast and lung. More cancer cases (67.7%) seen in Female but in Males found 52.5% in the broad age group 35 to 64 years. In young age leukemia and lymphoma were more common replaced by lung, oral and stomach cancer in middle age but in old age lung, stomach cancer were found in males but in females breast cancer in young, cervix uterus cancer in middle and followed by lung cancer in older age.
Conclusions: This type of study is the first time in Nepal to know the burden across a greater proportion of cancer from 7 major hospitals, but the coverage may not represent the whole country. More than 50% cancer patients were diagnosed in BPKM cancer hospital. Population based cancer registry is not yet established so, it is difficult to reflect the burden of cancer.

EP-172

IMPACT, AND MORTALITY TRENDS IN CHILDHOOD CANCER IN MIDWEST OF BRAZIL 1996 TO 2011, COMPARED WITH SEER DATA (U.S.A.)

F. Ramos Rezende[1], M.P. Curado[2]

[1]Health Sciences, Federal University of Goiás, Goiânia, Brazil; [2]Health Sciences, Federal University of Goiás/International Prevention Research Institute, Goiânia, Brazil

Objectives: There is a global trend of increased incidence and decreased mortality of pediatric tumors. The aim of this study is to analyze the incidence rates and trend in mortality of childhood cancer in Midwest of Brazil and compare the trends with USA (SEER).
Methods: Incidence data were obtained from the Cancer Registry Population-Based Goiânia, Cuiaba, Brasilia and Campo Grande. Mortality data were obtained from the Mortality Information System (DATASUS/MS). Standardized rates were calculated according to the 2000 U.S. Std Population. To analyze the mortality trend was used the logistic regression model of Poisson from join point software.
Results: Adjusted incidence rates from Midwest region of Brazil for all childhood tumors were about 67.60 per 100,000 in men and 63.58 per 100,000 in women. Mortality was higher in males (22.19 per 100,000) than in females (16.26 per 100,000). There was trend in reduction of mortality from childhood cancer in both genders, but not significantly. (Male: 0-19 years: APC: -1.5 (−3.1 to 0.0, p: 0.58). The incidence rates, in U.S.A. were lower than in Brazil. Males had higher rates (18.2 per 100,000) than in females (16.1 per 100,000). The mortality rates were 2.6 per 100,000 in males to 2.2 per 100,000 in females in the period of 2006 to 2010 in USA. Incidence trends, in USA (SEER) is increasing significantly (APC: 0.6, $p < 0.5$) and the mortality is decreasing (APC: -2.7, $p < 0.5$).
Conclusions: Trends in mortality for pediatric cancer in the Midwest of Brazil (developing country) is similar to the U.S.A. There was a reduction in mortality, although incidence and mortality rates in Brazil were higher. To analyse incidence trends in Midwest was not possible due to lack a long time series.

EP-173

EPIDEMIOLOGY OF PEDIATRIC MALIGNANCIES IN INDIA

P. Rent[1], S. Qureshi[2], E. Rent[2], A. Puri[2], A. Gulia[2], M. Bhagat[2], A. Moiyadi[2], G. Chinnaswamy[3], B. Arora[3], S. Banavali[3]

[1]Public Health, Tata Institute of Social Science, Mumbai, India; [2]Surgical Oncology, Tata Memorial Hospital, Mumbai, India; [3]Medical Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Not much is known regarding the epidemiology of childhood cancers in third world countries. There may be significant differences in the incidence of different malignancies in developing countries due to the different genetic and environmental factors. Data regarding disease pattern is the building block for forming public health strategies in any country. This study attempts to study the epidemiology of childhood malignancies in a third world country
Methods: A retrospective analysis was undertaken using data from a Tertiary Cancer centre in India collected from 1st Jan to 31st Dec 2012. 1445 cases of patients in the age group 0 – 18 years were taken into consideration. The case distribution of individual malignancies was evaluated. We also analysed the age of presentation of individual malignancies.
Results: Hematological malignancies were the most common, with Leukemia forming 32% and Lymphoma 11.7% of the total cases. Among solid tumors the top five were CNS (9.3%), PNET (8.5%), Osteosarcoma (7%), Neuroblastoma (4.8%) and GCT (4.4%). If the occurrence of malignancies is analyzed across different age groups we see that, 22.7% of the Retinoblastomas were found in the 4 to 12 years age group. Similarly for Lung 20% of the cases were in the 4 to 12 age group and 80% were in the above 12 age group. In case of Colorectal, 5.9% of the cases are in the 0 to 3 age group and 23.5% of cases were in the 4 to 12 group.
Conclusions: The trend in pediatric cancer is different in India than in developed countries with higher rates of PNET and Osteosarcoma and lower rates of CNS malignancies. Public Health programmes and strategies should be framed using country specific epidemiological data, for prevention, early detection and treatment of disease.

EP-174

CANCER IN EGYPTIAN CHILDREN:EPIDIMIOLOGY AND SURVIVAL INCIDENCE

Y. Saad-eldin Sadek[1]

[1]Pediatric Surgery & Pediatric Oncology, University of Alexandria, Alexandria, Egypt

Objectives: To report and clarify the prevalence of the different types of mailgnancy among the Egyptian children as well as the incidence of survival.
Methods: A retrospective study of the incidence of different types of cancer children admitted and treated in the Pediatric Oncology and the Pediatric Surgery Departments of University of Alexandria, Egypt over a pariod of 20 years was done.
The incidence of the overall 5 yeras survival was analysed, reported and compared to that of the western countries. The possible causes of low survival were studied and analysed.
Results: A total number 0f 1277 cases of cancer children had been reported over a period of 20 years in Alexandria University Hospitals, Egypt. They were treated in the Pediatric Oncology and Pediatric Surgery Departments. The relative incidence was as follows:leukemia 34%, brain tumors 19%, lymphoma 14.5%, bone tumors 11.5%, Wilms tumor 11.5%, Neuroblastoma 8.5%, sftt tissue tumors 3%, germ cell tumors 2.5% and liver tumors 1.5%. The overall five years survival rate was 39.8%, this is much lower when compared to that of the western countries which was proved to be 60-70%.
Conclusions: Egyptian cancer children have higher incidence of lymphoma than that reported in Uk and USA series. They also have higher incidence of Wilms tumor and a lower incidence of soft tissue tumors. Cancer children in Egypt have lower incidence of survival compared to that reported in the western countries. Among the important causes of this low survival is the delayed presentation and consequently delayed diagnosis and delayed treatment as well as the lack of specialized centers of Pediatric Oncology.

EP-175

DIAGNOSTIC DELAYS IN CHILDHOOD MALIGNANCIES: A HOSPITAL BASED STUDY

V. Sondhi[1], R. Kapoor[2], P. Suresh[3],. Dharmesh[3], T. Chaterjee[4], V. Manu[5], R. Tewari[5], V. Sharma[6], V. Nair[7]

[1]Pediatrics, Armed Forces Medical College, Pune, India; [2]Hematology, Command hospital, Pune, India; [3]Medical Oncology, Command hospital, Pune, India; [4]Immunohematology, Armed Forces Medical College, Pune, India; [5]Pathology, Armed Forces Medical College, Pune, India; [6]Radiodiagnosis, Armed Forces Medical College, Pune, India; [7]Dean, Armed Forces Medical College, Pune, India

Objectives: Timely diagnosis followed by effective treatment is essential for the management of childhood malignancies. However, diagnosis of childhood tumors often gets delayed, due to non-specificity of early symptoms and rarity of disease. The objective of this study was to investigate the diagnostic process of childhood malignancies with emphasis on the time from the onset of symptoms until the start of treatment.
Methods: This retrospective study was conducted in a tertiary care referral hospital in India. During the study period of Feb 2012-Feb 2014, 57 children were diagnosed as having malignancy. The study chronicled the events from initial symptoms, final diagnosis, treatment and current status of patient and disease. Treatment delay was defined as time from first symptom to the onset of treatment.
Results: Acute lymphoblastic leukemia (ALL) was the commonest malignancy, diagnosed in 22/57 (38.6%) children followed by brain tumors (9/57, 15.8%). Rhabdomyosarcoma accounted for 4 patients, while AML, Hodgkin Lymphoma, neuroblastoma, PNET, and Wilms tumor accounted for three patients each. Non-Hodgkin lymphoma and hepatoblastoma were the diagnosis in two children each; Osteosarcoma and langerhan cell histiocytosis contributed one patient each. The median delay in treatment for the entire study group was 15 days (range = 4-154days). The median delay among children with ALL was 13 (range = 4 = 51) days as compared to 19 (range = 6-116) days among children with brain tumors ($p = 0.13$). The treatment delay >21 days (three weeks) was associated with poor event-free-survival (Hazard ratio [HR] = 8.94; 95%CI = 3.17,25.27; $p < 0.0001$). For acute leukemia HR was noted to be 9.31 (95%CI = 0.26 to 338.3, $p = 0.22$), while the same for brain tumor was determined to be 34.1 (95%CI = 2.74,424.3; $p = 0.006$).
Conclusions: The long delay between onset of symptoms and treatment initiation is associated with poor outcome. High index of suspicion, and early initiation of diagnostic tests may aid in an early diagnosis and reduce the time to onset of treatment.

EP-176

A DESCRIPTIVE STUDY ON ESTABLISHING DEDICATED PAEDIATRIC ONCOLOGY SERVICES IN LOW INCOME COUNTRIES: GHANA, SOUTH AFRICA AND UGANDA

J. van Heerden[1], B. Neethling[1], V. Paintsil[2], J. Balagadde-Kambugu[3], G. Fadhil[3]

[1]Paediatric Haematology Oncology Service, Pietermaritzburg Metropolitan Complex Hospitals, Pietermaritzburg, South Africa; [2]Paediatric Oncology Unit Child Health Directorate, Komfo Anokye Teaching Hospital, Kumasi, Ghana; [3]Paediatric Oncology Unit, Uganda Cancer Institute, Kampala, Uganda

Objectives: This descriptive study evaluated the logistical, clinical, social and educational challenges in establishing paediatric oncology services in Africa.
Methods: A retrospective chart review was conducted of 946 children over an 8, 13 and 24 month period respectively in Kumasi, Ghana; Pietermaritzburg, South Africa and Kampala, Uganda in three newly established dedicated Paediatric Haematology Oncology services. The study was conducted in demographically varied countries to determine the burden of disease, nature of histology, presentation, co-morbidities and the ability to treat children with malignancies. It evaluated infrastructure, services and resources to treat children.
Results: The Kumasi, Pietermaritzburg and Kampala units respectively serviced 5.1 million, 1.1 million and 17.2 million children in their respective catchment areas with a ratio of 550 000 - 17.2 million children per Haematology-Oncology specialist, The most prevalent diagnosis in Ghana and Uganda was Endemic Burkitt's lymphoma whilst in South Africa it was Hodgkin lymphoma and Nephroblastoma. Stage 4 disease dominated at 65%. All three services had a malnutrition rate of 75%. Ghana had a 0% HIV rate amongst oncology patients whilst in Uganda and South Africa it was 10%. Most HIV cases were haematological malignancies. Malaria was the most common co-morbid disease in the equatorial countries and complicated the treatment of neutropenic fevers. In Pietermaritzburg all children were started on established protocols whereas in Kumasi and Kampala modified protocols were used due to drug unavailability and toxicity. Paediatric services had to compete with adult services for resources.
Conclusions: The burden of disease outweighs current staff and medical resources available to deliver comprehensive services. Various co-morbid diseases prevent the initiation of standard chemotherapy protocols and cause frequent modification of treatment. The treatment goal is mainly palliative. The future training of Paediatric Oncologists should include more interpretive application of standard treatment modalities in regards to co-morbid disease and treatment limitations.

EP-177

MISSING DATA AND SURVIVAL ANALYSIS OF CENTRAL NERVOUS SYSTEM TUMOURS AMONGST CHILDREN AND ADOLESCENTS IN YORKSHIRE, UK, 1990-2009

M. van Laar[1], D. Greenwood[1], D. Stark[2], R.G. Feltbower[1]

[1]Division of Epidemiology and Biostatistics, University of Leeds, Leeds, United Kingdom; [2]St James Institute of Oncology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Objectives: Severity of cancer at diagnosis is poorly recorded in medical records, often resulting in cases with this missing prognostic factor being excluded from analyses (complete case analysis (CCA)) creating potential bias. We investigated survival trends of central nervous system (CNS) tumours using multiple imputation (MI) to impute missing values of grade and ethnicity.
Methods: Children and adolescents (<30 years) diagnosed with CNS tumours were identified from a population-based cancer register (N = 795). Missing values were imputed using logistic regression, with age, sex, diagnosis year, deprivation, relapse and treatment as predictors. We performed 40 imputations; hazard ratios (HR) of Cox regression models were pooled and compared to CCA.
Results: Missing data occurred in 30% of cases. Survival analysis after MI showed a 2-fold increased risk of death for 'other' compared to 'white' ethnicity and an increased risk of death for grade II, III and IV tumours compared to grade I. Survival improved by 4% per year over the study period. Effects of ethnicity and grade were similar in CCA, however, improvements over time were not observed. MI reduced standard errors of coefficients by 18% on average compared to CCA.

	CCA			MI		
	HR	**95%CI**	**P-value**	**HR**	**95%CI**	**P-value**
Year of Diagnosis	1.02	0.99-1.05	0.29	0.96	0.94-0.98	<0.01
Ethnicity						
White	1			1		
Asian	1.33	0.76-2.33	0.32	1.43	0.81-2.50	0.22
Other	2.04	0.94-4.40	0.07	2.22	1.07-4.60	0.03
WHO Grade						
I	1			1		
II	3.66	2.24-5.98	<0.01	3.64	2.46-5.39	<0.01
III	6.93	3.75-12.78	<0.01	6.31	3.89-10.22	<0.01
IV	13.06	7.72-22.07	<0.01	11.02	7.35-16.53	<0.01

*Model was additionally adjusted for age, gender, diagnostic subgroup and socioeconomic status.

Conclusions: MI minimised bias and enhanced precision. Survival worsened exponentially with increasing grade of tumour and was poorer for 'other' compared to 'white' ethnicity. Survival improved significantly over the study period; importantly, this effect was not observed using the standard CCA method.

EP-178

CANCER DIAGNOSIS IN ADOLESCENCE IN THE EMERGENCY ROOM AT A NATIONAL INSTITUTE OF HEALTH

R. Cárdenas-Cardós[1], M. Zapata-Tarrés[1], L. Velasco-Hidalgo[1], L. Nevares-Juárez[1], M. Ramírez-Martínez[1], R. Rivera-Luna[1]

[1]Oncology, Instituto Nacional de Pediatría, Mexico City, Mexico

Objectives: In Mexico, the diagnosis of cancer in adolescent is late and it has been associated with a poor prognosis. The aim of our study was to describe the clinical characteristics at the diagnostic in adolescence with cancer.
Methods: We realized a descriptive retrospective study where we included all the patients between 12 and 17 years at the moment of cancer diagnosis from January to December 2013. We analyzed the clinical characteristics stratifying in two groups: patients diagnosed at the emergency room and in the outpatient clinic.
Results: We included 45 patients, 66% were diagnosed with an oncological emergency. The relation male: female was 2.7:1. The main oncological diagnosis was osteosarcoma followed by acute lymphoblastic leukemia and central nervous system tumors. The reason for visiting the emergency room was pain, headache, tumor and pallor. The association between diagnosis in the emergency room and the mortality was not statistically significant.
Conclusions: Adolescents were diagnosed more frequently in the emergency room with advanced stage of disease and the medical urgency. It is relevant to establish an early detection program in this population in order to reduce diagnosis delay.

GERM CELL TUMOURS

EP-179

COMPARISON OF GONADAL AND EXTRAGONADAL, EXTRACRANIALLY LOCALIZED GERM CELL TUMORS IN CHILDREN. MULTICENTER STUDY FROM POLAND

E. Adamkiewicz-Drozynska[1], M. Jezierska[1], E. Izycka-Swieszewska[2], W. Balwierz[3], A. Chybicka[4], J. Kowalczyk[5], J. Peregud – Pogorzelski[6], G. Sobol–Milejska[7], J. Wachowiak[8], M. Wysocki[9], J. Stefanowicz[10], K. Polczynska[10], L. Chelmecka – Hanusiewicz[3], M. Wieczorek[11], I. Karpinska –Derda[11], M. Krawczuk-Rybak[12], E. Leszczynska[12], J. Nurzynska – Flak[13], K. Peszynska[14], T. Szczepanski[15], A. Pobudejska – Pieniazek[15], M. Rychlowska – Pruszynska[16], A. Sokol – Jezewska[4], W. Mlynarski[17], J. Trelinska[17], T. Urasinski[18], K. Wachowiak – Szajdak[19]

[1]Paediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [2]Pathology and Neuropathology, Medical University of Gdansk, Gdansk, Poland; [3]Pediatric Oncology and Hematology, JU Medical College in Krakow, Krakow, Poland; [4]PediatricTransplantology Hematology and Oncology, Medical University of Wroclaw, Wroclaw, Poland; [5]Pediatrics Hematology and Oncology, Medical University of Lublin, Lublin, Poland; [6]Pediatrics Hematology and Oncology, Pomeranian Medical University in Szczecin, Szczecin, Poland; [7]Pediatrics, Silesian Medical University in Katowice, Katowice, Poland; [8]Pediatrics Hematology Oncology and Transplantology, University of Medical Sciences in Poznan, Poznan, Poland; [9]Pediatrics Hematology and Oncology, Nicolas Copernicus Medical University of Bydgoszcz, Bydgoszcz, Poland; [10]Pediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [11]Hematology and Oncology, Pediatrics and Oncology Center in Chorzow, Chorzow, Poland; [12]Paediatrics Hematology and Oncology, Medical University of Bialystok, Bialystok, Poland; [13]Paediatrics Hematology and Oncology, Medical University of Lublin, Lublin, Poland; [14]Paediatrics Hematology and Oncology, Nicolas Copernicus Medical University of Bydgoszcz, Bydgoszcz, Poland; [15]Paediatrics Hematology and Oncology, Silesian Medical University in Katowice, Zabrze, Poland; [16]Pediatric Oncological Surgery, Mother and Child Institute in Warsaw, Warsaw, Poland; [17]Paediatrics Hematology Oncology and Diabetology, Medical University of Lodz, Lodz, Poland; [18]Paediatrics Hematology and Oncology, Pomeranian Medical University in Szczecin, Szczecin, Poland; [19]Pediatrics Hematology Oncology and Transplantology, University of Medical Sciences in Poznan, Poznan, Poland

Objectives: To compare clinical characteristics, histology and treatment results of gonadal and extragonadal, extracranially localized malignant germ cell tumors (MGCT) in children.
Methods: Retrospective analysis of clinical and histological features with regard to the outcome in two groups of patients: group I with extragonadal (EG) and group II with gonadal (GN) MGCT.
Results: There were 152 patients from 15 Polish Paediatric Oncological Centresdiagnosed between 2008-2013 were evaluated. They were treated according to TGM-95 protocol. 42/152 were included to group I (EG tumors) and 110/152 to group II (GN tumors). Patients with GN tumors were older (median age 13 years 10 months) than patients with EG tumors (median age 4 years 1 month). In group I the females predominated (23/19), in group II - the males (23/87). Size of tumors was bigger in group I. Evaluation of serum markers indicated increased AFP in 66% from group I and in 82% from group II. Increased HCG was revealed in 23% from group I and in 64% from group II. High levels LDH (>2x normal value) were found in 9% and in 16% adequately. Uremic acid was increased in 10% vs 28%. 55% of patients from group I and and 49% from group II were qualified to high risk group. The most frequently recognized histological types were teratoma and yolk sac tumors (YST) in group I; in group II YST and dysgerminoma/seminoma. Relapses were noted in 2 patients in every group, primary resistance was observed in 2 GN tumors. Third line therapy was used in 6 patients from group I and in 1 from group II. Unsatisfactory outcome was seen in 5 patients.
Conclusions: Some significant differences in clinical and histological features were documented. Further studies are needed to explain if the prognostic factors are the same in gonadal and extragonadal tumors.

EP-180

TESTICULAR AND PARATESTICULAR TUMORS IN CHILDHOOD AND ADOLESCENCE

B. Aydin[1], H. Susam Sen[1], A. Varan[1], B. Yalcin[1], T. Kutluk[1], C. Akyuz[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: Testicular and paratesticular tumors are rare in childhood and have different characteristics from adult counterparts. We reviewed 41-year experience for testicular cancer in children and adolescents in our center.
Methods: Clinical characteristics and outcome of children who were treated between 1973 and 2014 were retrospectively evaluated.
Results: The median age of 149 patients with primary testicular and paratesticular tumors was 2.5 years (ranged 0-17). Histopathological diagnoses were yolk sac tumor (55.7%), teratoma (12.8%), mixed malignant germ cell tumor (7.4%), Leydig cell tumor (3.4%), granulosa cell tumor (0.7%), and paratesticular rabdomyosarcoma (10.7%). Three patients were diagnosed as primary testicular non-Hodgkin lymphoma and one patient as metastatic paratesticular Wilms tumor. The most common clinical presentation was painless scrotal mass (88%). Initial surgery in 83.2% of patients was radical inguinal orchiectomy. Patients with stage 2 and higher germ cell tumors received BEP regimen (cisplatin 100mg/m2/day on day 1, etoposide 120 mg/m2/day on days 1-3, bleomycin 15 mg/m2/day on day 2). Patients were followed median 25 months (1 day-23.5 year). 5-year EFS and OS for stages 1, 2, 3 and 4 were 86%, 100%, 53%, 75%, and, 100%, 100%, 67%, 63% respectively. Most of the patients with rhabdomyosarcoma (11/16) had stage 1 disease. OS at 5 years was 92% for patients with paratesticular rhabdomyosarcoma.
Conclusions: Most frequent testis tumor is yolk sac tumor in childhood. BEP is effective regimen in testicular germ cell tumors. Stage 1 and 2 tumors have excellent prognosis regardless of histology.

EP-181

PURE GONADOBLASTOMA WITH KARYOTYPE 46, XX AND XY CHIMERISM NEGATIVE INTO A GIRL - A CASE REPORT

D. Gasperini[1], G. Martins[1], E. Silva[2], N. Suarez[1], V. Kremer[3], M. Neto[4], L.U.I.Z. Lopes[5]

[1]Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Patholy Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Oncology Pediatric Surgeon, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [4]Cytogeneticist, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [5]Phd Medical Director, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: Gonadoblastoma are germ cell tumors intimately mixed with sex-cord stromal in circumscribed nests, usually with hyaline basal membrane and focal or diffuse calcifications. Despite not being metastatic gonadoblastomas tumors, other types of germ cell tumors associated with them can invade the stroma, especially when combined with disgerminomas (50%) or others. They usually appear in patients with dysgenetic gonads, phenotypically female with sexual or somatic abnormalities, most often in the karyotype 46XY (96%), but it has been observed individuals with absence of the Y chromosome (karyotype 46, XX,45, X45, X/46, XX), with structural abnormalities of X, (46, XX, del (11p)) and true hermaphrodites.
Methods: We report a case of an infant with pure gonadoblastoma, female, 8 months old, without gonadal dysgenesis, 46XX karyotype and negative XY chimerism, which was admitted to our hospital with a palpable mass in the pelvis discovered during surgery for correction right inguinal hernia. Alpha-fetoprotein (AFP) and beta-subunit of human chorionic gonadotropin (HCG) were normal. Ultrasonographical examinations revealed a large solid expansive training, adnexal right, heterogeneous, partially accurate and lobulated contour, measuring 7.3 x 3.5 x 5.8 cm, with a volume of 77 cm^3. At laparotomy, we found extensive tumor in the left ovary and right ovary tape, performed left salpingo-oophorectomy and biopsy of the right ovary. Histological examination showed gonadoblastoma in the left ovary and absence of neoplasia in other structures analyzed. Immunohistochemical examination with calretinin, CD113 (C-KIT), inhibin and OCT-4 positive, helped to diagnose this gonadoblastoma.
Results: She is currently being followed up with exams ultrasonagraphy and collecting AFP and HCG monthly to control possible relapse.
Conclusions: With this case, literature review was done to discuss treatment approach and additional research.

EP-182

GERM CELLS INDUCED FROM HUMAN UMBILICAL CORD MESENCHYMAL CELL-DERIVED INDUCED PLURIPOTENT STEM CELLS BY BMP4

L. Ma[1], T. Wang[2], Y. Chen[3]

[1]*Pediatrics, The Second Affiliated Hospital of Shantou University Medical College, Shantou, China;* [2]*Pediatrics, Capital Institute of Pediatrics, Beijing, China;* [3]*Pediatrics, Guangdong Maternity and Child Health Care Hospital, Guangzhou, China*

Objectives: To reprogramme the induced pluripotent stem (iPS) cells from Human umbilical cord mesenchymal cells (HuMSCs) and induce the iPS cells into germ cells by BMP4.
Methods: OCT4, SOX2, Klf4, c-myc, Nanog, Lin28 were transfected into HuMSCs with lentivirus to reprogram HuMSCs into iPS cells. Morphological observation, Alkaline Phosphatase staining, karyotype analysis, RT-PCR, immunofluorescence staining, tumor formation in vivo and embryniod body formation in vitro were performed to examine the pluripotency of the iPS cell lines. We then induced one of the iPS cells lines into germ cells by BMP4. Gene expression was measured by qRT-PCR at days 0, 3, 7, 10 and 14. Early-stage germ specific protein VASA and meiosis specific protein SYCP3 were assesssed by immunofluorescence staining.
Results: We obtained two iPS cell lines completely reprogrammed, HuMSC-iPS1 and HuMSC-iPS2. HuMSC-iPS1 expresses germ cell markers (DAZL, DPPA3, DDX4, SYCP3, PROTAMINE) at undifferentiated state. BMP4 (100ng/ml) can upregulate germ cell markers at different time points highly while the spontaneous differentiation just upregulate DPPA3, DAZL and VASA modestly at day 3. However, all of these genes were downregulated at day 14. VASA and SYCP3 immunofluorescence staining indicates there is a high VASA expression in BMP4 induced group in contrast to low expression in the spontaneous group at day 7. Meanwhile, there is a modest SYCP3 fluorescence in BMP4 induced group in contrast to no immunofluoresence in the spontaneous group.
Conclusions: OCT4, SOX2, Klf4, c-myc, Nanog, Lin28 can reprogram HuMSCs into iPS cells effectively. The MSC- iPS1 can differentiate into early germ cells spontaneously while the germ cells induced by BMP4 can enter meiosis.

EP-183

OUTCOME OF EXTRACRANIAL GERM CELL TUMOURS IN CHILDREN AT NATIONAL HOSPITAL OF PEDIATRICS, HANOI, VIETNAM

H.A. Nguyen[1], N. Bui[1]

[1]*Oncology, National Hospital of Pediatrics, Ha Noi, Vietnam*

Objectives: Germ cell tumour (GCT) account for approximately 3% of childhood cancer. It can be benign or malignant. The aim of this study was to evaluate outcome of extracranial GCT in children at NHP. All patients were treated according to the Germ Cell III protocol.
Methods: A retrospective review of 168 children with extracranial GCT had been treated at NHP between 2008 and 2013. Result of treatment, recurrence, death, overall survival (OS) and event free survival (EFS) 5 years were analyzed.
Results: All patients with mature teratoma underwent surgery alone, but there was 1.4% recurrence, 2.9% death. Patients with immature teratoma had 5,9% recurrence, no died. The patients with yolk sac tumours underwent excision tumour or surgical biopsy, followed by chemotherapy (96.1%), 7.8% recurrence, 5.9% death. 9 patients died (5.4%) and 9 patients were recurrence (5.4%). Mortality and recurrence rate were high with sacrococcygeal, mediastinal tumours and mixed malignant GCT. Cause of death were respiratory failure, coma due to metastases. Overall survival (OS) for the whole patient group was 88.9% and event-free survival (EFS) was 83.8% at 5 years. Patients with gonadal GCT had OS and EFS higher than those with extragonadal (OS:$p = 0.118$, EFS:$p = 0.011$). Patients with sacrococcygeal and mediastinal tumours had OS and EFS lower than those with gonadal and retroperitoneal GCT (OS:$p = 0.048$, EFS:$p = 0$). Patients with immature teratoma (OS:100%, EFS:92.6%) and yolk sac tumour (OS:94%, EFS:83.6%) had the highest probability of OS and EFS. Complication were infection and disorder of defecation and urination after operating tumour at sacrococcygeal.
Conclusions: The prognosis of GCT is quite good, especially with gonadal GCT.

EP-184

CHARACTERISTICS OF EXTRACRANIAL GERM CELL TUMOURS IN CHILDREN AT NATIONAL HOSPITAL OF PEDIATRICS, HANOI, VIETNAM

H.A. Nguyen[1], N. Bui[1]

[1]*Oncology, National Hospital of Pediatrics, Ha Noi, Vietnam*

Objectives: The aim of this study was to evaluate characteristics of extracranial GCT in children at NHP.
Methods: A retrospective review of 168 children with extracranial GCT had been treated at NHP between 2008 and 2013. Pathology, age, sex, primary tumour, metastases and stage were analyzed.
Results: There was 78.6% of children under 5 years old in this study. Male/female = 1.2/1. Clinical signs could include big testis (41.7%), abdominal distension (30.6%), touching abdominal tumour (25%) or sacrococcygeal (11.1%), defecation and urination difficulty (8.3%). Gonadal GCT hold 55.9%. Almost tumour at extragonadal were sacrococcygeal tumour (16.1%). Most of mature teratoma were found in ovary (50%), sacrococcygeal (55.6%) and mediastinum (61.5%). Tumour in testis almost were yolk sac tumour (56.5%). Children under 5 years old usually had tumour at testis (44.7%) or sacrococcygeal (18.9%). Children over 5 years old usually had tumour in ovary (55.6%) or mediastinum (19.4%). All tumours had imaging of sound mix, heterogeneous. AFP were normal in all patients with mature teratoma. AFP increased in 1/3 of immature teratoma, almost of yolk sac tumour and mixed malignant GCT. Teratoma were found most frequently (mature: 69, immature: 34), followed by Yolk sac tumour (n = 51), Mixed malignant GCT (n = 10), Dysgerminoma (n = 2) and Embryonal carcinoma (n = 2). The GCT were located in sites: testis (n = 62), ovary (n = 32), sacrococcygeal (n = 27), mediastinum (n = 13), retroperitoneum (n = 14), abdominal cavity (n = 13), neck (n = 3), shin (n = 1) and miscellaneous (n = 10). Most patients (81) were Stage I, 64 patients were Stage II, 13 patients were Stage III, 6 patients were Stage IV and 4 patients operated in other hospitals could not classified.
Conclusions: Extracranial GCT in children had variable pathology and primary location. Most of patients admitted in early stage.

EP-185

EXTRACRANIAL GERM CELL TUMORS: - THIRTEEN YEAR EXPERIENCE AT KANTI CHILDRENS HOSPITAL

K. Sah[1]

[1]*Oncology, Kanti Children Hospital, Kathmandu, Nepal*

Objectives: To evaluate the treatment outcome of children with extra cranial Germ Cell Tumors (GCT) treated in our center.
Methods: This was a retrospective analysis of treatment outcome of children with extracranial germ cell tumors who were registered in our center from March 1999 to March 2012. All the cases had undergone surgical removal of the masses and biopsy. Alpha-feto-protein and beta-HCG were done pre-operatively, post operatively, during chemotherapy and on each follow up. If the tumor markers were raised post-operatively, they received JEB (Carboplatin, Etoposide, Bleomycin) Chemotherapy, 3 weekly until the tumor markers normalized, and 2 more cycles were added thereafter. Stage I tumors and mature GCT with normal tumor markers were kept in regular follow up.
Results: Out of 755 childhood cancers, 45 (5.96%) were GCT. The median age group was 1-3 years (Range: 1 day – 13 yrs), M: F = 1:3. Based on histological findings the common tumor types were Yolk Sac tumor (49%), Immature Teratoma (22%), Mature Teratoma (11%), Mixed GCT (9%) and Embryonal Carcinoma (9%). The most common site was Sacrococcygeal (45%) followed by Gonads (35%) Mediastinal tumor (11%). Most common stage was II (40%). Forty cases received chemotherapy and 5 were kept on a close follow up. All those who were started with chemotherapy completed their treatment. At the end of thirteen years, 22 (49%) are alive and on regular follow up, 11 (24%) died and 12 (27%) lost to follow up.
Conclusions: Extracranial Germcell Tumour, GCT was the most common GCT with 49% over all survival rate.

EP-186

PRIMARY THYMIC GERMINOMA IN A BOY WITH LOWE SYNDROME

T. Takezoe[1], T. Watanabe[1], Y. Genma[2], T. Ohsumi[2], T. Mori[2], R. Horikawa[3], K. Matsuoka[4], T. Shimizu[1], M. Migita[1], M. Takahashi[1], M. Ohno[1], K. Sato[1], Y. Fuchimoto[1], Y. Kanamori[1]

[1]*Department of Pediatric Surgery, National Center for Child Health and Development, Tokyo, Japan;* [2]*Department of Oncology, National Center for Child Health and Development, Tokyo, Japan;* [3]*Department of Endocrinology and Metabolism, National Center for Child Health and Development, Tokyo, Japan;* [4]*Department of Pathology, National Center for Child Health and Development, Tokyo, Japan*

Objectives: Mediastinal germ cell tumors are relatively rare, and among them thymic germinoma is an extremely rare tumor. We report a case of thymic germinoma associated with Lowe syndrome. To our knowledge, this is the first case report of thymic germinoma complicated with Lowe syndrome.
Methods: Case report.
Results: An 11-year-old male who was diagnosed with Lowe syndrome has been followed at our outpatient clinic. Patients with Lowe syndrome have the following signs and symptoms: 1) renal tubular acidosis, 2) congenital cataract, and 3) intellectual disability. When he was 11 years and 9 months old, secondary sexual characteristics appeared rapidly in a few weeks. Serum HCG-b was high (278.2 pg/ml) and chest MRI showed a cystic tumor in the thymus. Although it was difficult to clarify whether the tumor was malignant or not, the tumor was functional and we decided to resect the tumor. The tumor was first biopsied and turned out to be a germinoma by prompt intraoperative diagnosis. We performed extended thymectomy with mediastinal lymph node dissection. After the operation, he was treated with four courses of JEB (carboplatin, etoposide, and bleomycin) chemotherapy; then, the dose was reduced by 40% considering his deteriorated renal function. He is now followed up at the outpatient clinic and has shown no recurrence.
Conclusions: We reported the first case of thymic germinoma complicated with Lowe syndrome.

EP-187

IMAGING FEATURES OF MATURE AND IMMATURE EXTRA-GONDAL TERATOMA IN PEDIATRIC AGE GROUP

A. Youssef[1], S. Abd Al Karim[2], S. Ahmed[3], T. Rafaat[4], M. EL Shafie[2], H. Taha[5], M. EL Wakil[4], I. Zaky[4]

[1]Diagnostic Imaging, National Cancer Institute, Cairo University, Cairo, Egypt; [2]Surgery, National Cancer Institute, Cairo University, Cairo, Egypt; [3]Pediaterics, National Cancer Institute, Cairo University, Cairo, Egypt; [4]Diagnostic Imaging, National Cancer Institute, Cairo University, Cairo, Egypt; [5]Pathology, National Cancer Institute, Cairo University, Cairo, Egypt

Objective: Teratoma is the most frequent germ cell tumors. The most accepted theory for their origin suggests that most are due to abnormal differentiation of embryonic germ cells that arise from the fetal yolk sac. Normally, these cells migrate to gonads yet it can migrate abnormally to other locations so there are gondal and extra gondal teratomas. Teratomas range from benign, mature, to immature, poorly differentiated lesions with solid components and malignant transformation. The prognosis, clinical outcome and the risk of recurrence were reported to be related to the degree of tumor maturity. Our objectives are to demonstrate the radiological features of the extra-gondal teratomas and to evaluate the potential accuracy of the imaging findings in differentiation between the mature and immature teratoma.
Methods: Seventy pediatric patients-30 male and 40 females- with pathologically proven teratoma who presented to our hospital in the past four years were included in this study. Their ages ranged from 20 days to 17 years. Retrospective review of their radiological studies was done and correlated with the pathological results.
Results: Gondal tertoma found in 14 cases, ovarian (n = 8), two of them were bilateral and testicular (n = 6). Sacrocoggeal location is the commonest site of extragondal teratomas (n = 22) followed by reteroperotineal (n = 13), intraperotineal lesion (n = 5), intraspinal (n = 6), intracranial (n = 4), neck (n = 3), orbital (n = 2) and penile (n = 1). Pathological diagnosis shows 55 mature teratoma and 15 immature teratoma. Most of the mature teratoma (53/55) show all fat, calcification, cystic and solid component whereas the immature lesion usually lake one of these component mostly the fat component.
Conclusions: Extra-gondal teratoma are more common than gondal ones in pediatrics unlike the adults. Awareness of the imaging feature of these lesions especially the immature teratoma is of importance in proper management and improvement of the patient outcome.

HISTIOCYTOSIS

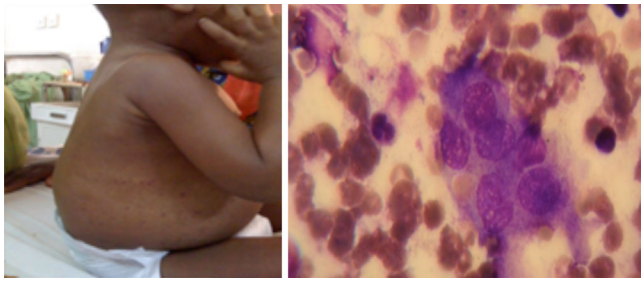
EP-188

MALIGNANT HISTIOCYTOSIS: REPORT OF TWO CASES

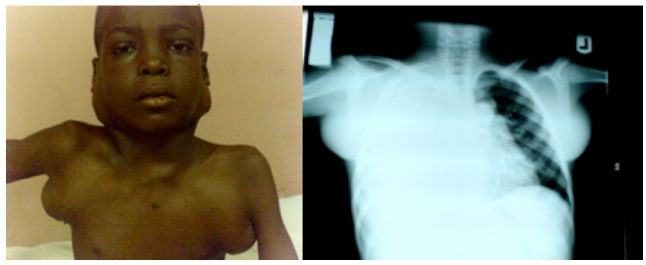
S. Abdullahi[1], U. Abdulsalam[1], M. Ibrahim[1], H.G. Dalhat[2]

[1]Paediatrics, Bayero University/Aminu Kano Teaching Hospital, Kano, Nigeria; [2]Haematology, Bayero University/Aminu Kano Teaching Hospital, Kano, Nigeria

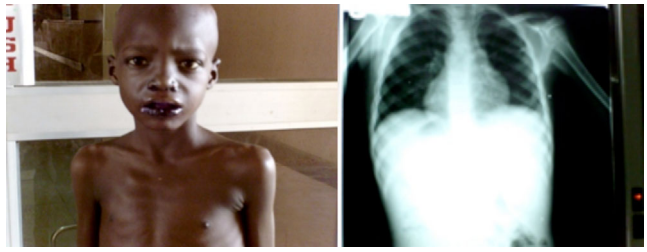
Background: Malignant Histiocytosis is a rare disorder characterized by a systemic proliferation of morphologically atypical histiocytes. The clinical presentations vary greatly, ranging from mild to life threatening.
Objective: To draw attention of clinicians particularly in developing countries to this rare disorder that can easily be confused with acute leukemia.
Case reports: Two males aged 2 and 8 years respectively were admitted to Aminu Kano Teaching Hospital. They presented with recurrent fever for 2 months and bilateral neck swellings. During the same period, they had repeated blood transfusions. On examination, the two were underweight with significant cervical lymph-node enlargement, generalized petechiael haemorrhages and hepato-splenomegaly. They were initially suspected to have acute leukemia. However bone marrow aspiration biopsy revealed a diagnosis of malignant histiocytosis. They were treated with Cyclophosphamide Oncovin Doxorubicin and Prednisolone. The parents of the first child abandoned the course of chemotherapy 5 days into the first course and the patient died at home 6 days after leaving the hospital. The second patient completed six cycles of chemotherapy and the repeat bone marrow aspiration biopsy and the full blood count after the first course showed significant improvement and the patient is still on follow up.



Patient 1 Bone marrow infiltration by histiocytes, engulfing both mature and immature haemopoietic cells



Patient 2 Patient's chest radiograph at diagnosis



same patient after completing treatment Patient's chest radiograph after completing treatment

Conclusion: Histiocytosis is rare, but should be suspected as a differential diagnosis in a patient with significant lymph node enlargement, recurrent anaemia and repeated blood transfusion.

EP-189

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR LANGERHANS CELL HISTIOCYTOSIS (EXPERIENCE OF EGE UNIVERSITY FROM TURKEY)

N. Cetingül[1], S. Aksoylar[1], S. Kansoy[1], M. Kantar[1], B. Demirag[1], B. Akinci[1]

[1]Pediatric Oncology, Ege University School of Medicine, Izmir, Turkey

Objectives: Langerhans Cell Histiocytosis (LCH) is characterized by heterogenous lesions including Langerhans cells. When the systems involved are "risk organs" and/or the patient is younger than 2 years at diagnosis, MS-LCH has been considered particularly devastating, and as carrying a potentially fatal prognosis.
Despite the treatment intensification, the mortality rate is approximately 40% in patients wiht MS-LCH. Refractory patients and those with multiple reactivations present a challenge. Cladribine, Cladribine –cytarabine arabinoside combination and clofarabine can be used as salvage therapy.
Methods: We report 3 refractory Langerhans Cell Histiocytosis patient who were treated successfully with hematopoetic stem cell transplantation using non myeloablative conditioning regimen.
Results:

Table 1.Patients characteristics

Patient no	Sex	Age at diagnosis	Type of LCH	Involved organs	6.th week response to frontline treatment	Therapy prior to HSCT
1	M	7,5 month	MS-HR	Liver, spleen, bone marrow, skin	Poor response	VBL+Prednisolone/MTX/CSA/ ARA-C/ CSA+ Cladribine+ARA-C Clofarabine
2	M	8 month	MS-HR	Liver, spleen, bone marrow, skin	Poor response	VBL+Prednisolone/MTX/CSA/ ARA-C/ CSA+ Cladribine+ARA-C Clofarabine
3	F	9 month	MS-LR	Skin, GIT	Good response	VBL+Prednisolon/ Cladribine/ clorafabine

Conclusions:

Table 2.Details of hematopoietic stem cell transplantation and outcome

Patient no	1	2	3
Age at HSCT	20,5months	30months	27months
Duration from diagnosis	13months	22months	18months
Findings before HSCT	Liver 14cm,spleen 14cm Skin lesions pancytopenia	Liver 4-5cm, spleen 7cm thrombocytopenia	Liver 3cm, spleen 4cm
Conditionin	Melphalan/fludarabine/Alemtuzum	Melphalan/fludarabine/AT	Melphalan/fludarabine/Alemtuzum
g	ab	G	ab
Sources	6/6 matched unrelated Cord blood	5/6 matched unrelated Cord blood	10/10 matched unrelated Peripheral stem cell
Infused NCC	6,5x107/kg	3,8x107/kg	6,4x108/kg
GVHD prophylaxis	CSA/MMF	CSA/MMF	CSA
Engraftmen t	+34'th day	+32'nd day	+17'th day
Post HSCT	+4 years	+12 months	+6 months
Outcome	Alive	Alive	Alive
Sequel	-	Liver, skin GVHD	-

MMFmicophenolate mophetile
HCST should be employed especially in high risk MS-LCH patients.

EP-190

ORBITAL EOSINOPHILIC GRANULOMA – CLINICAL PATHOLOGICAL STUDY

R. Fan[1], Y. Sun[2]

[1]Pathology, Indiana University School of Medicine, Indianapolis, USA; [2]Ophthalmology, Indiana University School of Medicine, Indianapolis, USA

Objectives: Orbital eosinophilic granuloma (aka: unifocal Langerhans cell histiocytosis) is a relatively rare entity among orbital tumors, with many unique clinical and pathological features and challenges. Currently the large scale clinicopathological study is missing.
Methods: We retrospectively collected 18 cases, nine cases in our institutional files from 1992 to 2013 and nine cases from medical literature. All cases have either electron microscopic confirmation with Birbeck granules or immunohistochemistry finding of CD1a and/or S100 positivity. The clinical information, selective radiology images and histopathology of cases from our institution were reviewed.
Results: The patients age ranges from 1 to 58 year old, with mean 9.3 years with male predominance (M/F = 14:4). The lesion are equally distributed at right or left side (9 cases for each side). Almost all patients have superior lateral orbital lesions. Eye lid or forehead swelling, proptosis are the most common symptoms, with visions unimpaired or mildly affected.
Conclusions: 1st and 2nd decade presentation, male predominance and the predilection of eosinophilic granuloma at superior lateral orbit with frequently remarkable adjacent bone destruction narrows down the differential diagnosis significantly. In contrast, rhabdomyosarcoma of orbit most commonly happens at superomedial quadrant if embryonal variant or at inferior if alveolar variant. Neuroblastoma, though the preferred metastatic location is the same, but the age are characteristically at the lower spectrum accompanied by higher frequency of bilaterality and hypertension caused by catecholamine secretion. From the pathologist's perspective, sparse Langerhans cell presentation and/or mixtures of other inflammatory infiltrates, inconspicuous eosinophils on frozen sections are major challenges.

EP-191

SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN CHILDREN WITH MALIGNANCY UNDERGOING INTENSIVE CHEMOTHERAPY

R. Kebudi[1], B. Cakir[2], O. Gorgun[1], O. Dogan[3]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Bezmialem Vakif University Medical Faculty, Istanbul, Turkey; [3]Pathology, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey

Objectives: Hemophagocytic lymphohistiocytosis (HLH) is a condition of uncontrolled immune dysfunction induced by a hyperinflammatory response. Secondary hemophagocytic lymphohistiocytosis may be associated with a systemic viral, bacterial, fungal, or parasitic infection in individuals with an underlying immunological disorder such as malignancy. We aim to document the characteristics of secondary HLH in children with malignancy and to point out early diagnosis and treatment.
Methods: The characteristics, HLH inducing factors, treatment and outcome of 4 (2 females, 2 males) children with cancer and secondary HLH were evaluated.
Results: 4 children (2 acute lymphoblastic leukemia with infection, 1 relapsed neuroblastoma with infection, 1 anaplastic large cell lymphoma at diagnosis) with fever, hepatosplenomegaly, anemia, thrombocytopenia, increased liver function tests, very high ferritin levels, high triglyceride levels and hemophagocytosis in bone marrow were diagnosed with secondary HLH. Infectious etiology was cytomegalovirus (CMV), CMV and probable invasive aspergillus, staphylococcus aureus infections, and malignancy itself. The treatment of hemophagocytic lymphohistiocytosis consisted of corticosteroids and/or intravenous immunoglobulins along with appropriate antimicrobial therapy and chemotherapy in these patients. One of the patients had a second reactivation of HLH during intensive chemotherapy due to concomitant CMV and fungal infections. All the symptoms and signs regressed gradually.
Conclusions: Secondary HLH can be diagnosed in up to 10% of patients with malignancy and may be life threatening. Patients with high fever and liver dysfunction should be further investigated and marrow aspiration samples carefully observed to detect hemophagocytosis. Earlier diagnosis and treatment may decrease the high mortality rate in these patients.

EP-192

IMPACT ON OUTCOME OF A MODIFIED LANGERHANS CELL HISTIOCYTOSIS (LCH) PROTOCOL WITH INTENSIFIED HIGH RISK INDUCTION AND AUGMENTED PROLONGED MAINTENANCE- A SINGLE INSTITUTION EXPERIENCE

G. Narula[1], B.A. Wanve[1], B. Arora[1], S.D. Banavali[1]

[1]Medical Oncology (Pediatric Division), TATA Memorial Hospital, Mumbai, India

Objectives: Relapses in LCH, and mortality in Multisystem- High Risk (MS-HR) remain problematic. Disease progression on early reassessment necessitates expensive salvage options including transplant. Etoposide showed modest benefit in MS-HR and prolonged maintenance reduced recurrences in earlier studies. Methotrexate proved equivocal in shorter maintenance. These strategies were discontinued after LCH trials I-III. A regime with metronomic Etoposide for MS-HR and prolonged maintenance including Methotrexate was devised to reduce need for salvage. Patients accrued over 5 years were analyzed.
Methods: LCH records of 5 years from Jan 2009 were studied. Single System (SS) and Multisystem Low Risk (MS-LR) received 25 weekly Vinblastine doses, Prednisolone for 4 weeks, tapered over 2, then continued as 3-day weekly pulses till week 12, and 5-day 3-weekly pulses till week 25. 3-weekly pulses continued in maintenance for MS-LR and HR for 6 and 18 months respectively. Additionally, 3-weekly Vinblastine, daily 6- Mercaptopurine and weekly Methotrexate were given throughout maintenance. MS-HR also received daily Etoposide for 21 of every 28 day cycle for one year. Responses were evaluated at 3, 6 and 12 months or end of therapy.
Results: 39 patients were evaluable. Median age was 36 months (4-189). 24 were SS, 4 MS-LR and 11 MS-HR. Five (3 MS-HR) were lost to follow up before first revaluation. 30 had improvement (Active Disease- Better or No Active Disease) and 3 had intermediate response at first reassessment. 1 MS-LR progressed in a risk organ, and was managed as HR. 1 MS-HR relapsed within 5 months requiring salvage. On a median follow up of 25 months (5- 54), all 34 evaluable patients were alive, 3 with sequelae.
Conclusions: Induction and maintenance augmentation with metronomic Etoposide for MS-HR and prolonged maintenance with additional Methotrexate has shown promise in reducing mortality and relapses respectively, avoiding expensive salvage treatments.

EP-193

A CASE OF SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) FOLLOWING INCOMPLETE KAWASAKI'S DISEASE (KD). IMPORTANCE OF DISTINGUISHING RECURRENT KD FROM HLH

B. Oflaz Sozmen[1], R. Kebudi[2], A. Dindar[3], F. Gurakan[4], O. Devecioglu[5]

[1]Pediatric Hematology - Oncology, Koc University and American Hospital, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and American Hospital, Istanbul, Turkey; [3]Pediatric Cardiology, Istanbul University Medical Faculty and American Hospital, Istanbul, Turkey; [4]Pediatric Gastroenterology, American Hospital, Istanbul, Turkey; [5]Pediatric Hematology - Oncology, Istanbul University Medical Faculty, Istanbul, Turkey

Objectives: Hemophagocyticlymphohistiocytosis (HLH) is potentially a life threatening disorder characterized by severe systemic inflammation caused by immune dysregulation. Secondary HLH is seen after various infections, rheumatologic disorders and malignancies.
Methods: We report a patient with secondary HLH developing after Kawasaki's disease (KD).
Results: A previously healthy one year old male was initially admitted to the hospital with prolonged unremitting fever and diffuse maculopapular rash. He was diagnosed with incomplete KD after his echocardiogram showed dilated left coronary artery. He was treated with intravenous immunoglobulin (IVIG) and aspirin with initial response. Five days after his hospital discharge and a week after initial therapy he started having fevers, worsening of rash and developed hepatosplenomegaly. He had cytopenia with hemoglobin of 6,9 g/dl and platelets of 55K/uL. His ferritin and triglyceride levels were elevated (2215ng/ml and 486mg/dl respectively). Bone marrow aspirate and biopsy were performed which revealed hemophagocytosis. IL-2Rs level was elevated at 2764 U/ml. Perforin mutation was negative. He was diagnosed with secondary HLH and started on IVIG and dexamethasone as per HLH 2004 protocol. He had a rapid response to treatment with improved general status, resolution of fever and cytopenias, decrease in ferritin and triglyceride levels.
Conclusions: HLH may be secondary to KD. Differentiating recurrent KD from secondary HLH may be difficult. It's important to recognize the clinical and laboratory criteria of HLH quite early and initiate treatment accordingly to avoid mortality and morbidity due to HLH.

EP-194

CENTRAL NERVOUS SYSTEM IMAGING IN CHILDHOOD LCH

L. Porto[1], A. Jurcoane[1], E. Hattingen[1], T. Lehrnbecher[1]

[1]Neuroradiology, University Children's Hospital, Frankfurt am Main, Germany

Objectives: Langerhans cell histiocytosis (LCH) is a systemic disease with variable impact on the central nervous system (CNS). The aim of this study was to evaluate the cerebral abnormalities on MR imaging in children with LHC.
Methods: Two experienced neuroradiologists retrospectively reviewed the 31 MR examinations available from 94 children and adolescents with LCH. The typical cerebral pathologies of LCH were recorded and rated regarding their signal intensity on T2-w images and on contrast-enhanced T1-w images.
Results The most common locations of the visible structural changes were osseous, followed respectively by pineal enhancement, enlarged pituitary stalk/mass, white matter hyperintensity, dentate nucleus, parenchymal enhancement, hippocampus and meningeal enhancement. The inter-rater agreement was 69-100%. The lowest agreement was found for the pineal region and dentate nucleus.

Conclusions: The most common site of manifestation in LCH after the bone was the hypothalamic-pituitary system. But other parts of the CNS such as the cerebellum or the white matter may also be involved, indicating initial neurodegeneration in childhood.

EP-195

LATE PRESENTATION PREDICTS ENDOCRINE DYSFUNCTION IN PATIENTS WITH LANGERHANS CELL HISTIOCYTOSIS (LCH) - A RETROSPECTIVE ANALYSIS OF THE WEST OF SCOTLAND LCH SERVICE 1998-2012

M. Ronghe[1], A. Coyte[2], D. Murphy[1], J. Sastry[1], F. Ahmed[2], G. Shaikh[2]

[1]Paediatric Oncology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [2]Paediatric Endocrinology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom

Objectives: Langerhans cell Histiocytosis (LCH) is a rare condition primarily affecting the paediatric population. It is characterised by clonal proliferation of Langerhans cells. Disease severity is dependent on the type and number of organs involved in addition to focality. Disease aetiology still remains unclear. We aimed to record the incidence and characteristics of West of Scotland LCH patients with a focus on predictive factors for endocrine dysfunction.
Methods: Consecutive diagnoses of LCH, at The Royal Hospital for Sick Children Glasgow, between January 1998 - December 2012 were selected. Patient notes were used to collect information on age, sex, postcode (Scottish index of deprivation-SIMD 1-most deprived, 6-least deprived), ethnicity, systems involved, signs and symptoms of presentation, disease progression, treatment and current status.
Results: Twenty-three patients were diagnosed with LCH. The median age of diagnosis was 2.7 years (Range: 1 month-15 years). 52% (n = 12) were female. Over half of patients 57% (n = 13) have SIMD scores of 1/2. 82% of the population were Caucasian, 13% South Asian and 4% of mixed origin. The head was the most common site of presentation. There was 1 mortality in the cohort. Common symptoms at presentation included skin rashes, lumps and musculoskeletal pain. *A*ll patients with high risk organ involvement (spleen, liver, hematopoietic system or lung) were females. Endocrine dysfunction, with diabetes insipidus being most common, was seen in 35% (n = 8). 62.5% (n = 5) were diagnosed with diabetes insipidus alone. Patients with endocrine dysfunctions had a longer symptom interval compared to those without endocrine dysfunction; with 62.5% (n = 5) diagnosed after 4 months compared to 13.3% (n = 2) without endocrine dysfunction. (p = 0.052)
Conclusions: Deprivation is associated with an increased incidence of LCH, with females more likely to develop high risk organ disease. A third of paediatric LCH patients develop endocrine dysfunction and these patients have a longer symptom interval. Further studies are required.

EP-196

SEVERE DISSEMINATED CNS JUVENILE XANTHOGRANULOMA PRESENTING WITH BRAINSTEM DYSFUNCTION AND COMA

S. Siddaiahgari[1], D. Makadia[1], L. Lingappa[2]

[1]Pediatric Hematology- Oncology, Rainbow Childrens Hospital, Hyderabad, India; [2]Pediatric Neurology, Rainbow Childrens Hospital, Hyderabad, India

Objectives: to see the outcome of Juvenile xanthogranulomatosis (JXG) presenting with brainstem dysfunction and coma.
Methods: 3 years child presenting with coma, hemiparesis secondary to non langerhans cell histiocytosis has been treated with LCH 3 protocol.
Results: Three years male, presented with nodular lesion on face since 9 months of age, gradually progressing to trunk, back and extremities. No abnormality at birth. There was history of polyuria& polydipsia from 18 months of age, frontal headache & vomitings for 4 months and weakness of left half of the body, pooling of secretions for 1 month prior to presentation. On examination, had diffuse Xanthogranulomatous lesions over skin and eyes. Mouth was normal. There was no organomegaly. CNS examination revealed, GCS of 7/15, swallowing difficulty, restricted horizontal gaze, left hemiparesis with power of grade 3/5 with right facial palsy. His CBP, CRP, electrolytes, bichemistry, Lipid profile were normal. CXR, USG abdomen, 2D Echo were normal. MRI brain showed diffuse circumscribed lesions in cerebrum, cerebellum, subcortex and ependymal region. Large lesion in right CP angle causing compression of IVth ventricle, mild hydrocephalus with distortion of brain stem. The skin and brainbiopsy report revealed juvenile xanthogranuloma. Immunohistochemistry demonstrated histiocytic cells were positive for CD68, negative for CD1a & S-100. These combined results confirmed histiocytes are non-Langerhan's cells. In light of the clinical and histological findings, a diagnosis of JXG was made. He was started on chemotherapy as per LCH III protocol. Treated diabetes insipidus with desmopressin. Bulbar dysfunction, hemiparesis, consciousness improved within 3 weeks. skin lesions gradually improved. MRI showed near total resolution of lesions. Maintenance was extended for 2 years as per neuroimaging findings. Currently he is off treatment for 6 months and well.
Conclusions: Severe disseminated CNS disease with JXG responds to chemotherapy with significant neurological improvement with near total MRI and skin lesions resolution.

EP-197

CYTOSINE-ARABINOSIDE, VINCRISTINE, AND PREDNISOLONE IN THE TREATMENT OF CHILDREN WITH MS LCH NOT RESPONDING TO FIRST LINE TREATMENT: EXPERIENCE OF A TERTIARY CARE HOSPITAL IN INDIA

A. Singh[1], G. Pai[1], L. Dawman[1], R. Seth[1]

[1]Pediatrics, All India institute of Medical sciences, New Delhi, India

Objectives: The purpose of our study was to find the treatment outcome of patient of MS-LCH treated on VCR-Ara C steroid protocol after failure of first line treatment.
Methods: The medical records of 54 patients with a diagnosis of LCH, was examined to find the treatment response with first line protocol (steroid, VBL) and treatment of refractory LCH with subsequent course, survival, and late sequelae. They were followed up and outcomes assessed.
Results: Multisystem LCH was seen in 36 patient's. Duration of symptoms ranged from 2 months- 4.5 years (mean 10 months). Multisystem LCH was seen in 36 patients. 7 patients had refractory/recurrent LCH. One patient had low risk recurrent LCH which responded to steroids only. 3 patients were treated with AraC VCR protocol and other three received Cladribine based therapy. Both groups treated with cladribine and AraC VCR showed comparable response radiologically, clinically and in adverse reactions. Episodes of Febrile neutropenia were less with AraC VCR protocol. Risk organ most affected was liver. 25% of patients with multisystem disease had some residual lesion or active disease.
Conclusions: AraC VCR based treatment for refractory LCH is a good alternative to cladribine based protocol. Cost benefit, less myelosuppression are advantages over cladribine. Low risk recurrent LCH can be treated with less cytotoxic regimes. Treatment of refractory LCH presents a challenge and treatment protocol needs to be decided based on risk organ involvement, organ dysfunction and response to less intensive protocols.

EP-198

TREATMENT OF RELAPSED LANGERHANS CELL HISTIOCYTOSIS ACCORDING TO LCH III PROTOCOL DID NOT PREVENT SUBSEQUENT RELAPSES; SINGLE CENTER EXPERIENCE

K. Svojgr[1], H. Mottl[1], M. Kyncl[2], R. Kodet[3], V. Smelhaus[1], J. Stary[1], J. Malis[1]

[1]Pediatric Hematology and Oncology, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic; [2]Radiology, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic; [3]Pathology and Molecular Medicine, Charles University 2nd Faculty of Medicine and University Hospital Motol, Prague, Czech Republic

Objectives: Langerhans cell histiocytosis (LCH) is a rare disease characterized by accumulation of malignant dendritic cells. In our study we analyzed the outcome of patients with LCH treated on LCH III protocol.
Methods: From12/2002 to 1/2012 24 patients with LCH were treated at our institution. Eventfree survival (EFS) and overall survival (OS) was analyzed using Stat Viewstatistical program.
Results: Patients with LCH were treated on LCH III protocol, 20 patients were treated at diagnosis, 4 patients underwent primary local therapy for osteolytic bone lesion first and then relapsed (in median 4.36 months); the protocol was used subsequently as the salvage therapy. Single-system (SS) LCH was diagnosed in 14 patients (bones, skin, lungs, pericardium), multi-system LCH had 10 patients (bones, skin, lymph nodes, thymus, lungs, liver, pituitary gland). 'Risk organs' were affected in 3 patients (2 lungs, 1 liver). Median age at diagnosis was 2.7 years (0.5-14.6), median follow up was 7 years (1.5-13.3). Tree patients were stratified to therapeutic group 1: MS-'risk'-LCH, 10 patients to group 2: MS-'low risk-LCH, 11 to group 3: SS multifocal bone or 'central nervous system special'-LCH. EFS of all patients is 75%, OS is 95.8%. EFS SS-LCH is 92.0%, MS-LCH 50.0%, P = 0.02. Therapeutic group 1: 2 from 3 patients relapsed, group 2: 3 from 10 relapsed, group 3: 1 from 11 patients relapsed, P = 0.04%. EFS of 4 patients that were treated for LCH progression is 25.0% in comparison to 85.0% in primary treated patients, P = 0.004.
Conclusions: Patients with LCH treated on LCH III protocol have excellent prognosis at our institution. On the other hand LCH III protocol did not prevent subsequent progressions when used as a salvage treatment for relapsed LCH after primary local therapy. Large number of patients is needed to confirm our findings.
Supported by MHCZ – DRO, University Hospital Motol, Prague, Czech Republic 00064203.

EP-199

STEM CELL TRANSPLANTATION IN PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: EXPERIENCE FROM A TERTIARY CARE CENTRE IN INDIA

D. Thakkar[1], N. Radhakrishnan[1], M. Kalra[1], A. Gupta[1], V. Dinand[1], A. Sachdeva[1]

[1]Pediatric Hematology-Oncology and BMT Unit, Sir Ganga Ram Hospital, New Delhi, India

Objectives: Hemophagocytic lymphohistiocytosis (HLH) can be primary or secondary. For primary HLH and refractory secondary HLH, hematopoietic stem cell transplant (HSCT) is the only curative treatment.
Methods: Retrospective review of our HSCT data was done. Out of 34 patients who underwent HSCT between 2010-2013, 3 were for HLH. All 3 patients were diagnosed as HLH based on the HLH 2004 criteria. Genetic workup was done whenever feasible.
Results: F, 11 month old female, diagnosed as HLH, underwent Matched Sibling Donor (MSD) HSCT (Donor-elder brother;6/6 match) after conditioning with Fludarabine, Melphalan and Anti-Thymocyte Globulin with a peripheral blood stem cell dose of 6.9 x 10^6 / kg. Neutrophils engrafted on Day +22. Her GVHD (skin+gut) responded to immunosuppresion. At present she is alive at 2yr post HSCT.S, 15 months old male, with abnormal NK cell activity and STX11 mutation underwent a double umbilical cord blood (UCB) HSCT post conditioning with Campath, Fludarabine, Melphalan. (Cord A: 5/6 match; nucleated cell (NC) dose 62.4 x 10^7, Cord B: 4/6 match; (NC) dose 120.44 x 10^7). Post transplant, he had CMV reactivation. He died 1 month post transplant of acute renal failure.N, 3 year old male, with Munc 13.4 mutation underwent an unrelated UCB HSCT (5/6 match) after conditioning with Busalphan, Cyclophosphamide and Etoposide. Post transplant, he had complications of BK virus cystitis, skin & gut GVHD, hypertensive encephalopathy and vision impairment. He had neutrophil and platelet engraftment at day +24 and +40 respectively. He died of cardiogenic shock on day +198 post transplant.
Conclusions: Patients with HLH undergoing HSCT have many co-morbidities which need to be intricately managed. Success rates of transplants in these patients are improving with the evolving experience.

EP-200

MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS (LCH): CASE SERIES AND REVIEW OF LITERATURE FROM INDIA

D. Thakkar[1], N. Radhakrishnan[1], M. Kalra[1], S. Agarwal[1], D. Tarangini[1], V. Dinand[1], A. Sachdeva[1]

[1]Pediatric Hematology-Oncology and BMT Unit, Sir Ganga Ram Hospital, New Delhi, India

Objectives: The outcome of LCH in children varies from excellent response in single-system disease to poor response in multisystem disease. We analyzed patients diagnosed with multisystem LCH at our center and compared outcomes to published literature from India.
Methods: Retrospective analysis of patients diagnosed with LCH at our centre between 2006 to 2013 was done. All patients were stratified and managed as per LCH-III protocol.
Results: Thirty-five patients were diagnosed with LCH. M:F ratio was 2.5:1 and median age of presentation was 4.13 years. 20 patients (57%) had multisystem disease and 18 had risk-organ involvement. 5 patients (25%) had anemia (Hb<10gm%) and 10 (50%) had anemia with thrombocytopenia at presentation. Other features included fever (n = 9), breathing difficulty (n = 7), hepatomegaly (n = 6), splenomegaly (n = 1), skin rash (n = 6), bone lesions (n = 7), diarrhoea (n = 6), rectal bleeding (n = 2), bleeding from ears (n = 1), neck swelling (n = 2) and seizures (n = 1). All patients received 2 courses of induction with prednisolone & vinblastine. Maintenance chemotherapy was given in 16 patients. 4 patients were switched to salvage protocol (2 relapses, 2 active disease). 5 patients (25%) completed treatment and are in remission, 3 (15%) are on treatment, 6 (30%) expired, 1 (5%) abandoned treatment and 5 (25%) were lost to follow up. We identified 2 case series from Indian literature which described outcome of chidren with LCH. Bansal D., reported 69 LCH patients over 19 years of whom 48 (69.6%) had multisystem involvement. They were treated with prednisolone and vinblastine or etoposide over 6-8 weeks. 41.6% had a fatal outcome. The 2nd case series by Singh T., reported 40 patients of LCH over 5 years, of whom 5 had multisystem disease. 3 received treatment; one is in remission, one relapsed and the other died.
Conclusions: Multisystem involvement is seen in >50% of pediatric patients presenting with LCH. The outcome of these patients from our series as well as that reported from the subcontinent continues to be poor.

EP-201

2-CHLORODEOXYADENOSINE AND CYTOSINE ARABINOSIDE COMBINED CHEMOTHERAPY FOR TREATMENT OF REFRACTORY OR RECURRENT LANGERHANS CELL HISTIOCYTOSIS

M. Urbieta[1], M. Garcia Lombardi[1], G. Rey[1]

[1]Oncology Unit, Hospital de Niños R. Gutierrez, Ciudad Autónoma de Buenos Aire, Argentina

Objectives: Children with Langerhans cell histiocytosis (LCH) may become refractory to standar therapy or present with repeated recurrences. Reports indicate that 2-chlorodeoxyadenosine (2-CDA) and cytosine arabinoside (Ara-C) combined chemotherapy is effective in this cases. The purpose of this review was to describe the experience in our Unit
Methods: Retrospective analysis on records from 5 patients admitted between January 2008 - December 2012. Patients had a confirmed diagnosis of LCH that had recurred several times or not responded to standard therapy. Patients were given a dose of 5 mg/m2 daily 5 days plus concurrent Ara-C 100 mg/m2/day for 4 days with profilactic filgrastim A total of 6 courses were programmed, and courses were repeated every 3 weeks.
Results: 28 patients with LCH were admitted during the refered period, 5 patients used the scheme with 2-CDA plus Ara-C (3 for multiples reactivation, 2 for progression of disease). Median age of diagnosis was 54 months (range 3 months to 15 years) 3 patients had initial involvement of high-risk organs and 1 Central Nervous System (CNS) mass 3 patients completed 6 courses, 1 change per progression after two courses and one discontinued for severe (grade 3) liver toxicity in the first dose of the first course All but one had myelosuppression as the main toxicity even the patient who does not complete the course (grade 2-3): Three patients are free of active disease 6,14 and 36 months after completing 6 courses of chemotherapy (2 of the high risk organ involment patients and the one with CNS mass). refractory patient and the patient with liver toxicity are alive conducting other lines of treatment.
Conclusions: Patients with refractory LCH or with multiple subsequent reactivations to standard therapy have high chances of achieving remission with 2-CdA and Ara-C combined scheme as reports in the literature, with acceptable toxicity.

EP-202

CLINICAL STUDY ON TREATMENT EFFICACY OF 15 CASES WITH MALIGNANT EOSINOPHILIC GRANULOMA OF ORBIT IN CHILDREN

D. Huang[1], Y. Zhang[1], W. Zhang[1]

[1]Pediatric, Beijing Tongren Hospital Capital Medical University, Beijing, China

Objectives: To study clinical character and analysis efficacy of orbit malignant eosinophilic granuloma for first symptom with orbit mass in children.
Methods: A total of 15 patients with orbit malignant eosinophilic granuloma in children were diagnosed using pathology in our hospital from Apr. 2007 to Apr. 2013.11 cases of male, 4 cases of female. The median age was 2.25 years old (1-12y). In 15 cases, 4 cases of chemotherapy using MVP project (methylamine [M]+vincristine[V]+prednisone[p]), and 11 cases of chemotherapy using DAL-HX 83/90 project (etoposide [VP-16], prednisone, and vinblastine). 13 cases were treated using surgery and chemotherapy, and 2 cases were treated using single chemotherapy. Statistics analysis clinical characters, efficacy and prognosis of 15 cases of malignant orbit eosinophilic granuloma in children.
Results: 1) First symptom: 13 cases of orbit mass and extruded with eyeball, (86.7%), 3 cases of strabismus and diminution of vision and eyes pain (13.3%), and no fever of all patients (100%). **2)** Eye of the disease come on: right orbit was 7 cases, account for 46.7%, and left orbit was 8 cases, account for 53.3%.**3)** Follow up to October 2013, median time was 17 months (8-71months), 15 cases were followed. The niduses of 13 cases were complete absorbed, the niduses of 2 cases were most absorbed. In 15 cases, no patient was relapse. Five patients with strabismus and diminution of vision and eyes pain were recover after chemotherapy and no function obstruction.
Conclusions: Malignant orbital eosinophilic granuloma in children insidious onset, and atypical clinical manifestations, should pay attention to the differential diagnosis. Orbital eosinophilic granuloma in children sensitive to chemotherapy. The focus absorption rate by comprehensive treatment and follow-up is higher.

ICCCPO (PARENT/SURVIVORS)

EP-203

LATE EFFECTS OF RADIATION THERAPY AND THE POWERS OF NEUROPLASTICITY

L. Cadogan[1]

[1]Pediatric Oncology, BC Children's Hospital, Vancouver, Canada

Objectives: Description of the late effects that radiation therapy bears on adults who survived cancer as children and how it impacts their quality of life. Presentation will include current research, personal struggles faced as a childhood cancer survivor and information on different methods/programs that promote neuroplasticity.

EP-204

REHABILITATION OF CHILDHOOD CANCER PATIENTS- COLLABORATIVE EFFORTS OF SRCC -CENTRE FOR CHILD DEVELOPMENT (CCD) WITH TATA MEMORIAL HOSPITAL (TMH), & UGAM-CHILDHOOD CANCER SURVIVORS SUPPORT GROUP

S. Jha[1], E. Rawat-Pawar[1], S. Goswami[2], V. Dhamankar[2], M. Prasad[2], P. Kurkure[2], R. Jalali[3], A. Nagrulkar[3], S. Joshi[4], A. Garware[4]

[1]Survivorship, Ugam-Indian Cancer Society, Mumbai, India; [2]Pediatric oncology, Tata Memorial Hospital, Mumbai, India; [3]Neuro Oncology, Tata Memorial Hospital, Mumbai, India; [4]Rehabilitation, SRCC-Centre for Child Development (CCD), Mumbai, India

Objectives: To rehabilitate young cancer patients whose psychological and locomotor functions are affected due to treatment by providing therapy sessions in collaboration with SRCC- CCD rehabilitation centre

Methods: TMH collaborated with SRCC-CCD, multi specialty rehabilitation therapy centre in Mumbai to offer therapy for young cancer patients who have disturbance of their psychological and locomotor functions. Ugam-childhood cancer survivors support group under survivorship programme of Indian Cancer Society is responsible for implementation. An executive administrator of Ugam who is childhood cancer survivor is in charge of facilitating collaboration. The centre conducts physiotherapy, occupational therapy, speech therapy and educational therapy sessions to evaluate the patients. Patients are given ratings (Good, Fair, Poor) based on the aforesaid evaluation. A monthly report is sent to the hospital giving details of the assessment and the recommendation for follow up. The patient may or may not be advised follow up after giving due consideration to his/her sensory, Activities of Daily Living (ADL), psychological, and locomotor functions during the evaluation. These evaluations are done free of cost by SRCC-CDC.
Results: A total of 26 patients, median age 8Years (Range 2-15) are beneficiaries. There were 22/26 (85%) with brain tumors and 4/26 (15%) are non brain tumors, who received cranial irradiation; 12 reside in Mumbai & 14 are from outside Mumbai. Parental feedback regarding these sessions have been good in 80.8% and fair in 19.2%. Patients have shown overall improvement in their Activities of Daily Living after these therapy sessions.
Conclusions: SRCC-CCD has taken exceptional steps for rehabilitation of active cancer patients. These sessions have not only been a boon to the patients and their parents but also to the treating oncologists as they are able to deliver holistic care to the patients. It is expected that several eligible cancer patients will get benefited by this ongoing collaboration.

EP-205

LONG TERM TOLERANCE OF WHOLE ABDOMINO-PELVIC IRRADIATION IN CHILDREN WITH CANCER

V. Martin[1], V. Minard-Colin[2], N. Caussin-Bellier[3], O. Oberlin[4], J.L. Habrand[5], S. Sarnacki-Feray[6], H. Martelli[7], S. Bolle[8]

[1]Radiation Oncology, Institute Gustave Roussy, villejuif, France; [2]Pediatric Oncology, Institute Gustave Roussy, villejuif, France; [3]Pediatrics, Hôpital André Mignot, Le Chenay, France; [4]Pediatric Oncology, Institute Gustave Roussy, Villejuif, France; [5]Radiation Oncology, Centre François Baclesse, Caen, France; [6]Pediatric Surgery, Hôpital Necker Enfants Malades, Paris, France; [7]Pediatric Surgery, Hôpital du Kremlin-Bicêtre, Le Kremlin-Bicêtre, France; [8]Radiation Oncology, Institute Gustave Roussy, Villejuif, France

Objectives: To analyse the long-term sequelae in children who received whole abdomino-pelvic irradiation (WAPI) for cancer.
Methods: All patients with a follow-up longer than 5 years and treated during childhood for cancer with multimodal approach including WAPI at Gustave Roussy were reviewed. Data were collected from medical and technical files. Long-term toxicities were graded with the CTCAE v3.0.
Results: Twenty-six children were treated with WAPI between 1974 and 2006. Mean age at the time of irradiation was 5.9 years (1-17.5 years). Histologies were Wilm's tumor for 19 patients, Desmoplasic tumor (2), Clear cell sarcoma (1), Seminoma (1), Rhabdoïd tumor (1), Rhabdomyosarcoma (1) and Mesoblastic Nephroma (1). WAPI was delivered at the dose of 10 to 30 Gy by an anterior and a posterior field, with a boost in case of residual tumor. Contralateral kidney was protected at 12 Gy. Median follow-up was 13 years (5-26.4 years). Long term renal failure concerned 3 patients (1 grade I, 2 grade III) of whom 1 grade III also received nephrotoxic chemotherapy. Digestive disorders occurred in 5 patients: 1 grade I, 1 grade II and 3 grade III. On the 11 females, 6 needed treatment to induce puberty while the other 5 are still in prepubertal age. No endocrine disorder has been reported in males. Short stature, defined by height < 2 DS for age and sex, occurred in 4 patients. Scoliosis was observed for 2 patients. Secondary tumor occurred twice, one urothelial carcinoma and one chondrosarcoma of the ilium, both within the radiation fields.
Conclusions: Long-term sequelae of WAPI are limited except growth troubles (15.4%), secondary tumors (7.7%) and loss of ovarian function in all females. Thus, those patients need a close and prolonged follow-up and an ovarian tissue cryopreservation (at least for future in vitro oocyte maturation) for may be appropriate for females who underwent WAPI.

EP-206

RECEIVE, GIVE AND SUPPORT - A GERMAN CONCEPT THAT WORKS

F. Mauersberger[1]

[1]Deutsche Kinderkrebsstiftung/DLFH (German Childhood Cancer Foundation), Deutsche Kinderkrebsstiftung/DLFH (German Childhood Cancer Foundation), Halle/S., Germany

Objectives: The presentation will be about the concept "receive, give and support "of the Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation). The main goal of the concept is to have a good mixture of giving support to the young adults and getting back their experiences and initiatives to support other concerned youths.
Methods: The young adults receive special medical and social law support. The "give" includes the "tour on the Rainbow" and the mentoring-project. On the other handside, there is the support with seminars, camps and different topic courses for teaching the young adults.
Results: To have cancer as a young adult is a very difficult experience. The concept wants to gain a multidimensional view of the possibilities that can be achieved with this experience: the things we can learn during cancer and how to spread those impressions to others.
Conclusions: The aim of the concept is, that the young adults with and after cancer get a platform of exchange (receive), invest their own time and experience to support other concerned youths (give) and are supported in their personality (support). I like to strengthen this idea and present it to you.

EP-207

SURVEY PROJECT ON THE FATE OF MOROCCAN CHILDHOOD CANCER SURVIVORS

F. Msefer Alaoui[1], N. Benaicha[2], A. El Khattabi[3], L. Hessissen[4]

[1]childhood cancer, Association l'Avenir, Rabat, Morocco; [2]epidemiology and clinical research, CHU Hassan II, Fes, Morocco; [3]Survivors, Association l'Avenir, Rabat, Morocco; [4]Pediatric Oncology, Children Hospital of Rabat, Rabat, Morocco

Objectives: The present survey objectives are to establish a database of Moroccan childhood cancer survivors, to gather information about their current status, to meet their needs for treatment or prevention, and to lay-out a strategy of long-term monitoring in terms of prevention, early detection, treatment, and social-emotional support.
Methods: The survey will target Moroccan patients who have been treated completely or partially in Rabat from childhood cancer, which diagnosis has been put at least 10 years ago. The data to be collected will include civil status at diagnosis, cancer's characteristics, its treatment and evolution, and current medical and social status. In order to reach the survivors, we will be using several means including phone, email, social networks, and postal mail. The questionnaire would be completed by the survivors themselves, their parents or their physician. We have hired as project coordinator a fellow epidemiologist who will write her thesis on this survey subject. The project duration is expected to be about 12 months including: survey preparation, distribution and collection of the questionnaire, analysis of the results, writing and publishing the survey's findings. The project budget includes the coordinator's salary, training and meetings expenses and it would be financed by the Terry Fox Run which took place in Rabat, Morocco, on February the 16th 2014 as International Childhood Cancer Day's event.
Results: In 2010, when "the Path of Hope" association was founded, 300 Moroccan childhood cancer survivors attended the meeting or gave information by phone or mails. Many of them were doing well, but others were suffering from medical, educational or behavioral problems.
Conclusions: In conclusion, this survey will be crucial to establish a database on the Moroccan childhood cancer survivors in order to have a long-term monitoring system that will include key referential information, medical and social support at the national level.

EP-208

THE L'AVENIR ASSOCIATION: 28 YEARS SUPPORTING CHILDREN WITH CANCER IN MOROCCO

F. Msefer Alaoui[1], F. Chraibi[1], L. Hessissen[1]

[1]Childhood Cancer, Association l'Avenir, Rabat, Morocco

Objectives: In the developed countries, parents' groups are created to enhance research and well being of their children. In developing countries, associations of families are very rare and their first aim is to provide financial resources for treatments.
Methods: "L'Avenir' Association is one of the first parents of children with cancer associations in developing countries. It was established in 1986 by caregivers and parents of cancer patients. At that time, the State had many other problems to face such as infectious and nutritious diseases. Since its creation, the 'l'Avenir' has been getting stronger and more efficient; services provided are numerous: drugs, equipment, schooling, entertainment, housing, awareness, early diagnosis training and financial support. It has developed partnership with 'St Jude Research Children Hospital' to improve education, diagnosis and care in paediatric oncology. The 'l'Avenir' works with the hospital's caregivers, other cancer organizations and state departments. It has set up a local section in Fes and initiated a group of survivors 'the Path of Hope'. In 1995, 'l'Avenir' has built a parents' house to provide accommodation for families who don't live in Rabat, to soften treatment conditions and to decrease treatment and follow up abandonments. 'La Maison de l'Avenir' is spacious: 22 bedrooms, a kitchen, dining room, living room, playroom,. It provides meals to the families who have to pay only about 1 USD a day per adult. Since its opening, 3000 families have spent 10 days (1 to 60 days), 5 times a year (1 to 16 times). The house is run by the 'l'Avenir' which organizes fund raising events.
Results: La Maison de l'Avenir has significantly allowed to decrease treatment abandonment, and so, contributes strongly to cure children with cancer.
Conclusions: Parents or friends groups in developing countries can achieve remarkable results improving social and medical conditions of the patients.

EP-209

HAYIM FOR CHILDREN WITH CANCER IN ISRAEL ASSOCIATION - IN THE SERVICE OF CHILDREN WITH CANCER IN ISRAEL

D. Orren[1]

[1]Hayim Association, Ramat Gan, Israel

Objectives: The Hayim Association was founded by parents of children with cancer in 1984. This voluntary organization is active in all Children's Oncology wards throughout Israel with the goal of assisting and reducing the suffering of children and their families, and to improve the quality of health care. The association operates in all the medical centers nationwide, and is part of the oncology wards. The association is a member of ICCCPO.
Methods: Main activities: Supporting the Israel Medical Association for Pediatric Hematology and Oncology in gathering and coordinating medical information on child cancer. Purchase of sophisticated equipment for improving diagnosis and treatment. (i.e. PFAX for early diagnosis of Leukemia, Vapor-Phase Refrigerators for storing stem cells etc.) Funding studies and development of sophisticated methods for improving diagnoses and directing optimal care. Improving the professional standards of medical, paramedical and psychosocial personnel, by funding participation in local and international conventions and seminars. Fostering and improving the children's welfare and supporting surroundings: Supporting families with financial problems due to their child's disease. Funding transport for treatments. Funding support groups for better coping with the disease. Arranging trips and fun days for children and their families in Israel and abroad. Monthly fun flights of children. Assistance in classes and play corners in hospitals. Individual tuition of children during and after treatment. Grants and scholarships for children during their rehabilitation.
Results: The association's achievements include: Assistance in establishing a night care ward for children with cancer, the first of its kind in Israel, in the Rabin Medical Center. Assistance in setting up a bone marrow transplant ward for children in Schneider Hospital, the first in Israel. Standardization of medical and psychosocial care among the various centers in Israel. Improvement of child welfare and hospitalization conditions.
Conclusions: Much more must be done.

EP-210

OVERVIEW OF PEDIATRIC AND ADOLESCENT MALIGNANCY AND ITS SCOPE AND CHALLENGES IN NEPAL

S. Panthee[1], K.S. Sharma[1]

[1]*NA, Children cancer foundation -Nepal, Bharatpur, Nepal*

Objectives: To find occurrence and type of pediatric malignancies, estimated cancer burden and facility required to treat.
Methods: We have collected data from hospital based national cancer registry of Nepal from 2003 to 2010 and division of pediatric oncology of B P Koirala memorial Cancer Hospital (BPKMCH) from 1999 to 2013. Data were analyzed for the occurrence and relative frequency of pediatric cancer in Nepal.
Results: 2000 new pediatric cancer reported from 2003 to 2010 in HBCR, and 2000 new cases reported at BPKMCH (1999 to 2013), division of pediatric oncology. In BPKMCH there were leukemia (28%), Lymphoma (18%), Bone sarcoma 166 (12%), Brain tumor (6%), Retinoblastoma (6%), Germ cell tumor (4%), wilms tumor (4%), Skin and epithelia neoplasm (2%), Hepatoblastoma (1%), Neuroblastoma (2%), ENT and others (15%). In national wide HBCR, there was leukemia 502 (34%), Lymphomas 172 (12%), Bone sarcomas 166 (11%), Brain tumors 96 (7%), Retinoblastoma 94 (6%) GCT 65 (4%), Neuroblastoma 42 (2%), epithelial neoplasms 28 (2%), Hepatoblastoma 20 (1%) and Others 116 (9%). As there were 26 million of children 19 years of age in 2011 census, average incidence of childhood cancer are about 120/millions/year. There are 1459 new cases each year.
Conclusions: here are 4 pediatric oncologists and 50 beds available within Nepal, which is very much insufficient. Present bed capacity and oncologists can't cure more than 200 patients in a year. Large number of patients does not have treatment access due to inadequate human recourses and facilities. To give cancer treatment and care to 1450 new cases each, there should be 500 beds and 60 pediatric oncologists along with other supporting subspecialty experts and resources. We can cure more than 70% of pediatric cancer at low cost, this will save almost 1000 life each year.

EP-211

PSYCHOSOCIAL NEEDS OF AND SERVICES FOR LONG-TERM SURVIVORS (AGE > 27 YRS.)

D. Schmid[1]

[1]*Deutsche Kinderkrebsstiftung, Bonn, Germany*

Objectives: Today, the majority of children with cancer become long-term survivors. However, long-term survivorship often comes with different psychosocial problems beside medical side effects of the cancer treatment. Even adult survivors of childhood cancer are at risk for various social and psychological sequelae. Therefore there is a need for services especially for this steadily increasing group. This presentation is about the psychosocial needs of long-term survivors (age > 27 yrs.) and shows the services of the Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation) for long-term survivors.
Methods: The Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation) owns the Waldpiratencamp, a camp for childhood cancer patients, survivors and their family. At this camp in Heidelberg there are also camps especially for adult survivors of childhood cancer. Since 2011 there is one seminar yearly for long-term cancer survivors > 27 years, arisen through urgent questions of survivors: How do I tell people (especially my malefriend/ femalefriend) I am a cancer survivor? What are people going to think? Will anyone want to date me? Is it okay for me to have sex or be on birth control pills? Etc. Open and frank discussions of these sensitive topics may prevent unnecessary hurt and stress.
Results: Older childhood cancer survivors have other needs than younger ones. Seminars that are exclusively for adults > 27 years are always fully booked.
Conclusions: Services especially for long-term survivors age > 27 years are essential.

EP-212

YOUTH AND THEIR FUTURE - GUIDANCE INTO WORKFORCE FOR CHILDHOOD CANCER SURVIVORS IN AUSTRIA

C. Schneider[1], A. Kienesberger[1]

[1]*Österreichische Kinder-Krebs-Hilfe, Österreichische Kinder-Krebs-Hilfe, Vienna, Austria*

Objectives: Former childhood cancer patients often face difficulties to enter workforce. Some have to deal with cognitive impairments, others have to cope with reduced long-bearing capacity. Further, many patients have problems communicating "gaps" in their CVs due to recent cancer treatments. In some cases patients also have to deal with prejudiced employers and co-workers, who "stigmatize" former childhood cancer patients and underestimate their abilities. So there is an urgent need for an initiative that supports former patients on their way entering workforce.
Methods: We had been looking for a suitable solution for former patients in Austria for a long time. Finally, an appropriate project was found in Munich, Germany, which has been running successfully since 2006. Therefore, we used the German model as a base for the Austrian intervention.
Results: In Austria the project 'Youth and their Future' started in the beginning of 2012 – in cooperation with local hospitals, the Austrian Childhood Cancer Organization (ACCO) and 'die Berater' (a leading consultancy focusing on coaching and training). In the context of this collaboration the three institutions adopt different roles: While the hospitals recommend former patients to the ACCO (which funds the project), the consultancy provides, based on many years of experience, individual support for the clients. Amongst other things, their service includes personality development, clarification of physical and psychological abilities, career advice and application coaching.
Conclusions: The Austrian Childhood Cancer Organization feels obligated to support former childhood cancer patients also after their medical treatment. Especially former brain tumor patients need professional support to find "their" place in the world of workforce. For these patients a fixed trainee position or a regular working condition is of great importance by means of gaining economic independence, financial security and a stronger position within society.

EP-213

WORKING TOGETHER TO WIN THE BATTLE AGAINST CANCER - LIVING A BETTER LIFE AND GIVING BACK TO THE COMMUNITY

M. Wan[1]

[1]*mutual support, Little Life Warrior Society, Hong Kong, Hong Kong China*

Objectives: To carry on our vision "Working Together to Win the Battle Against Cancer – Living A Better Life and Giving Back to the Community"
Methods: Ever since the establishment in 2002, the Little Life Warrior Society (LLWS) has grown from a relatively modest self-help and basically run by voluntary helpers to a unique model of providing mutual support services to cancer children and their parents in the community. The LLWS provides a much-needed platform where cancer children and their parents can get support from other families going through the same experience. In 2009, the LLWS, was registered as a charity society in Hong Kong. In 2010 Home of the Little Life Warriors was officially opened at the Cancer Centre to provide a comfortable area for the patients and their family members to rest and to play while waiting for outpatient treatment. Also, tutorial classes are arranged to help children catch up their schoolwork.
Results: With the generous help of many supporters over the decade, the Little Life Warrior Society has raised public awareness of childhood cancer and reached out to the Mainland China and the International stage. The numbers of our members was 1249 people in 2013. Nine Little Life Warrior Societies in the Mainland China were established and the impact of their work on the many childhood cancer patients and their families.
Conclusions: After all these years, the vision of Little Life Warrior Society has remained solid. The small warriors have grown up into big warriors and become volunteers of the Society to serve the childhood cancer patients in the hospital. Using the Home of Little Life Warrior as a reference to set up a Children Cancer Patients Resources Centre in Hong Kong Children Hospital which is can be put into service in 2018.

EP-214

FIGHT YOUR SPIRIT TO CONQUER YOUR CANCER

S. Zakaria[1]

[1]*Foundation, Indonesian Childhood Cancer Foundation (YOAI), Jakarta, Indonesia*

Objectives: As survivor I would like to motivate other cancer patients to have the same spirit as when I was a patient. After the diagnosed, I have so many new goals that I want to complete in my life. I want to help all of my friends who suffered from cancer by giving them support. I think that supporting is one thing they needed most to keep their spirit, so they don't give up in the middle of their treatment.
Methods: Its obvious that during the medical treatments there were times when I felt so sad and even depressed. My sister asked me to write something like a journal to help me to feel better. And to be honest I didn't think that writing would really do, until I finally began to write after a couple of days. Since I love singing I was thinking why don't I make my writing into something that everyone can enjoy? So I started writing a couple of songs based on my experience and the diary that I have been writing. After gathering all the songs that I wrote I made an album.
Results: With the help of my family I was able to produce an album that I made. My thought was when I sell my album I will donate 40% of the income for the cancer patients through the Indonesian Childhood Cancer Foundation (YOAI). In fact I would love to be able to donate for other children with cancer throughout the world through their foundation.
Conclusions: Up to present I am still Writing songs in English and Indonesian. And for the time being I have been distributing my album to several friends. I was able to give several album to the foundations at ICCCPO Conference in Hongkong. I wish my idea will inspire other cancer patients.

LATE EFFECTS

EP-215

RISK FACTORS ASSOCIATED WITH ANTHRACYCLINE INDUCED CARDIAC DYSFUNCTION IN PEDIATRIC PATIENTS

A. Shaikh[1], M.M. Alam[1], A. Saleem[1], M. Ahmed[1]

[1]Pediatric & Child Health, Aga Khan University Hospital, Karachi, Pakistan

Objectives: Anthracyclines have significant impact on outcome in many pediatric chemotherapy protocols and therefore remain the mainstay of treatment. The aim of this study was to identify the risk factors for anthracycline induced cardiac dysfunction in pediatric oncology patients.
Methods: We performed a prospective cohort study during July 2010- Jun 2012 at Aga Khan University Hospital, Pakistan. All pediatric oncology patients aged 0 to 16 years, who received anthracycline as a chemotherapy and remain in regular follow up for at least 1 year post chemotherapy, were included for final analysis.
Results: Out of 110 patient, 75 (66%) were males and mean age was 74 ± 44 months. ALL ($n = 70$, 64%) was the most common primary diagnosis followed by lymphoma ($n = 19$; 17%) and AML ($n = 12$, 11%). Doxorubicin alone or in combination was used in ($n = 94$, 85%) of patients and cumulative doses 300mg/m2 ($p < 0.001$, OR: 7) and mode of delivery (p 0.048, OR 9.7) were also found statistically significant.
Conclusions: Anthracycline induced cardiac dysfunction is mostly related to cumulative dose > 300mg/m2, radiation therapy and sepsis. Regular long term follow up with cardiologist is the key point for early diagnosis and therapy for a long term survival.

EP-216

ANTHRACYCLINE INDUCED ACUTE AND EARLY ONSET MYOCARDIAL DYSFUNCTION IN CHILDHOOD MALIGNANCIES

S. Shaikh[1], M.M. Alam[1], A. Saleem[1], S. Mohsin[1], M. Ahmed[1]

[1]Pediatric & Child Health, Aga Khan University Hospital, Karachi, Pakistan

Objectives: Anthracyclines (i.e., doxorubicin, daunorubicin) are the backbone of chemotherapy for most childhood malignancies but are well known for their cardiotoxicity, which includes cardiomyopathy with systolic and/or diastolic dysfunction, arrhythmias and pericardial effusion. The objective of this study was to identify anthracycline induced acute and early onset chronic progressive cardiotoxicity in various childhood malignancies.
Methods: All children who received anthracycline as chemotherapy and three echocardiographic evaluations (baseline, one month and 1 year) at Aga Khan University, Karachi between July 2010 and June 2012, were prospectively analyzed for cardiac dysfunction. Statistical analysis across systolic and diastolic dysfunction at baseline, 1 month and 1 year were made by repeated measures analysis of variance (ANOVA).
Results: Among 110 study participants,75 (68.2%) were males. Mean age was 74 ± 44 months, majority 70 (64%) of them were Acute lymphoblastic leukemia (ALL). Doxorubicin alone was used in 59 (54%) and combination therapy was used in 35 (32%). Fifteen (14%) children developed cardiac dysfunction at 1 month while 28 (25%) children within a year. Of these 10/15 (66.6%) & 16/28 (47.2%) had isolated diastolic dysfunction respectively while 5/15 (33.3%) and 12/28 (42.8%) had combined systolic and diastolic dysfunction at 1 month and 1 year echocardiography respectively. Seven (6.4%) patients expired due to severe cardiac dysfunction.
Eight (14%) children receiving doxorubicin showed dysfunction mostly related to higher cumulative dose ($p < 0.001$).
Conclusions: Our study reports a high incidence of anthracycline induced cardiotoxicity. Presence of ALL, high cumulative dose, doxorubicin alone or in combination with daunorubicin and patients with trisomy 21, AML, Ewing sarcoma were identified as high risk.

EP-217

EVALUATION OF IRON OVERLOAD IN ACUTE LYMPHOBLASTIC LEUKEMIA AFTER THE END OF TREATMENT

K. Arjmandi Rafsanjani[1], L. Rohani[2]

[1]Hematology Oncology, Iran University of Medical Sciences, Tehran, Iran; [2]MD, Tehran University of Medical Sciences, Tehran, Iran

Objectives: Leukemia is the most common malignancy in children. Treatment of the disease causes bone marrow suppression that necessitates excessive blood transfusion. The aim of this study was to evaluate iron overload by assessing serum ferritin level in Acute Lymphoblastic Leukemia (ALL) and its correlation with number of blood transfusion in children under 15 years of age.
Methods: During this study patients who were referred to oncology department of Ali-Asghar children hospital and had known ALL were enrolled. Serum level of ferritin, serum iron, TIBC and transferin saturation at the end of treatment, 6 months and 12 months after treatment were evaluated. Patients with signs of infection or any inflammation were excluded. At the end all data were analyzed by SPSS version 18 software.
Results: 50 patients were evaluated (30 males and 20 females). Mean serum iron was 94.8 ± 14.3. Mean TIBC was 316.1 ± 15.5. Transferin saturation was 30%. Mean value of ferritin were 637.1 ± 179.2, 380.4 ± 146.4 and 201 ± 73.3 at the end of treatment, 6 months and 12 months after treatment. Mean number of transfusion was 7.9 ± 1.02 (2-16). There was significant correlation between serum level of ferritin and number of transfusion.
Conclusions: Present study showed that after treatment of ALL serum level of ferritin is high comparing normal values. Number of blood transfusion was proved to be the only determining factor for iron overload.

EP-218

A FEASIBILITY PILOT STUDY OF SETTING UP A FERTILITY CLINIC FOR SURVIVORS OF CHILDHOOD CANCER TREATMENT IN INDIA

P. Arora[1], R. Misra[2], S. Mehrotra[3], S. Sharma[3], P. Bagai[3], R. Arora[4]

[1]Reproductive Medicine, Nova IVI Fertility Clinic, New Delhi, India; [2]Medical Oncology, Medanta - The Medicity, Gurgaon, India; [3]Parent Support Group, Cankids…Kidscan, New Delhi, India; [4]Medical Oncology, Max Super-Speciality Hospital, New Delhi, India

Objectives: Cancer in children and its treatment has implications for their future fertility. Hitherto, there have been no studies on fertility preservation or infertility management for these patients from India. This study was a pilot initiative to address this gap.
Methods: Childhood cancer survivors who either work or whose parents work for Cankids…Kidscan were invited to attend a late-effects clinic focussed on fertility from Dec 2013 to Mar 2014. The survivor was seen by a paediatric oncologist and a reproductive medicine specialist.
Results: 20 survivors (70% males) with median age 18.5 years (range 13-30 years) who were off treatment for median 7 years (range <1-16 years) were seen. Original diagnosis was ALL 12 (including 2 relapses), AML 2, NHL 3, Retinoblastoma 1, Wilms 1, Bone sarcoma 2, Gonadal GCT 1. Any alkylating agent exposure was seen in 14 (70% survivors), most commonly cyclophosphamide median dose 3000mg/m^2 (range 900-6600mg/m^2). Any radiotherapy exposure was seen in 12 (60%), 18Gy cranial radiotherapy for ALL in all and testicular radiation in one. One survivor had gonadal surgery for ovarian dysgerminoma. No one had a HSCT. Based on clinical and treatment variables 14 (70%) survivors were classified as low risk for infertility, 4 (20%) as medium risk and 2 (10%) as high risk. All except one (13 year old) had achieved puberty. Hormonal and semen analysis was requested where appropriate. None was planning to start a family. None had received counselling on fertility preservation at the time of diagnosis.
Conclusions: A late-effects fertility clinic for survivors of childhood cancer treatment in India is feasible and can be part of an overall survivors clinic. When resources are limited, appropriate risk grouping can identify which children can benefit from fertility preservation and which need early intervention once cancer treatment is complete.

EP-219

AN INSIGHT INTO THE BIOMARKERS OF OBESITY IN SURVIVORS OF ACUTE LEUKEMIA

A. Batra[1], R. Shrivastava[1], A. Tyagi[1], D. Dhawan[1], L. Ramakrishnan[2], S. Bakhshi[1]

[1]Medical Oncology, Dr. BRA IRCH AIIMS, New Delhi, India; [2]Cardiac biochemistry, All India Institute of Medical Sciences, New Delhi, India

Objectives: Acute lymphoblastic lymphoma (ALL) survivors are predisposed to obesity, and consequently increased risk of death due to cardiovascular diseases. The exact mechanism of

obesity is not known, although it has been attributed to steroids, cranial irradiation and consequent hypothalamic disturbances. The study was done to assess the prevalence and potential biomarkers of obesity in the survivors of acute leukaemia patients.
Methods: This is a cross-sectional study conducted at All India Institute of Medical Sciences in the survivors of acute myeloid leukaemia (AML) and ALL who had completed the treatment atleast one year before enrolment in this study. The prevalence of obesity was studied by determining the body mass index (BMI). A BMI of more than 85th percentile is classified as overweight and more than 95th as obese. Potential biomarkers were studied by assessing serum leptin, resistin and adiponectin levels by ELISA and were compared between the obese and non-obese leukaemia survivors.
Results: 159 acute leukaemia (126 ALL and 33 AML) patients were enrolled in the study with a median follow up of 36.8 months post treatment. The median age was 10 (range: 3-18) years. 123 (77.3%) patients were males. The prevalence of overweight/obesity in acute leukaemia survivors was 27%, compared to 10% in 40 normal healthy controls. The mean serum leptin and resistin levels were similar in obese and non-obese leukemia survivors (3.7 vs 2.85 pg/mL, $p = 0.064$; 8.01 vs 9.33 ng/mL, $p = 0.36$). However, the mean serum adiponectin levels were significantly lower in the obese leukaemia survivors as compared to non-obese leukaemia survivors (7.97 vs 11.5 (g/mL, $p = 0.023$).
Conclusions: The prevalence of obesity is higher in acute leukaemia survivors. The lower levels of adiponectin in obese leukemic survivors may be one of the mechanisms for predisposition in the survivors of acute leukaemia.

EP-220

HEALTH-RELATED QUALITY OF LIFE AND FUNCTIONAL OUTCOMES OF CHILDREN/ADOLESCENT SURVIVORS OF MALIGNANT BONE TUMORS

P. Berlanga[1], M. Salom[2], A. Cañete[3], V. Castel[1]

[1]Cancer Clinical and Translational Research Group, Instituto de Investigacion Sanitaria La Fe, Valencia, Spain; [2]Pediatric Orthopedics Unit, Hospital La Fe, Valencia, Spain; [3]Pediatric Oncology Unit, Hospital La Fe, Valencia, Spain

Objectives: Health-related quality of life (HRQL) is an important outcome measure due to increasing survival rates. Although HRQL in long term-survivors of pediatric cancer is mostly comparable with that of the general population, bone tumors HRQL is relatively poor compared with other cancer survivors. We aim to assess HRQL and functional performance in these survivors in order to establish individualized programs to promote early detection of chronic health problems.
Methods: Prospective cross-sectional study of a cohort of malignant bone tumor survivors, < 21 years old at diagnosis and > one year off therapy with no evidence of disease at inclusion in study. All patients were interviewed by a pediatric oncologist and an orthopedic surgeon. The Health Utilities Index (HUI3) was used to measure HRQL and the Musculoskeletal Tumor Society Score (MSTS) to assess physical disability. Bone tumor HRQL was compared to age- and sex- matched leukemia/lymphoma survivors. Data was analyzed using SPSS 20.0.
Results: Fifteen osteosarcoma and eleven Ewing sarcoma patients were included, median age at diagnosis of 10.8 y (2.4-20.8), at evaluation of 22.6 y (range: 11.1-45.5) and follow-up of 10.0 years (range: 2.1-27.6). Fourteen were male and twelve females. Seven patients had undergone amputation. 81% of bone tumor survivors rated their health state as good/very good/perfect compared to 100% of leukemia/lymphoma group ($p = 0.019$). HUI3 multi-attribute score in bone tumor group was significantly lower (0.74 vs 0.89, $p = 0.038$) as well as ambulation and pain single-attribute scores (0.95 vs 1.00 $p = 0.026$; 0.93 vs 0.98, $p = 0.044$, respectively). Median MSTS score was 83% (range: 13-100%).
Conclusions: Malignant bone tumor survivors have poorer overall HRQL compared to age- and sex- matched leukemia/lymphoma survivors, however most consider their health state as good/very good/perfect. Long-term follow-up focused in adequate pain control and impairment-driven rehabilitation in this group of patients is needed.

EP-221

UTILISING A REQUIREMENTS MANAGEMENT APPROACH TO INTEGRATE USER AND PROFESSIONAL VIEWS INTO THE DESIGN OF A TEENAGERS AND YOUNG ADULTS (TYA) CANCER SURVIVORSHIP SERVICE

P. Beynon[1], L. Hartley[1], J. Cheshire[1], A. Cameron[2], S. Dolby[3], A. Badger[1], C. Ewer-Smith[1], P. Spencer[1], E. Fynn[1], M. Stevens[1]

[1]On Target, University Hospitals Bristol NHS Trust, Bristol, United Kingdom; [2]TYA Cancer Service, University Hospitals Bristol NHS Trust, Bristol, United Kingdom; [3]Psychological Health Services, University Hospitals Bristol NHS Trust, Bristol, United Kingdom

Objectives: Interventions applied early after cancer diagnosis may be the most effective way to help TYA patients re-establish life-trajectory during and after treatment. These should be informed by patient/professional experience but integrating such views into delivery of patient care demands a structured approach to the collection and prioritisation of data. Requirements Management (RM), a systems engineering process, was used to evaluate and develop a regional TYA clinical service.
Methods: Data was sought by postal questionnaire/interview/focus group (patients $n = 108$; family/friends $n = 32$); online questionnaire/interview (professionals, $n = 219$). Each data item was extracted and summarised as a 'Finding' then assessed for underlying 'Requirements' for change to care/delivery of the service. For example, a patient 'Finding' about exercise: 'Going to a public gym wouldn't be comfortable. Fears about being exposed/judged' generated two different, possible 'Requirements': (1) 'Patients need access to sports/health facilities which afford a sense of privacy/protection from the public' and (2) 'Patients should be offered psychological support to help them deal with feelings of being different and/or perceptions of being judged negatively'. All Requirements derived in this way were evaluated against factors reflecting health policy and practical applicability, including: Benefits achievable in terms of Quality/Innovation/Productivity/Prevention/Personalised care (QIPPP); Difficulty (Very Difficult-Very Easy); Priority (Must/Should/Could/Would do); Benefit to Service (None-High); Benefit to Patient (None-High).
Results: There were 1,764 individual findings generated 3,332 requirements, reduced to 184 unique requirements after review/de-duplication. These were then prioritised (selecting those considered easiest to achieve with high direct benefit to patients) and used to design interventions to modify/enhance patient care in areas such as physical and psychological wellbeing, work mentoring and staff training.
Conclusions: RM is a useful tool to support service development based on user/professional views using large volumes of data and when applied alongside methodologies such as co-creation/co-design accurately responds to user needs. An audit trail links each 'Finding' to a final step in service change.

EP-222

USING THE FATIGUE THERMOMETER TO SCREEN ADOLESCENT AND YOUNG ADULT BRAIN TUMOR SURVIVORS

S. Brand[1], C. Chordas[2], C. Liptak[1], P. Manley[2], C. Recklitis[2]

[1]Psychosocial Oncology, Dana-Farber Cancer Institute, Boston, USA; [2]Pediatric Oncology, Dana-Farber Cancer Institute, Boston, USA

Objectives: Cancer related fatigue (CRF) is one of the most common and distressing symptom experienced by adolescent and young adult (AYA) cancer survivors and may disproportionately affect brain tumor survivors. While national guidelines recommend screening for CRF during routine follow-up, data supporting specific screening measures is limited. The objective of this study is to assess the validity of a one-item Fatigue Thermometer (FT) measure for assessing fatigue in AYA brain tumor survivors.
Methods: 142 survivors (age 12-32) with a median time since diagnosis of 10.5 years (range 2.4 – 28 years) completed the 1-item Fatigue Thermometer (FT) and the 18-item Multidimensional Fatigue Scale (MFS) at a single clinic visit.
Results: 57 survivors (40%) were identified as clinically fatigued on the MFS. ROC analysis indicated good concordance between the FT ratings and the MFS criterion ($AUC = 0.812$), but no FT cut-off score to reliably identify survivors with elevated MFS scores was identified. A low FT cut-off score of 1 had good sensitivity (93%), but poor specificity (59%), and higher FT cutoff scores of 3 had good specificity (78%), but missed too many cases of fatigue identified by the MFS (sensitivity = 65%). No FT cutoff score met study criteria for screening accuracy (sensitivity $\geq$.85 & specificity $\geq$ 0.70).
Conclusions: Results from this study indicate the FT, a single-item screening measure for fatigue, is not able identify clinically significant fatigue in AYA brain tumor survivors. Results are discussed in the context of research on other "ultra-brief screening measures as well as clinical and research implications of the findings.

EP-223

ANTICANCER CHEMOTHERAPY AND DEVELOPMENTAL ANOMALIES OF TEETH IN CHILDREN

E. Krasuska-Slawinska[1], A. Brozyna[2], B. Dembowska-Baginska[2], D. Olczak-Kowalczyk[3]

[1]Dental Surgery Clinic for Children, The Children's Memorial Helath Institute, Warsaw, Poland; [2]Pediatric Oncology Department, The Children's Memorial Helath Institute, Warsaw, Poland; [3]Department of Pediatric Dentistry, Medical University of Warsaw, Warsaw, Poland

Objectives: Anticancer treatment during childhood carries a risk of dental anomalies and denticles. Aim: correlation of developmental anomalies of teeth with type of anticancer drugs administered and chemotherapy related early complications
Methods: Sixty patients who completed anticancer treatment (median 4.9 ± 3.4 yrs from treatment completion) and 60 healthy children aged 6-18 years were assessed. Clinical and radiological evaluation was performed and included assessment of enamel anomalies (DDE-Index), anomalies in the number, size and tooth structure. Medical records were reviewed and data collected on; tumor type, age at diagnosis and treatment, chemotherapy duration, type/doses of anitcancer agents, emesis and mucositis during treatment and its severity (according to CTCAE v 4.0 criteria). Statistical analysis was performed using U Mann –Wihitney and Spearman test.
Results: Children treated with chemotherapy had statistically higher incidence of enamel anomalies, teeth agenesis, microdontia, root shortening, taurodontism and denticles as compared to health controls. Administration of vincristine and its total dose correlated with every type of tooth anomaly, cyclophosphamide, ifosfamide, doksorubicin, with hypodontia, microdontia, root shorteneing and enamel anomalies, etoposide and cisplatin with microdontia, root shortening, enamel anomalies, methotrexate, teniposide with root shorteneing and carboplatin with denticles and enamel anomalies. Mucosistis and emesis potentiated root shortening, microdontia and enamel anomalies.

Conclusions: Chemotherapy and its early complications (emesis and mucosistis) result in development of dental anomalies. Vincristine, cyclophosphamide/ifosfamide and doxorubicin are anticancer agents which most likely have the greatest impact on the incidence of these complications. Mucositis and emesis add to the severity of the anomalies.

EP-224

HEALTH OUTCOMES OF CHILDHOOD MEDULLOBLASTOMA/PNET. ONE CENTER RESULTS

B. Dembowska-Baginska[1], A. Brozyna[1], M. Drogosiewicz[1], M. Perek-Polnik[1], E. Swieszkowska[1], I. Filipek[1], M. Tarasinska[1], J. Korzeniewska[1], D. Perek[1]

[1]Pediatric Oncology Department, The Children's Memorial Helath Institute, Warsaw, Poland

Objectives: Assessment of health outcomes in survivors of childhood medulloblastoma/PNET (MB/PNET).
Methods: 113 MB/PNET patients (70 males 43 females) at least 2 yrs (median 5.5 yrs) from treatment completion were examined. Median patient's age at MB/PNET diagnosis was 8 yrs 2 m, at assessment 14.5 yrs. All patients were treated with surgery, cranio-spinal irradiation, chemotherapy and followed-up in our clinic. Health problems were assessed and graded according to CTC AE v 3.0 criteria.
Results: The following health problems were recorded: decreased physical activity -38% of patients, neurological disorders- 32%, fatigue - 60%, IQ below average -40%, short stature <3percentile – 46.6%, hypothyreoidism- 17%, renal dysfunction-15%, hearing impairment-87%, requiring hearing aids-56%, dental caries 100%, other dental 68%, musculoskeletal 23%, skin -60%, BMI <18 - 28%, >25-16%, second malignancy 4pts. Among 112 patients there were 678 adverse health events. Ninety% of patients demonstrated at least 1 health problem, 75% more than 5 (median 6 health problems to one patient) of which 15% were severe and life-threatening (CTC AE- grade3 and 4). Four patients developed second malignancy –AML-2 pts, 2 pts MDS.
Conclusions: Survivors of childhood MB/PNET are at high risk of developing various, multiple, chronic and acute health conditions. Due to complexity of the observed adverse health problems lifelong, careful follow-up of children cured from MB/PNET is essential.

EP-225

HEALTH PROBLEMS IN SURVIVORS OF CHILDHOOD SOLID TUMORS

A. Brozyna[1], B. Dembowska-Baginska[1], I. Daniluk[1], O. Rutynowska[1], A. Kolodziejczyk-Gietka[1], O. Gryniewicz-Kwiatkowska[1], M. Drogosiewicz[1]

[1]Pediatric Oncology, The Children's Memorial Helath Institute, Warsaw, Poland

Objectives: Evaluation of health status of 151 consecutively presenting children followed-up after treatment of solid tumor (excluding CNS tumors).
Methods: 151 patients (79 males, 72 females), median age at examination of 15yrs (8 yrs 2m at tumor diagnosis) were examined. At least 2 years elapsed since treatment completion. There were survivors of NHL -30pts (B-22, T-7, DLBCL-1), Hodgkin Lymphoma- 20, Soft Tissue Sarcoma (STS) - 27, Bone sarcoma -17 (Ewing/PNET-8, osteosarcoma-9), Wilms tumor-13, Hepatoma -7 (HBL-6, HCC-1), Retinoblastoma-16, Mixed Germ Cell Tumors-13 (ovary-10, testes-3) and other-8. Their treatment followed tumor specific protocols. Patients were examined by physician and their health status was assessed and graded according to CTC AE v3.
Results: Among the 151 survivors there were 5 children with genetic syndromes (NBS-1 pt, NF1-4). Nutritional status was normal in 65%, obesity-23.8%, undernurished-11.2%. Short stature was observed in15.8%. All but 4 patients (2.6%) presented with at least one of the following health issues: endocrinopathy (33%), nephropathy (15.9%), skin abnormalities (21.2%), bone and skeletal deformations (34.4%), osteoporosis (9.3%), immunological and *hematological* (5.3%), neurological (13.2%), gastrological (16.5%), cardiological (27.1%) disorders, hearing and sight impairment (9.8%), dental caries (10%), psychosocial (7.2%) and psychiatric (5.3%) problems. Two patients had a history of second malignant neoplasm (Ewing sarcoma/PNET-1, AML-1). Over 97% of patients presented with at least one disease and therapy related health problem requiring treatment and close follow-up.
Conclusions: Disease and treatment related complications are common in survivors of childhood malignancy. Due to a wide spectrum of observed health problems children cured from solid tumor should be followed up lifetime and when transitioning to adults care specific recommendation should be given for further medical and psychosocial assistance.

EP-226

SECOND MALIGNANT NEOPLASMS (SMN). REPORT FROM ONE CENTER

B. Dembowska-Baginska[1], A. Brozyna[1], I. Filipek[1], M. Drogosiewicz[1], M. Perek-Polnik[1], W. Grajkowska[2]

[1]Pediatric Oncology Department, The Children's Memorial Helath Institute, Warsaw, Poland; [2]Pathology Department, The Children's Memorial Helath Institute, Warsaw, Poland

Objectives: Second malignant neoplasms (SMN) are the most serious complications of anticancer treatment. Since childhood malignancies have a cure rate of 75% and since there is a growing number of patients with SMN assessing the risk of such conditions is mandatory. The aim of our study was to review patients with SMN treated in our department.
Methods: Clinical features of patients with SMN; gender, age, primary diagnosis, treatment of first disease, time from primary tumor to SMN, SMN type, treatment and outcome were analyzed. Pathology of primary and SMN were reviewed.
Results: Among 3,316 patients treated between 1997-2013 44 children (21 females, 23 males), aged 2 yrs 8 months- 27 yrs (median 12.5 yrs) were diagnosed with SMN. 19 patients had a primary diagnosis of CNS tumor, 6–lymphoma, 4–soft tissue sarcoma (STS), 3–neuroblastoma, 3-Wilms tumor (WT). There were 2 cases of osteosarcoma, hepatoblstoma, germ cell tumor, ALL and 1-retinoblastoma. 22 patients (50%) had radiotherapy for primary tumor, 2 had CNS prophylaxis, 40 (91%) received chemotherapy. Time from diagnosis of primary disease to SMN ranged from 6 months to 15.5 years (median- 5.5 years). The following SMNs were diagnosed: hematologic malignancies 20 pts (45.4%) (AML- 13, ALL-3, MDS-2, NHL-T-2 pts), malignant brain tumors-12 (27.3%), osteosarcoma – 4 (9%), STS-2 (4.5%), thyroid cancer -2 (4.5%), WT, clear cell sarcoma and renal cell carcionoma -3 (7%), ovarian cancer – 1 (2.3%). In 9 patients SMN occurred in irradiated field (7 pts CNS, 2 pts thyroid). Seven (37%) of 19 pts with primary CNS tumors developed AML or MDS. Out of 44 SMN patients 22 are alive from 2 years 5 months to 21 years, median 8 years.
Conclusions: Our observations confirm the risk of SMN in children cured of cancer. Long latency period for some SMNs warrants lifelong surveillance for these conditions.

EP-227

PULMONARY COMPLICATIONS IN LONG- TERM SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER

N. Çetingül[1], F. Ergin[1], E. Demir[1], M. Kantar[1], H. Alper[2], S. Aksoylar[2], A. Sayiner[3], S. Kansoy[3]

[1]Pediatric Oncology, Ege University School of Medicine, Izmir, Turkey; [2]Pediatric Radiyology, Ege University School of Medicine, Izmir, Turkey; [3]Chest, Ege University School of Medicine, Izmir, Turkey

Objectives: Pulmonary complications are among the most common and serious sequelae seen in childhood cancer survivors (CCSs). Cancer types, age at diagnosis, thoracic involvement, pulmonary metastasis at diagnosis and type of treatment modality (chemotheraphy, pulmonary/thoracic radiotheraphy and surgery) are affective in pulmonary complications.
Methods: In this study, we examined the pulmonary complications of 50 cancer patients over 7 years old whose treatment had been completed and were in remission for at least 3 years. Their physical examination, chest X-ray and pulmonary function tests (PFT) (spyrometric testes and DLCO) evaluated in Ege University, Department of Pediatric Oncology. Also 40 healthy and within the same age range children and young adult were evaulated as control group.
Results: Our patients were 16 acute leukemias, 15 lymphomas, 10 bone and soft tissue sarcomas, 4 CNS tumors and 5 other solid tumors. In the surviving patients the disorders of PFT were found to be 52%, (24% small airway disease, 14% diffusion disorders and 14% combined disorder; restrictive disorder + other disorders) and in the control group disorders of PFT were 22,5% (p:0,007). Being diagnosed with cancer at under 2 years of age increased the risk of restrictive disorders and small airway disease ($p = 0.027$). In bone and soft tissue sarcomas increased the risk of small airway disease (SAD), in other solid tumors observed especially diffüsion disorder ($p = 0.01$). Receiving high doses of alkilating agents increased the risk of restrictive disorders. Also pulmonary/thoracic RT increased the risk of impaired PFT. We saw that follow up time can cause variable impaired PFT.
Conclusions: Pulmonary disfunctions in CCSs are prevelant. Diagnostic age, pulmonary RT/surgery and high doses of alkilating agents are important risk factors. CCSs have to be followed up late pulmonary function impairment and complications.

EP-228

SECOND NEOPLASMS: A SINGLE CENTER EXPERIENCE

S.A. Tekgündüz[1], C. Bozkurt[1], G. Sahin[1], N. Yuksek[2], S.I. Özdemir[3], S. Yesil[1], G. Tanyildiz[1], M.O. Candir[1], S. Toprak[1], A.U. Ertem[1]

[1]Pediatric Hematology-Oncology, Dr. Sami Ulus Woman's Health and Children Education and Research Hospital, Ankara, Turkey; [2]Pediatric Hematology-Oncology, Medical School University of Bülent Ecevit, Ankara, Turkey; [3]Pediatric Hematology-Oncology, Konya Research and Training Hospital, Ankara, Turkey

Objectives: Despite to improvement of childhood cancer patient survival at the same time second cancers are being another problem. Radiotheraphy, epipodophyllotoxins and alkylated agents are most responsible factors. In the United States, secondary malignancies percentage is about 6% to%10. This percentage is increasing to 30% when the diagnosis is Hodgkin lymphoma. Aim of this study to evaluate second neoplasm and affecting factors in our center.
Methods: The files of patients with diagnosed second neoplasm were evaluated retrospectively between 1985-2004. Mostly diagnosis of patients is performed during regular follow up. Only diagnosis of two patients are performed in adult oncology center. First diagnosis of patient are including seven acute leukemia (six acute lymphoblastic leukemia;

one mixt type leukemia), two Wilms tumor, two non-Hodgkin lymphoma, one Hodgkin lymphoma, one ganglioneuroblastoma, one Langerhans cell histiocytosis respectively.
Results: In this period totally 2356 childhood cancer patients diagnosed in our center between 1985-2014. Fourteen second neoplasm were diagnosed during this period. Eight out of fourteen patients were male. Median period between the cessationof theraphy of the initial disease and the diagnosis of the secondary neoplasm were was 74,8 month (range,0 to 314 month) Two patient developed second malignancies during treatment of first diagnosis. In all, Six had AML, three soft tissue sarcoma, one osteoblastoma, one paraganglioma, one Hodgkin lymphoma, one squamoous cell carcinoma of tongue, one papillary type carcinoma of thyroid respectivly. Four out of the 14 patients who diagnosed acute myeloid leukemia (AML) were died. Three out of the 14 patients are under the treatment.
Conclusions: In our series, epipodophyllotoxins, alkylated agents and radiotheraphy seems risk factors of second neoplasm. Results of second AML are dismal. Our number of second cancer likely under the estimation because of insufficient number of follow up. All childhood cancer patients are need to regular follow up during lifetime.

EP-229

TRIPTORELIN TO PRESERVE FERTILITY IN ADOLESCENTS TREATED WITH CHEMOTHERAPY FOR CANCER

M. Meli[1], M. Caruso[2], M. La Spina[1], L. Lo Nigro[1], P. Samperi[1], S. D'Amico[1], F. Bellia[1], V. Miraglia[1], G. Russo[1], A. Di Cataldo[1]

[1]Pediatric Hematology and Oncology, University of Catania, Catania, Italy; [2]Pediatric Endocrinology, University of Catania, Catania, Italy

Objectives: Triptorelin, a GnRH agonist analogue, may be administered to post-pubertal females with cancer who receive chemotherapy in order to obtain menstrual suppression and decrease the hemorrhage risk due to thrombocytopenia. Our objective is to evaluate if triptorelin administration has also a protective role against gonadotoxicity of chemoterapeutic drugs.
Methods: This retrospective observational analysis includes all females who received chemotherapy for cancer in our Unit from 2000 to 2013, aged between 10-17, who already had the menarche. After informed consent, they received monthly depot intramuscular triptorelin at the dose of 3.75 mg. This report includes patients who concluded their treatment since at least one year and who are still alive. We evaluated the long-term ovarian function looking for clinical signs and symptoms of ovarian damage as amenorrhea or menstrual changes. We also searched for possible pregnancies and abortions. We made a laboratory follow-up, dosing serum FSH, LH, PRL, E2 and progesterone, and an ovarian ultrasound.
Results: Patients evaluable according to eligibility criteria are 29 (15 lymphomas, 11 leukemias, 1 PNET, 1 Ewing sarcoma, 1 rhabdomyosarcoma). Four of them received high-dose chemotherapy (HDCT). Over the 25 patients who did not receive HDCT, only one developed amenorrhea. The others maintained a normal ovarian function at clinical, laboratory and ultrasound evaluation. Three of them achieved spontaneous, physiologic pregnancy and gave birth to healthy babies. Three of the 4 patients who made HDCT developed premature ovarian failure (POF).
Conclusions: During HDCT, it seems that triptorelin is not able to preserve the ovarian function. In this case it could be recommended triptorelin followed by cryopreservation of ovarian tissue or oocytes. Our study suggests that GnRH-a during chemotherapy may prevents POF in patients treated without HDCT, indicating both the appropriateness and the need of a prospective randomized trial with a larger population.

EP-230

LONG TERM FOLLOW- UP OF CHILDHOOD CANCER SURVIVORS IN LEBANON

R. Farah[1], R. Kouzy[2], P. Kiwan[3], R. Bejjani[4], C. Saddi[4], J. Triolet-Varin[4]

[1]Pediatrics, St George Hospital University Medical Center, Beirut, Lebanon; [2]Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon; [3]Faculty of Medicine, University of Balamand, Beirut, Lebanon; [4]CHANCE, CHildren Against Cancer Association, Beirut, Lebanon

Objectives: Despite high survival rates of pediatric cancers, evaluation of the long-term medical and psychosocial effects on survivors in Lebanon is scarce.
Methods: Children treated for various types of cancer, cured and over 5 years from diagnosis at three major hospitals in Lebanon were identified. Data collection was based on chart review and extensive questionnaire administered to the parents or the patient. Excel sheets were filled and data was analyzed.
Results: There were 93 eligible cancer survivors identified with an average follow-up period of 8 years (range 5 to 15 yrs). 42 patients were included in the initial survey. Mean age was 17 (range 7 to 30 yrs). There were 17 females and 25 males. 36.5% had leukemia, 12.9% lymphoma, 19.5% sarcoma and the rest had various malignancies. Most common physical symptoms reported were weight problems (48.8%) and chronic fatigue (24.2%). Emotional manifestations included anxiety in 38.1% (16), while 54.8% felt adventurous and confident. 80.5% of the patients complained that the treatment affected their education: 58.5% (24) repeated their academic year, 16.6% (7) had trouble continuing education and dropped out, while 29.2% (12) of the patients attended college. Only one was a smoker and none were drug abusers. Out of 42 survivors only 27 (64%) knew the truth about their previous cancer. All had a positive insight about their medical treatment and follow-up, the hospital team and the family support during and after therapy.
Conclusions: This study is the first in Lebanon looking at long-term outcome of childhood cancer survivors. Although many are successful and leading a normal life, there is a significant number whose health, overall well-being and education were affected. Medical and psychological follow-up is critical for reintegration into the society. Long-term follow-up programs are lacking in our country and need to be developed further.

EP-231

PULMONARY FUNCTION AFTER TREATMENT FOR EMBRYONAL BRAIN TUMORS ON SJMB03 THAT INCLUDED CRANIOSPINAL IRRADIATION

D. Green[1], T.E. Merchant[2], C. Billups[3], D.C. Stokes[4], A. Broniscer[5], U. Bartels[6], M. Chintagumpala[7], T.E. Hassall[8], S. Gururangan[9], G.B. McCowage[10], J.A. Heath[11], R.J. Cohn[12], M.J. Fisher[13], A. Srinivasan[14], G.W. Robinson[5], A. Gajjar[5]

[1]Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [2]Radiological Sciences, St. Jude Children's Research Hospital, Memphis, USA; [3]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA; [4]Pediatrics, University of Tennessee School of Medicine, Memphis, USA; [5]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [6]Haematology and Oncology, The Hospital for Sick Children, Toronto, Canada; [7]Pediatric Medicine, Texas Children's Hospital, Houston, USA; [8]Haematology and Oncology, Royal Children's Hospital, Brisbane, Australia; [9]Pediatrics, Preston Robert Tisch Brain Tumor Center Duke University Medical Center, Durham, USA; [10]Pediatrics, Children's Hospital at Westmead, Sydney, Australia; [11]Oncology, Royal Children's Hospital, Melbourne, Australia; [12]Clinical Oncology, Sydney Children's Hospital, Sydney, Australia; [13]Oncology, Children's Hospital of Philadelphia, Philadelphia, USA; [14]Bone Marrow Transplantation & Cellular Therapy, St. Jude Children's Research Hospital, Memphis, USA

Objectives: Treatment of children with embryonal brain tumors (EBT) includes craniospinal irradiation. There are limited data regarding the effect of radiation therapy (RT) on pulmonary function.
Methods: Protocol SJMB03 enrolled patients 3 to 21 years of age with EBT. Pulmonary function tests (PFTs) [forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) by spirometry, total lung capacity (TLC) by plethysmography and diffusing capacity of the lung for carbon monoxide corrected for hemoglobin ($DLCO_{corr}$)] were obtained. Differences between PFTs obtained following the completion of RT and 24 or 60 months ACT were compared using exact Wilcoxon signed rank tests.
Results: There were 303 eligible patients (spine dose: $\leq$ 2345 cGy – 201; $>$ 2345 cGy – 102; proton beam, N = 20) were enrolled between June 24, 2003 and March 1, 2010, 260 of whom had at least one PFT. Median age at diagnosis - 8.9 years (range, 3.1 to 20.4 years). Median spinal RT dose - 23.4 Gy (range, 23.4 to 50.4 Gy). Median cyclophosphamide dose was 16.0 g (range, 0 to 17.9 g/m^2). 24 and 60 months after completion of treatment, DLCO was $<$ 75% predicted in 23% (27/118 evaluated) and 25% (21/84 evaluated), FEV1 was $<$ 80% predicted in 21% (32/154 evaluated) and 29% (32/109 evaluated), FVC was $<$ 80% predicted in 27% (46/172 evaluated) and 28% (30/108 evaluated) and TLC was $<$ 75% predicted in 9% (13/138 evaluated) and 11% (10/92 evaluated) of patients. DLCO was significantly decreased 24 (median difference (MD) in% predicted, - 3.00%; $p = 0.028$) and 60 months ACT (MD in% predicted, - 6.00%; $p = 0.033$) compared to the end of RT.
Conclusions: DLCO was significantly decreased 24 and 60 months after completion of spinal RT compared to immediately post-RT. TLC was marginally decreased 60 months ACT ($p = 0.072$). Continued monitoring of this cohort is planned.

EP-232

PREVALANCE OF HYPERTENSION AMONG CHILDHOOD CANCER SURVIVORS

E. Guler[1], N. Araz[2], M. Buyukcelik[3], A. Balat[3]

[1]Pediatric Oncology, Akdeniz University School of Medicine, Antalya, Turkey; [2]Pediatrics, Gaziantep University School of Medicine, Gaziantep, Turkey; [3]Pediatric Nephrology, Gaziantep University School of Medicine, Gaziantep, Turkey

Objectives: There are limited number of studies regarding prevalance of hypertension among childhood cancer survivors. The aim of this study is to determine prevalance of hypertension and its relationship with obesity.
Methods: The patients treated and followed at least two years without relapse or second malignancy were included in the study. In all patients ambulatory blood pressure monitoring was performed over 24 h using the Microlife WatchBP03 oscillometric device. Hypertension was defined as a systolic blood pressure and/or diastolic blood pressure of $>$ 95 the percentile. The weight was measured by bioelectrical impedance analysis (BIA) and BIA was determined by Tanita TBF 300 body composition device. Obesity was defined as indicated in International Obesity task force's international standarts and in diagnostic crietaria of International Diabet Foundation, respectively.
Results: The average age of 52 patients (female/male, 25/27) were 12.84 ± 3.88 years. Time off therapy ranged 24-125 month (median: 54.50). The diagnosis of patients were hematologic malignacies (33), Wilms tumor (9) and other solid tumors (10). Thirty six (69.2%) of patients

were normotensive while 16 (30.8%) patients had hypertension. Hypertension prevalence was 44.4%, 28.5%, 27.7% in patients with Wilms tumor, other solid tumors and hematologic malignancy, respectively. Forty three (82.7%) patients were at standart weight whereas 15.4% (8) was overweight and 1.9% (1) was obese. Fourteen (30.4%) patients had abdominal obesity being particularly high in hematologic malignancies. No relationship between hypertension and obesity or waist circumference was found ($p>0.05$).
Conclusions: Childhood cancer survivors are at increased risk for the development of obesity, abdominal obesity and hypertension. Hypertension prevalence in patients with Wilms tumor is higher than the patients with other malignancies. These results might point out the importance of follow up and early diagnosis of hypertension especially in Wilms tumor survivors.

EP-233

PATTERNS AND PREDICTORS OF WHO ACCOMPANIES ADULT SURVIVORS OF CHILDHOOD CANCER TO ROUTINE LONG-TERM FOLLOW-UP CLINIC VISITS

K. Haines[1], H.R. Mitchell[1], L. Balsamo[1], J. Rotatori[1], N.S. Kadan-Lottick[1]

[1]Pediatric Hematology-Oncology, Yale University School of Medicine, New Haven, USA

Objectives: Many adult survivors of childhood cancer have difficulty transitioning to health care independence. As an indication of patient dependency, we determined 1) patterns of attending long-term follow-up clinic with others, and 2) associated predictors, among survivors.
Methods: In this cross-sectional study of survivors of childhood cancer, age $\geq$18 years at follow-up, attending their first routine Yale HEROS Survivor Clinic visit, the presence of family and non-family member companions was routinely ascertained from 8/1/2003 through 3/31/2014 as part of the standard evaluation for 152 (98%) of 155 eligible patients. Frequencies of who attended clinic with others were calculated overall, and stratified by patient and disease characteristics. Potential predictors of attending clinic with others were analyzed in logistic regression.
Results: The participants were a mean age of 11.2 ± 5.4 years at diagnosis, 62% female, with a history of leukemia/lymphoma (61%), CNS tumor (11%), sarcoma (19%) or other solid tumors (9%). Age at follow-up was 25.7 ± 6.7 years (range 18.1-49.2). Overall, 52% of patients $\geq$18 years attended clinic with other (s): parent (81%), spouse/significant other (15%), other relative (10%), friend (3%) [categories not mutually exclusive]. Patients aged 18-25 were more likely than those $\geq$25 years to attend with another (68% vs. 28%, $p < 0.0001$), but parents and spouses/significant others comprised >75% and >10% of companions, respectively, for both age groups. History of a CNS tumor was significantly associated with attending survivor clinic accompanied ($p = 0.04$). Age at diagnosis, gender, and insurance type were not significantly associated with attending clinic with others.
Conclusions: We found a high percentage of adult childhood cancer survivors, particularly with CNS tumors, accompanied by others at routine survivor care visits. Research is needed to evaluate the role of family and other companions in childhood cancer survivors' health care and how to assist young adult patients' transition to independent management of their own health.

EP-234

THE SURVIVORSHIP PASSPORT FOR LONG-TERM CARE OF CHILDHOOD CANCER SURVIVORS. AN INITIATIVE OF THE EUROPEAN NETWORK FOR RESEARCH ON CANCER IN CHILDREN AND ADOLESCENTS (ENCCA)

R. Haupt[1], C. Dellacasa[2], S. Karner[3], L. Kremer[4], C. Bergeron[5], S. Caruso[6], D. Saraceno[2], V. Morsellino[6], R. Skinner[7], L. Hjorth[8]

[1]Epidemiology and Biostatistics Unit, G. Gaslini Institute, Genoa, Italy; [2]Health Care Systems, Cineca, Bologna, Italy; [3]Project Management, Icccpo, Vienna, Austria; [4]Pediatric Oncology, Emma Children's Hospital Academic Medical Center, Amsterdam, Netherlands; [5]Pediatric Hematology/Oncology, Centre Leon Berard, Lyon, France; [6]Epidemiology and Biostatistics Unit, G. Gaslini Institute, Genoa, Italy; [7]Paediatric and Adolescent Haematology and Oncology, Great North Children's Hospital Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom; [8]Paediatric Haematology and Oncology, Lund University, Lund, Sweden

Objectives: As 80% of young people with cancer are now surviving and at least half have reached or are entering adulthood, it is essential that health systems are able to inform survivors and all relevant stakeholders about possible risks or late effects of the cancer treatment received.
Methods: A partnership among professionals, survivors, parents and IT experts has been established through the ENCCA network to create the "Survivorship Passport". It is a paper and electronic-based document, and designed to be given to each patient after the planned end of treatment containing simple cancer history and therapy information. The passport includes recommendations for indivualised follow-up based on up-to-date clinical guidelines developed within the PanCareSurFup project and the International Guideline Harmonization Group (IGHG) to facilitate the prevention, early detection and treatment of potential late effects.
Results: An international ballot involving expert clinicians was held to define the passport template. The passport is generated through a secured web-based platform which is patient-oriented, accessible in multiple languages by all type of users and can be integrated with national/hospital, and clinical trials databases. Linkage with guidelines for screening of some relevant possible late complications (secondary breast cancer, cardiomyopathy, premature ovarian insufficiency) has been established, and new guidelines will be implemented as soon as they will become public.
Conclusions: The Survivorship Passport aims to harmonize follow-up of former cancer patients across Europe by promoting homogeneous criteria and evidence-based guidelines from clinical practice for prevention, early detection and treatment of physical and psychosocial late adverse effects. In the age of personalized medicine, this simple and accessible tool can enhance age-appropriate healthcare and address individual patient issues specific for pediatric cancer survivors, possibly leading to important breakthroughs in the monitoring and cure of childhood cancer survivors in the long-term, which will contribute to an optimal health-related quality of life for survivors.

EP-235

CENTRALISED LONG TERM FOLLOW-UP CLINICS FOR CHILDHOOD CANCER SURVIVORS: WHY DO SO MANY SURVIVORS NOT ATTEND?

J.K. McLoone[1], J. Jones[2], C.E. Wakefield[1], K. Johnston[3], R.J. Cohn[4]

[1]School of Women's and Children's Health UNSW Medicine, University of New South Wales, Sydney, Australia; [2]Australian and New Zealand Haematology/Oncology Group, MIMR-PHI Institute of Medical Research, Clayton, Australia; [3]Kids Cancer Centre, Sydney Children's Hospital, Randwick, Australia; [4]Behavioural Sciences Unit Kids Cancer Centre, Sydney Children's Hospital, Randwick, Australia

Objectives: Childhood cancer survivors remain at elevated riskof developinglife-threatening chronic disease after the completion of cancer treatment. As such, long term follow up (LTFU) care is recommended for early detection/intervention. However, many childhood cancer survivors (CCSs) do not remain engaged with LTFU services in the decades post-treatment completion. This national study assessed CCSs perceived benefits and barriers to attending specialised LTFU care.
Methods: Childhood cancer survivors (>5 years from diagnosis), including adult CCSs and parents of CCSs <16 years of age, from four paediatric oncology hospitals completed a mailed questionnaire. Data was analysed using SPSS20.
Results: $N = 209$; 47% male; 64% adult survivors (mean age 32-years, $SD = 9.5$, mean time since diagnosis 24-years, $SD = 10.9$), 36% parents (mean age of child 13-years, $SD = 4.8$, mean time since diagnosis 10-years, $SD = 3.4$). Many CCSs (42%) do not currently attend LTFU clinic, despite dissatisfaction with the alternate care they currently receive (65% dissatisfied, versus 11% of LTFU clinic attendees). Non-attendees recognised LTFU clinic attendance as 'important'/'very important' to learn about late-effects (96%), to learn about screening/diagnostic tests (91%), and to check they had not developed a second cancer (91%). CCSs also reported unmet information needs in the area of late effects (80%) and second cancers (65%) and the follow-up care they should receive (57%). However, lack of awareness regarding the availability of a LTFU clinic (57%) and prompts/reminders to attend once disengaged (51%) were reported as key barriers to attending LTFU.
Conclusions: The current model of centralised LTFU care does not meet the needs of over 40% of CCSs. Future research designed to engage and empower survivors to seek and receive care through alternate LTFU care pathways, including multidisciplinary, nurse-led, or primary care clinics or community health services, to overcome their barriers to receiving care, while meeting their needs, is critical.

EP-236

THE PREVALENCE OF ABNORMAL GONADAL HORMONES IN YOUNG MALE CANCER SURVIVORS

M. Krawczuk - Rybak[1], M. Plonowski[1], J. Sadowska[2], J. Wachowiak[2], D. Sega-Pondel[3], A. Chybicka[3], T. Stachowicz-Stencel[4], E. Adamkiewicz-Drozynska[4], I. Malinowska[5], M. Matysiak[5], A. Koltan[6], M. Wysocki[6], A. Pobudejska-Pieniazek[7], T. Szczepanski[7], B. Przybyszewski[8], W. Badowska[8], A. Czajnska-Deptula[9], D. Perek[9], D. Szymanska-Miller[10], J. Kowalczyk[10]

[1]Pediatric Oncology & Hematology, Medical University of Bialystok, Bialystok, Poland; [2]Pediatric Oncology & Hematology and Hematopoietic Stem Cell Transplantation, Medical University of Poznan, Poznan, Poland; [3]Pediatric Oncology & Hematology and Bone Marrow Transplantation, Medical University of Wroclaw, Wroclaw, Poland; [4]Pediatrics Pediatric Oncology & Hematology, Medical University of Gdansk, Gdansk, Poland; [5]Pediatrics Pediatric Oncology & Hematology, Medical University of Warsaw, Warsaw, Poland; [6]Pediatric Oncology & Hematology, Collegium Medicum Nicolaus Copernicus University, Bydgoszcz, Poland; [7]Pediatric Oncology & Hematology, Medical University of Silesia, Zabrze, Poland; [8]Pediatric Oncology & Hematology, Children State Hospital, Olsztyn, Poland; [9]Pediatric Oncology, Children's Memorial Health Institute, Warsaw, Poland; [10]Pediatric Hematology &Oncology, Medical University of Lublin, Lublin, Poland

Objectives: The gonadal function can be affected by chemotherapy, radiation to the pelvic or head area and total body irradiation, leading to temporary or permanent oligospermia and

deleterious changes in sperm quality in males. Anticancer protocols include some cytostatics that exert various effects on the gonads. The most frequent pediatric cancers was divided into three groups according to their gonadotoxic treatment: high (HR), middle (MR) and low (LR) risk. In our study gonadal and pituitary hormones were analyzed in young cancer survivors.
Methods: We evaluated gonadal function in 231 young (mean age 16.0 ± 8.6 years, > 2 years after the end of treatment) cancer survivors and 57 controls by measuring the levels of gonadotropins (FSH, LH), testosterone and inhibin B.
Results: The entire cohort of cancer survivors, independently of risk group, had (as compared to the control group) lower mean inhibin B (86.56 ± 67.42 ng/L vs. 127.8 ± 72.6 ng/L; $p = 0.0001$), higher FSH (7.67 ± 11.72IU/L vs. 2.7 ± 2.46IU/L; $p = 0.0001$) and LH (3.78 ± 3.49IU/L vs. 2.25 ± 2.35 IU/L; $p = 0.001$). Testosterone levels were comparable to the control. Abnormal levels of inhibin B were found in 40.8% of the survivors: 35% in LR group, 32%-in MR and 80.6% in HR group. Elevated FSH levels were observed in 46.3% of the survivors (26.7%- in LR,47.8% - in MR, 85.2% - in HR group). The inhibin B:FSH ratio was lowered in all risk groups, most profoundly in HR group. Taking consideration the age of treatment as well as the time that passed since treatment termination, survivors in comparable risk groups presented similar hormonal abnormalities.
Conclusions: after anticancer treatment the risk of gonadal damage is increased (particularly in high risk group). The patients and parents have to be informed about the possibility of lowered reproductive function and pretreatment semen cryopreservation sould be recommended.

EP-237

ADOLESCENT & YOUNG ADULT (AYA) SURVIVORS OF CHILDHOOD CANCERS- A CHALLENGE IN AFTER COMPLETION OF THERAPY (ACT) CLINIC

P. Kurkure[1], M. Prasad[1], V. Dhamankar[1], S. Goswami[1], N. Dalvi[1]

[1]ACT Clinic-Pediatric Oncology, TATA Memorial Hospital, Mumbai, India

Objectives: To assess the evoluation of late effects in childhood cancer survivors who have transitioned to AYA age group on longitudinal follow up in ACT clinic at Tata Memorial Hospital, Mumbai.
Methods: ACT clinic database was analyzed for childhood cancer survivors who have attained 15-30 yrs age at last follow up for demographics, grade of late effects & impact on QOL.
Results: Of 1614 childhood cancer Survivors (> 2 yrs off therapy & disease free) registered in ACT clinic from Feb1991-Feb2014, 776 (48%) survivors are in AYA group, M.F = 563/213 (2.7:1), Hematolymphoid:Solid tumours = 428/348 (1.2:1), Mumbai: Non Mumbai based = 249:527 (1:2). Median age at diagnosis 7yrs, current median age 20yrs, median duration of follow up since ACT clinic registration 12 yrs (range 2-27 yrs). At registration 343 (44%) had no late effects. 205 (26%) had gradeI, 58 (7.5%) gradeII 161 (21%) had gradeIII. Only 9 (1.2%) had gradeIV late effects which increased to 46 (6%) at last follow up mainly due to recurrence 20/46 (43.5%) second neoplasia 21/46 (46%) death due to late effect 1/46 (2%) & 4 (8.7%) due to other medical reasons & accident. Only 25 (3%) were at low risk of developing potential late effects. 319 (41%) were in intermediate risk & 56% (432) fell in high risk category requiring at least annual follow up. Nearly 60% of survivors registered in first decade had stopped follow up as compared to 16% registered in subsequent decade ($p < 0.01$).
Conclusions: AYA survivors of childhood cancers form major (48%) group in Long Term Follow up clinic. The increasing incidence of life threatening late effects on longitudinal follow up combined with statistically significant increasing trend of stopping follow up over period of time since ACT registration is alarming & calls for innovative approaches for maintaining good follow up through survivor-centric approaches such as use of IT based communication & formation of support groups like Ugam.

EP-238

PREVALENCE AND MONITORING OF COMPONENTS OF THE METABOLIC SYNDROME IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER

Y.-H. Lee[1], H. Shin[1], H. Kang[1], S. Yang[2]

[1]Pediatrics, Hanyang University Seoul Hospital, Seoul, Korea; [2]Pediatrics, Hallym University Kangdong Sacred Heart Hospital, Seoul, Korea

Objectives: The components of metabolic syndrome (MS) have been tended to increase and associated with cardiovascular risks in long-term survivors of childhood cancer. We investigated the prevalence of components of MS in adolescent survivors of childhood cancer and tried to monitor them periodically.
Methods: We investigated 44 adolescent survivors of childhood cancer, median age 14.9 years (range 10–19.8 years) and median follow-up time elapsed after off-therapy 7.4 years (range 5–16.5 years). We measured body mass index (BMI), systolic and diastolic blood pressure, triglycerides (TG), high-density lipoprotein (HDL) –cholesterol, and fasting glucose. Fatty liver was evaluated by ultrasound examinations during follow-up period.
Results: No survivors demonstrated MS with 3 components, however, 18% of survivors (8/44) have 2 abnormal components and 43% (19/44) have 1 abnormal components, respectively. The frequency of each component was: increased BMI, 11%; elevated blood pressure, 0%; elevated TG level, 41%, low HDL cholesterol, 27%; and elevated fasting glucose, 9.3%. Among these components, the increased TG levels were highly prevalent in survivors than in general population ($p = 0.000$). Fatty liver was identified in 8 survivors (18.2%). Sixteen of 44 survivors (36.4%) received at least 3 repeated examinations annually. Twelve out of 16 survivors have 1 or 2 abnormal components at initial examination. Their number of metabolic components have been shown to decrease in 4, persisted in 3, and increased in 5 survivors. Three of 4 survivors who have no components of MS at initial examination showed at least 1 abnormal component during follow-up.
Conclusions: We observed the high incidence of increased TG level in adolescent survivors of childhood cancer, and detected abnormal components of MS during periodic follow-up. Lifestyle interventions and periodic long-term follow-up monitoring would be needed to reduce the metabolic risks in childhood cancer survivors.

EP-239

RISK-TAKING BEHAVIOURS AMONG CHILDHOOD CANCER SURVIVORS: A META-ANALYSIS

S. Marjerrison[1], E. Hendershot[2], P. Nathan[2]

[1]Division of Hematology/oncology, McMaster Children's Hospital, Hamilton, Canada; [2]Division of Haematology/oncology, Hospital for Sick Children, Toronto, Canada

Objectives: Survivors of pediatric cancer are at risk for late effects of their therapy, some of which may be exacerbated smoking, alcohol or drug use. We undertook a meta-analysis of the literature to determine whether survivors of childhood cancer engage in these risk-taking behaviours at rates different from their peers.
Methods: MEDLINE (1946-), EMBASE (1947-), PsychINFO (1806-) and CCTR were examined for studies comparing engagement in risk-taking behaviours between cancer survivors and sibling or matched peer controls. Two reviewers assessed studies for inclusion, and extracted data independently. Studies were combined with Forrest plots in Review Manager 5.2, using inverse variance weighting, and a random effects model to determine the odds ratio (OR) and incidence rates of risk-taking behaviors in survivors compared to controls. Risk of bias was assessed with the Health Evidence Bulletins – Wales: Critical Appraisal of Observational Studies tool.
Results: Of 1562 studies identified, 14 met criteria for inclusion. Twelve studies assessed smoking rates, 6 binge drinking and 7 drug use. Compared to their siblings, childhood cancer survivors were less likely to smoke (OR 0.72 [95% confidence interval 0.52, 0.98]) or binge drink (OR 0.77 [0.68, 0.88]), but similarly likely to use drugs (OR 0.33 [0.03, 3.28]). Compared to matched peers, survivors were less likely to smoke (OR 0.54 [0.42, 0.70]) or use drugs (OR 0.57 [0.40, 0.82]), but equally likely to binge drink (OR 0.97 [0.38, 2.49]). Among survivors, 21% [0.17, 0.25] smoked, 20% [0.08, 0.51] binge drank and 15% [0.10, 0.23] used drugs. Studies included had a generally low risk of bias.
Conclusions: Survivors of childhood cancer generally engage in similar or lower rates of risk-taking than their siblings and peers. Future studies should examine which youth are engaged in risk-taking behaviours and use this information to focus intervention strategies to minimize these activities among survivors.

EP-240

SUBSEQUENT NEOPLASMS AFTER CHILDHOOD CANCER: A 20-YEAR EXPERIENCE AT HOSPITAL INFANTIL DE MEXICO FEDERICO GOMEZ

A. Medina-Sanson[1], M. Preza-Sánchez[1], E.M. Dorantes-Acosta[1], D. Covarrubias-Zapata[1], J.J. Loeza-Oliva[1], S. Sadowinski-Pine[2]

[1]Hematology and Oncology, Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico; [2]Pathology, Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico

Objectives: To assess patient characteristics and outcome of subsequent neoplasms (SN) in survivors of pediatric cancer at our institution.
Methods: We reviewed the records of all patients who developed a SN after treatment for childhood cancer. Clinical characteristics, leukemia subtype or histology, latency, treatment and outcome were recorded.
Results: From a total of 5,121 malignant neoplasms diagnosed between January 1993 and December 2012, 27 patients developed 28 SN (cumulative incidence = 0.54%), 25 of them occurred from 2003-2012. Mean age at diagnosis of the primary neoplasm was 6.2 years. The most common primary was Retinoblastoma (7) followed by Acute Lymphoblastic Leukemia (6), Langerhans Cell Histiocytosis (3), Brain Tumors (3), non-Hodgkin's Lymphoma (2), Germ Cell Tumors (2), Soft Tissue Sarcomas (STS) (2) and Osteosarcoma (2). Genetic susceptibility could be identified in 7 cases. The average interval between diagnosis of the first and second malignancy was 5.1 years for all patients and 4.3 for those with genetic predisposition. The second malignancies included AML (11) STS (4), Brain Tumors (4), Osteosarcoma (2), Thyroid Carcinoma (1), Ewing Sarcoma (1) Hepatocellular Carcinoma (1) Gastric Carcinoma (1), nonmelanomatous Skin Cancer (1) and Lymphoma (1). A Retinoblastoma patient developed AML as a third malignancy. Eight secondary AML cases had received high doses of etoposide, cyclophosphamide or platinum compounds for the treatment of their first neoplasm and 8 out of 16 secondary solid tumors received radiotherapy. Nine patients are alive and disease free and 18 died due to their second malignancy. The risk of dying was higher among the patients who developed AML (91%).

Conclusions: We found a low cumulative incidence of SN and differences in the types of primary and secondary neoplasms with respect to other series. Ten years ago we had 30% of abandonment and higher mortality rates, consequently, patients died before the development of SN.

EP-241

THE ASSOCIATIONS BETWEEN COGSTATE COMPUTERIZED TESTS OF COGNITION AND STATE STANDARDIZED ACHIEVEMENT TEST SCORES IN SURVIVORS OF CHILDHOOD CANCERS

H.-R. Mitchell[1], L. Balsamo[1], N. Kadan-Lottick[1]

[1]Pediatric Hematology Oncology, Yale University School of Medicine, New Haven, USA

Objectives: Childhood cancer survivors are at risk for impaired neurocognitive functioning that can impact educational performance, but screening by neuropsychologists is time-intensive and costly. We sought to determine if the Cogstate battery, a computerized measure of neurocognitive functioning, is associated with academic achievement.
Methods: Patients with a history of chemotherapy, cranial radiation, or neurosurgery for a CNS tumor at ≤21 years who were at least 2 years after diagnosis were administered the 25-minute Cogstate computer battery (5 tasks measuring neurocognitive functioning; see table) in the Yale Pediatric Oncology Clinic. Connecticut state standardized assessments for math and reading achievement were obtained; performance was categorized as *at/above* vs. *under* the state-defined goal.
Results: The 39 participants (74.0% male) were a median of 15.9 (range 8.5-26.3) years old and 7.0 years after diagnosis. Overall, state-defined goals in math and reading were achieved in 60.5% and 61.5% of participants, respectively. T-tests revealed significant associations between achievement scores and Cogstate tests of cognition (see table). Students under goal for math performed significantly worse on the problem solving/reasoning test. Those under goal for reading performed significantly worse on the processing speed, attention, and working memory tests. The effect sizes for these associations were moderate to large.

	Math		Reading	
Cogstate Test	**p**	**Effect-Size~**	**p**	**Effect-Size~**
Problem Solving/Reasoning (errors)	**.03***	**0.78**	.07	0.64
Visual Associative Memory (errors)	.07	0.64	**.11**	0.54
Processing Speed (seconds)	.43	0.27	**<.01***	**1.15**
Attention/Vigilance (seconds)	.88	0.06	**<.01***	**1.07**
Working Memory (seconds)	.62	0.17	**.04***	**0.69**

~Cohen's *d*: 0.2 = small, 0.5 = medium, 0.8 = large

Conclusions: Our results suggest that the 25-minute Cogstate computer battery is a significant predictor of academic achievement. Large effect-sizes suggest worse performance on at least 4 Cogstate tests may be helpful in identifying children vulnerable to academic difficulties.

EP-242

BONE TOXICITY EVALUATION IN BRAZILIAN PATIENTS TREATED ON TWO CONSECUTIVE STUDIES: GBTLI 93 AND GBTLI 99

P.C.C. Molinari[1], M.L.M. Lee[1], E.M.M. Caran[1]

[1]Pediatric Oncology, Instituto de Oncologia Pediátrica/UNIFESP/EPM, São Paulo, Brazil

Objectives: To evaluate the impact of therapy on bone mineral density (BMD) in acute lymphoblastic leukemia (ALL) survivors treated according to the Brazilian Cooperative Childhood Protocols – GBTLI LLA-93 and 99.
Methods: BMD by dual energy X-ray absorptiometry was performed in 101 treated patients in a cross-sectional study and it values were evaluated according to clinical and treatment characteristics and body composition. Correlations between BMD values and all variables were tested using χ^2 test, Fisher's exact test, likelihood ratio and t-Student test with significancy level of 5%.
Results: Sixty patients were female and 78% were white, current mean age was 17 ± 4.7 years. Fourty-four patients were treated according to GBTLI LLA-93 and 57 according to GBTLI LLA-99. Twenty patients (19.8%) received cranial radiotherapy. The nutritional diagnosis was 22.8% overweight and 15.8% obesity. It was observed 2% of fractures and 2% of osteonecrosis in assessment of bone toxicity. In group younger than 20 years of age, three patients (3.8%) had low BMD and 16 (20.2%) had risk values for low BMD (Z-score between -1.1 and -1.9). This group had lower lumbar spine ($p = 0.01$) and total body ($p = 0.005$) BMD compared to the group with normal values. Moreover that group had lower lean body mass ($p = 0.03$). In group older than 20 years of age, ten patients (45.4%) had osteopenia and they were older that the group with BMD normal values ($p = 0.001$).
Conclusions: It was characterized a risk group for low BMD comprising 15.8% that presented significant low values of BMD. The study suggest that this group needs a better attention in monitoring bone loss and they may be benefit through preventive actions to avoid bone loss and to promote good habits of life. Furthermore it encourages the development of protocols for longitudinal monitoring of these patients.

EP-243

HEPATIC FOCAL NODULAR HYPERPLASIA IN PATIENTS PREVIOUSLY TREATED FOR PEDIATRIC SOLID TUMORS

C. Moscheo[1], M. Casanova[1], M. Terenziani[1], C. Morosi[2], M. Podda[1], C. Meazza[1], E. Schiavello[1], V. Biassoni[1], S. Chiaravalli[1], N. Puma[1], L. Bergamaschi[1], G. Gotti[1], A. Marchianò[3], M. Massimino[1]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [2]Radiology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [3]Radiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Objectives: Focal nodular hyperplasia (FNH) is a benign condition of the liver which may occur in patients previously treated for malignancies. The aetiopathogenic mechanism underlying FNH is poorly understood.
Methods: In our Institution, FNH was diagnosed in 14 patients (6 male, 8 female) previously treated for a pediatric cancer: 3 patients were treated for neuroblastoma, 3 for Ewing sarcoma, 3 for medulloblastoma, 2 for Wilm tumor, 1 for osteosarcoma, 1 for hepatoblastoma, and 1 for malignant mesothelioma. Median age at the time of the original cancer diagnosis was 7 years (range 3 months to 15 years). All patients received multi-agent chemotherapy, 8 underwent myelo-ablative regimens (with busulphan, melphalan or thiotepa) and 9 also received radiotherapy.
Results: The median age of FNH diagnosis was 14 years (range 4-23) and the median interval between the diagnosis of cancer and FNH was 5 years (range 3-18). In 2 cases, radiological findings, including MRI scanning, were inconclusive and liver biopsies were performed. Four patients had a single liver lesion, while in 10 patients FNH was multifocal. The median of the maximum nodule diameter (of the largest lesion in the case of multifocality) at time of diagnosis was 20 mm (range 8-40). After a median of 45 months follow-up (range 3-100) the median diameter was 30 mm (range 10-70), driven by 9 cases that increased size. This increase was not linear over time, with a median increase of 3.5 mm/year (range 1.8 to 9.6). Interestingly, in 3 out 4 cases with single lesion FNH became multifocal. No patients received surgical treatment and all patients remain on active follow-up.
Conclusions: Our experience is consistent with the concept of focal nodular hyperplasia as a benign condition. Biopsies improve diagnostic accuracy in cases where radiological findings are not conclusive. With regard to treatment, we recommend a conservative, "wait and see" approach.

EP-244

NUTRITIONAL STATUS, DIETARY INTAKE AND PHYSICAL ACTIVITY IN CHILDHOOD CANCER SURVIVORS

A. Murphy[1], L. Lockwood[2], A. Hallahan[3], P.S.W. Davies[1]

[1]Children's Nutrition Research Centre, Queensland Children Medical Research Institute The University of Queensland, Brisbane, Australia; [2]Division of Oncology, Children's Health Queensland Royal Children's Hospital, Brisbane, Australia; [3]Division of Oncology Children's Health Queensland Royal Children's Hospital, Queensland Children's Medical Research Institute The University of Queensland, Brisbane, Australia

Objectives: Nutrition related late effects are an important consideration in childhood cancer survivors (CCS). The aim of this study was to examine the nutritional status, dietary intake and physical activity levels of CCS.
Methods: This cross-sectional study involved 43 CCS (n = 14 solid tumors). Measurements included body mass index (BMI), body cell mass index (BCMI) via measures of total body potassium, percent fat (%fat) via the Bodpod® and energy intake and Physical Activity Level (PAL) by three day diet and physical activity diaries.
Results: The population had a mean (+/- SD) age of 14.6 ± 3.7 years and a mean (+/- SD) time since active treatment of 9.7 ± 3.0 years. The mean height, weight and BMI Z score fell within the range of 0.00 ± 1.00. Based upon BMI, no patients were obese and two were classified as thin. However, when%fat was measured, 49% were considered obese (>20% males; >30% females) and when BCM was measured, 54% were considered to be malnourished (BCMI Z score <-2). Sixty-six percent of CCS consumed between 75-110% of estimated energy requirements. The mean (+/- SD) PAL of the group was 1.46 ± 0.13 and 88% of the subjects were classified as having a sedentary/lightly active lifestyle (PAL<1.70). There was a positive relationship between BCMI Z score and PAL ($r = 0.34$; $p = 0.03$) and a negative relationship between%fat and PAL ($r = -0.32$; $p = 0.03$).
Conclusions: Malnutrition, both under and over nutrition, is a problem for CCS, which is under recognized by assessment of BMI. Childhood cancer survivors appear to have dietary intakes similar to the general population but have a sedentary lifestyle, with decreased BCMI and increased%fat related to decreased activity levels. It is recommended that physical activity interventions in combination with dietary guidance should be a focus both during and after cancer treatment to minimize the level of malnutrition seen in CCS.

EP-245

RELATIVE DIFFERENCES IN RISK FOR NEUROPSYCHOLOGICAL OUTCOMES POST PROTON RADIATION FOR INFRATENTORIAL VERSUS SUPRATENTORIAL PEDIATRIC BRAIN TUMORS

I. Paltin[1], C.E. Hill-Kayser[2], R.A. Lustig[2], J.E. Minturn[3], J.B. Belasco[3], K.A. Cole[3], P.C. Phillips[3], A.J. Waanders[3], M.J. Fisher[3]

[1]Child and Adolescent Psychiatry and Behavioral Science, Children's Hospital of Philadelphia, Philadelphia, USA; [2]Radiation Oncology, Hospital of the University of Pennsylvania, Philadelphia, USA; [3]Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, USA

Objectives: Describe neuropsychological (NP) outcomes after proton radiation (PRT) for infratentorial and supratentorial pediatric brain tumor patients.
Methods: Fifty-four patients completed NP evaluations pre-PRT; 22 patients completed evaluations 1-3 years post-PRT (infratentorial n = 13, 9 males, median age 7.0 years [range, 3.2-29.4]; supratentorial n = 9, 6 males, median age 16.4 years [range, 12.7-20.4]). Cumulative tumor bed dose ranged from 5400-5940cGy. Neuropsychological measures included: Adaptive Behavior Assessment System-2, Behavior Assessment System for Children-2, Beery-Buktenica Developmental Test of Visual-Motor Integration, Behavior Rating Inventory of Executive Function, California Verbal Learning Test-C/II, Purdue Pegboard Test, Rey Complex Figure Test, and Wechsler IQ measures.
Results: At baseline, IQ ranged from impaired to superior (infratentorial: n = 30, range 70-128, mean = 103.8, SD = 14.6; supratentorial: n = 24, range 67-127, mean = 96.1, SD = 14.1). Both groups struggled with visual-motor integration and fine motor functioning. The infratentorial group's performance on measures of attention, inhibition, visual and verbal memory, problem solving, organization, social-emotional and executive functioning was average to superior. The supratentorial group consistently demonstrated average abilities with some variability (impairment) on a task of visual organization. At follow-up, the infratentorial group demonstrated low average to superior intelligence (range 86 to 121, mean = 103.1, SD = 11.4); the supratentorial group demonstrated average to high average intelligence (range 94-118, mean = 106.1, SD = 7.8). Both groups evidenced below age expectation fine motor dexterity, list learning and visual organization/memory, and average reported executive and social-emotional functioning. Infratentorial group's inhibition and visual and verbal memory abilities declined to the average range, with low average adaptive functioning. Supratentorial group's performance remained average, with continued visual-motor integration weakness.
Conclusions: Post-PRT supratentorial mean group performance was stable. Despite strong pre-PRT performance, the younger, infratentorial group declined, with greater variability between group members. A subset of the infratentorial population was uniquely vulnerable to early PRT cognitive late-effects.

EP-246

SYMPTOMATIC OSTEONECROSIS IN CHILDREN UNDERGOING CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

E. Papakonstantinou[1], M. Lambrou[1], I. Athanasiadis[1], N. Laliotis[1], V. Sidi[1], A. Anastasiou[1], D.E. Koliouskas[1]

[1]Paediatric Oncology, Hippokration General Hospital, Thessaloniki, Greece

Objectives: Osteonecrosis (ON) has been increasingly documented in pediatric acute lymphoblastic leukemia (ALL) as it can results in joint dysfunction and subsequent impairments in activities of daily living among long-term survivors. Risk factors for ON include age above 10 years, female sex, and use of dexamethasone. We report the incidence of symptomatic osteonecrosis in children treated for with acute lymphoblastic leukemia in our department.
Methods: We retrospectively assessed the incidence of symptomatic ON in a total of 115 patients with acute lymphoblastic leukemia treated with protocols BFM 95 and ALLIC 2009. Symptomatic ON was diagnosed in 5 patients with ALL. They were 2 males and 3 females with median age 12 years (range, 7.5 to 14). The ON patients were identified based on clinical symptoms such as persistent bone pain, limping and limited motion of joints. Osteonecrosis was further confirmed with diagnostic imaging studies (x-ray and magnetic resonance imaging [MRI]).
Results: The cumulative incidence of ON was 4.3%. ON was diagnosed at median treatment weeks 66.5 (range, 24 to 108). The most commonly affected joints and bones were the hip joint (60%) and the knee joint (40%). Two patients (40%) exhibited multiple lesions. All patients underwent weight bearing restrictions and pain management. One patient (20%) needed surgical intervention. With the median follow-up times of 29 months (range 6 to 65), the clinical outcomes of ON were as follows: n1 with amelioration of ON, n4 with stable disease and n1 with deterioration of ON.
Conclusions: A significant number of patients develop ON during or after treatment for childhood ALL. Weight-bearing joints are most commonly affected. Clinical screening of ALL patients especially within 3 years from diagnosis is necessary for early recognition of ON.

EP-247

SCARS IN CHILDHOOD CANCER SURVIVORS

M. Peretz-Nahum[1], S. Moalem[2], Y. Melamed[1], E. Krivoy[1], N. Arad[1], S. Postovsky[1], A. Ben Barak[1], I. Zaidman[1], M. Weyl Ben-Arush[1]

[1]Pediatric Hemato-oncology, Rambam Health Care Campus, Haifa, Israel; [2]School of Behavioral Science, Tel Aviv-Yafo Academic College, Tel Aviv, Israel

Objectives: Childhood cancer survivors have to cope with scars, with at least one chest scar from a central venous catheter (CVC). Scars cause esthetic discomfort and are a visual reminder of disease. The impact of scars on cancer survivors' quality-of-life (QOL) has rarely been investigated. We evaluated coping with scars and their effect on body self image and health-related QOL in survivors of pediatric cancer.
Methods: Thirty-four survivors of childhood cancer, aged 15-30 years, 56% (19) females and 44% (15) males, on long-term follow-up (LTFU) completed a questionnaire concerning demographic details, disease and treatment, and scars: number, length (in cm), localization, psychological impact of scars on esthetic aspect, self body-image, affective and social life and health-related QOL. Statistical analysis of variants was performed by the SPSS method.
Results: Patients showed 1-9 scars, but 44% (15) had only one chest scar from the CVC. Forty-seven percent (16) had at least two scars, one from the solid tumor resection and one from the chest CVC. Average scar length was 4.42 cm (range, 1-50 cm). Most survivors ignored or hid the scars, even if they were not found to influence the self body-image, activities or social life. For 52% of survivors, the scars were at the origin of health concern. Coping with scars and hiding scars were found to be related with a statistical significance to self body image (p
Conclusions: Forty-seven percent of childhood cancer patients had at least two scars. Survivors cope with scars ambivalently: by hiding the scars, they decrease their negative impact esthetically, and ameliorate the self body image, affective and social QOL, but they remain a health concern.

EP-248

LONG-TERM FOLLOW-UP OF PEDIATRIC HEMATOPOIETIC CELL TRANSPLATION CANCER SURVIVORS

M. Peretz-Nahum[1], N. Arad[1], S. Postovsky[1], A. Ben Barak[1], R. Elhasid[2], A. German[3], M. Weyl Ben-Arush[3], I. Zaidman[3]

[1]Pediatric Hemato-oncology, Rambam Health Care Campus, Haifa, Israel; [2]Pediatric Hemato-oncology, Sourasky Medical Center, Tel Aviv, Israel; [3]Pediatric Endocrinology, Rambam Health Care Campus, Haifa, Israel

Objectives: Increasing numbers of hematopoietic cell transplantation (HCT), autologous as well as allogeneic, are being performed with a greater number of long-term survivors. The purpose of this study was to review late effects secondary to treatment exposure before HCT and to the HCT conditioning therapy.
Methods: Subjects included 38 childhood cancer survivors on long-term follow-up (LTFU) who had HCT; 28 patients had autologous and 20 had allogeneic HCT.
Results: Median age at diagnosis was 9 years (y) (range, 0-21y). Median age at LTFU was 27y (range, 8-37y). Median years of LTFU was 16 (range, 5-27). Male to female ratio was 1.1. We found 40 late effects in 23 survivors, 27 late effects in 13/19 cancer patients post-chemotherapy, radiotherapy and HCT; 13 late effects in 10/19 cancer patients post-chemotherapy and HCT without radiotherapy. Of 40 late effects, 26 were found in patients post-autologous and 14 in patients post-allogeneic HCT. Late effects were: 2 cataracts,1 hemianopsy, 1 hemiparesis, 1 convulsive disorder post Acute Disseminated Encephalomyelitis, 1 attention deficit disorder, 2 dental problems, 2 avascular necrosis, 1 leg length discrepancy, 6 hypothyroidism, 1 cardiac valve insufficiency, 4 chronic hepatitis, 5 oligo-azoospermia, 4 primary ovary failure, 3 second cancer, 4 osteoporosis (female), 1 failure to thrive, 1 obesity. Survivors who received radiotherapy had more late effects, mainly musculoskeletal disorders, hypothyroidism, cataract and second cancer. Osteoporosis was reported in females. Infertility rate was almost equal in both genders. No case of metabolic syndrome, hyperlipidemia or diabetes mellitus was reported.
Conclusions: Conclusion: This study reported 60% late effects in childhood cancer survivors post-HCT, the most in those treated by radiotherapy pre-HCT. The few cardiovascular late effects reported may be explained by median LTFU of 16y. High risk of late effects in HCT survivors warrants lifelong structured LTFU.

EP-249

MUSCULOSKELETAL SEQUELAE OF SOLID TUMOURS AND CANCER REHABILITATION OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY, SURGERY AND RADIATION THERAPY

A. Petrichenko[1], E. Bukreeva[2], N. Ivanova[1], T. Sharoev[1], A. Prityko[3]

[1]Oncology, Child Health Care Research Clinic, Moscow, Russia; [2]Rehabilitation, Child Health Care Research Clinic, Moscow, Russia; [3]Director, Child Health Care Research Clinic, Moscow, Russia

Objectives: Recommendations for screening, prevention, and management of survivors.
Methods: The study included 95 children and adolescents at the mean age of 13.7 years with solid tumours were treated between 1987 and 2013 years, followup of 6 to 324 months. 36

patients had metastases, 19 patients had solitary metastases, 17 –multiple. Treatment consisted of chemotherapy, radiotherapy, oncologic surgery, included limb-sparing procedures. The most common late effects we had observed were: scoliosis - in 75 cases, muscular hypoplasia – 66, osteopenia – 47, limb-length discrepancy in spite of usage of growing endoprosthesis - 46, deformation of chest wall and limbs – 32, pathological fractures - 6, poor joint movement – 61, neurological disturbance - 22, lymphedema - 5, deforming osteoarthrosis - in 3 cases. 20 patients had more, than 6 late effects. 43 patients underwent individual combined rehabilitation program. Patients underwent a course of postoperative inpatient physical therapy. This study evaluated the short and long-term changes in physical fitness of a child with a childhood malignancy, using an individual rehabilitation program, consist with combined physical exercise, kinesiotherapy, aquatic rehabilitation implemented shortly after treatment. Training is performed individually, under the supervision of an experienced paediatric physical therapist.
Results: We suggest that the usage an individual rehabilitation program can decrease pain, improve muscle strength and range of motion in joints, an increased supply of blood to the muscles, higher muscle metabolism, and more circulation in the limbs, improves tissue nutrition and helps the healing process.
Conclusions: Long-term survival is possible, even for patients with metastatic disease. All long-term survivors of childhood cancer should attend a specialized therapy in rehabilitation clinic.

EP-250

THYROID CARCINOMA AFTER TREATMENT FOR CHILDHOOD AND ADOLESCENT MALIGNANCIES: THE EXPERIENCE OF FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI OF MILAN

M. Podda[1], M. Terenziani[1], L. Gandola[2], N. Pizzi[3], C. Meazza[1], R. Luksch[1], A. Ferrari[1], M. Casanova[1], F. Spreafico[1], D. Polastri[1], E. Schiavello[1], V. Biassoni[1], M. Massimino[1]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Pediatric Radiotherapy Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [3]Otolaryngology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Objectives: To describe natural history, therapeutic approach and histopathology of secondary thyroid cancers in individuals who had a malignant disease in childhood and adolescence.
Methods: We conducted a retrospective analysis of patients treated at our Institute who developed a thyroid neoplasm between 1980 and 2012 after being treated for malignancy in pediatric age.
Results: Thirty-six patients with secondary cancer of the thyroid were identified. Most of the primary cancers had been Hodgkin's lymphomas. All patients had received radiotherapy for their first malignancy. Total thyroidectomy was performed in 27 cases (6 with lymphadenectomy), hemithyroidectomy in 9 (1 with lymphadenectomy); 12 patients received radiometabolic therapy, and all but 2 had TSH-suppressive therapy. The histological diagnoses were 31 papillary and 5 follicular carcinomas. OS was 100% and 95%, and PFS 96% and 83%, at 5 and 10 years, respectively. None of the patients died of their thyroid disease. Nodal involvement at onset was the only factor correlating with recurrence. Surgical sequelae only occurred in patients who underwent total thyroidectomy.
Conclusions: Survival did not depend on the aggressiveness of surgery. Our data confirm a good prognosis for secondary thyroid cancer, prompting us to encourage a 'minimalist' approach to the treatment of these particular patients, wherever possible.

EP-251

VALUES OF HIGH SENSITIVE TROPONIN T IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER TREATED WITH ANTHRACYCLINES

M. Pourier[1], L. Kapusta[2], A. van Gennip[1], J.P.M. Bökkerink[1], J. Loonen[1], L. Bellersen[3], A.M.C. Mavinkurve-Groothuis[1]

[1]Department of Pediatric Hematology and Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [2]Children's Heart Centre, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; [3]Department of Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

Objectives: Cardiac biomarkers can play an important role in the early detection of subclinical heart failure. In this study we aim to 1) obtain values of high sensitive cardiac Troponin T (hs-cTnT) in long-term survivors of childhood cancer 2) investigate the potential role of this biomarker in the detection of subclinical late-onset cardiotoxicity.
Methods: Hs-cTnT and N-terminal-pro-brain natriuretic peptide (NT-pro-BNP) were measured in 75 survivors of childhood cancer. Electrocardiography and echocardiography were performed to evaluate cardiac function.
Results: Mean follow-up period was 9.4 years (range 4.5 - 34.1 years). All survivors were clinically asymptomatic and had no history of heart failure during or immediately after treatment with anthracyclines. Electrocardiography was available in 59 of 75 survivors and showed no signs of myocardial injury related to ischemia or abnormal QTc. Echocardiography was performed in 64 of 75 survivors. Mean left ventricular shortening fraction (SF) was 34% (range 28 - 43%); mean ejection fraction (EF) was 61% (range 48 - 74%). Seven survivors had a mildly decreased EF between 48% and 55%. Normal hs-cTnT levels were detectable in all 75 survivors (range 3 - 13 ng/L). The hs-cTnT concentration did not differ among the different anthracycline dosage groups: $\leq$120, 120-300 and $\geq$300 mg/m^2. Yet, 7 of 75 survivors (9.3%) had elevated NT-pro-BNP levels (range 7 - 25 pg/ml). Of these 7 survivors one had a mildly abnormal EF of 51%. The other EF's, all SF and all ECG findings were normal in these 7 survivors.
Conclusions: Hs-cTnT concentrations are normal in long-term survivors of childhood cancer, even in the subpopulations with elevated NT-pro-BNP and/or a mildly decreased EF, indicating that it is not a sensitive marker for late onset subclinical anthracycline induced cardiotoxicity.

EP-252

LATE EFFECTS IN LONGTERM SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA: A SINGLE CENTRE EXPERIENCE

M. Prasad[1], V. Dhamankar[1], S. Goswami[1], N. Dalvi[1], B. Arora[2], G. Narula[2], S.D. Banavali[2], P. Kurkure[1]

[1]ACT Clinic Paediatric Oncology, Tata Memorial Hospital, Mumbai, India; [2]Paediatric HaematoLymphoid DMG, Tata Memorial Hospital, Mumbai, India

Objectives: To assess the spectrum of late effects in long-term survivors of Childhood Hodgkin Lymphoma (HL), treated with combination chemotherapy+/- radiation therapy (RT).
Methods: Retrospective analysis of all survivors of HL registered in After Completion Therapy (ACT) Clinic of a Paediatric Oncology Department between February1991 and February2014. Records were analysed for demographics as well as late effects and their possible causative factors.
Results: Of a total 1,614 survivors registered during this period,385 (23.8%) had a diagnosis of HL. The median age at diagnosis was 8years (range2-19y) and age at last followup was 19years (7-53y). The median followup was 10years (range2-40y).A disproportionate male enrolment (M:F ratio 8:1) was noted. Patients had been treated between 1972 and 2010;all had received chemotherapy (doxorubicin in 240/385;alkylating agent in 98/385) and 217 (56.4%) had received RT. Although only 38 (10%) of patients had severe/life-threatening complications (grade3/4) at ACT registration,66 (17.1%) had grade3/4 complications at last followup.30 patients had multiple significant issues. The common problems in this cohort included impaired growth in 42 (10.9%) and chronic HepatitisB and complications in 24 (6.2%). Hypothyroidism was detected in 106/209 tested (50%) and was significantly associated with RT to neck (p
Conclusions: Childhood HL has a high cure rate, and therefore more longterm survivors with potential for late effects. The high incidence of late effects, especially with older modalities of treatment, is an impetus for risk-adapted, response-based therapy with less intensive and toxic treatment protocols.

EP-253

LONG-TERM RENAL TUMOURS FOLLOW-UP: A SINGLE INSTITUTION STUDY

A. Schiavetti[1], F. Patriarchi[1], G. Varrasso[1], G. Megaro[1], L. De Luca[1], P. Versacci[1]

[1]Pediatrics, Sapienza University of Rome, Rome, Italy

Objectives: Late morbidity and mortality in renal tumors (RT) treated following five consecutive SIOP protocols.
Methods: A single-institutional retrospective cohort study, assessed RT survivors diagnosed from 1978 for mortality, subsequent malignant neoplasms, cardiac function, musculoskeletal effects, fertility and pregnancy and renal function. Out of 82 pts with RCC (6), CCS (1), WT (73), synchronous BWT (2), 12 died of disease, 1 of renal failure (WAGR) and 2 of accident. At mean FU of 19 yrs the OS is 81.7%. Sixty-seven survivors were previously treated with: unilateral nephrectomy (53), nephrectomy in one side and partial nephrectomy in the other one (1), nephron sparing surgery (13); local RT (9), lung RT (2), whole abdomen RT (1). Twenty pts received anthracyclines (14 with cardioxane association).
Results: Out of 67 survivors, 8 did not participate and 4 with short FU were excluded, 55 (M24/F31) mean age 22 yrs were evaluated. Second neoplasm: 2 cases (3.6%) presented an osteosarcoma and a colon carcinoma, respectively, in irradiated site. Cardiac function: FE ranged from 56% to 77% in 18 cases it was borderline in 2 (50% and 52%). FS ranged from 30% to 48% in 18 cases, it was borderline in 2 (25% and 27%). Fertility and pregnancy: 3 females had successful pregnancy, 1 male an abortion for Dandy-Walker malformation. Infertility in a whole abdomen irradiated case. Musculoskeletal Effects: 5 irradiated cases had scoliosis and flank hypotrophy. Renal function: out of 40 uncomplicated uninefrectomized cases, 23 (53.7%) presented eGFR<90 ml/min/1.73m^2, but only 5 (12.5%) had stage 2-3 chronic kidney disease (CKD). One BWT case had stage 2 CKD. One NSS case had eGFR<90 ml/min/1.73m^2.
Conclusions: In our series of pts with a long FU, second tumor is the main problem in RT survivors. In contrast with other similar reports we found a good cardiac function.

EP-254

ADVERSE EVENTS OF LOCAL TREATMENT IN HEAD AND NECK RHABDOMYOSARCOMA SURVIVORS AFTER EXTERNAL BEAM RADIOTHERAPY OR AMORE TREATMENT

R.A. Schoot[1], O. Slater[2], C.M. Ronckers[1], A.H. Zwinderman[3], A.J.M. Balm[4], B. Hartley[5], M. van de Brekel[4], S. Gupta[5], P. Saeed[6], E. Gajdosova[7], B.R. Pieters[8], M.N. Gaze[9], H.C. Mandeville[10], R. Davila Fajardo[8], Y.-C. Chang[9], S.D. Strackee[11], D. Dunaway[12], C. Abela[12], C. Mason[12], L.E. Smeele[4,13], J.C. Chisholm[14], G. Levitt[2], L.C.M. Kremer[1], M.A. Grootenhuis[15], H. Maurice-Stam[15], C.A. Stiller[16], P. Hammond[17], H.N. Caron[1], J.H.M. Merks[1]

[1]Department of Paediatric Oncology, Emma Children's Hospital Academic Medical Centre Amsterdam, Amsterdam, Netherlands; [2]Department of Paediatric Oncology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [3]Department of Clinical Epidemiology and Bio-Statistics, Academic Medical Centre, Amsterdam, Netherlands; [4]Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute, Amsterdam, Netherlands; [5]Department of Otorhinolaryngology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [6]Orbital Centre Department of Ophthalmology, Academic Medical Centre, Amsterdam, Netherlands; [7]Department of Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [8]Department of Radiation Oncology, Academic Medical Centre, Amsterdam, Netherlands; [9]Department of Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [10]Department of Radiotherapy, The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; [11]Department of Plastic Reconstructive and Hand Surgery, Academic Medical Centre, Amsterdam, Netherlands; [12]Dental and Maxillofacial department, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [13]Department of Oral and Maxillofacial surgery, Academic Medical Centre, Amsterdam, The Netherlands; [14]Children and Young People's Department, Royal Marsden Hospital, Sutton, United Kingdom; [15]Paediatric Psychosocial Department, Emma Children's Hospital, Academic Medical Centre, Amsterdam, The Netherlands; [16]The Childhood Cancer Research Group, Department of Paediatrics, University of Oxford, Oxford, United Kingdom; [17]Molecular Medicine Unit, UCL Institute of Child Health, London, United Kingdom

Objectives: The majority of head and neck rhabdomyosarcoma (HNRMS) patients need radiotherapy to achieve local control. Radiotherapy is a well-known cause of adverse events (AEs). To reduce AEs, an innovative local treatment was developed in the Emma Children's Hospital Amsterdam (EKZ-AMC): Ablative surgery, MOuld brachytherapy and surgical REconstruction (AMORE). Aims: to determine the prevalence of AEs in HNRMS survivors and to compare AEs between survivors treated with the international standard: external beam radiotherapy (EBRT-based: London) and survivors treated with AMORE if feasible, otherwise EBRT (AMORE-based: Amsterdam).
Methods: All HNRMS survivors, treated in London or Amsterdam between January 1990 and December 2010 (N = 153), and alive ≥2 years post-treatment were eligible (N = 113). A predefined list of AEs was assessed in a multidisciplinary clinic and graded according to the Common Terminology Criteria for Adverse Events v4.0.
Results: Eighty HNRMS survivors attended the clinic (median follow-up 10.5 years); 63% experienced ≥1 grade 3/4 event, and 76% had ≥5 AEs (any grade). Survivors with EBRT-based treatment experienced significantly more frequent and more severe AEs than survivors with AMORE-based treatment (p = 0.019 and p = 0.028 respectively). Five year overall survival (source population) after EBRT-based treatment was 75.0% and after AMORE-based treatment 76.9%, p = 0.56.
Conclusions: This study is a baseline for new methods of local control and can be used in the future to assess AEs caused by novel local treatment modalities. AMORE-based local treatment resulted in similar overall survival and a reduction of AEs secondary to local treatment.

EP-255

RADIATION-INDUCED HEARING LOSS IN SURVIVORS OF CHILDHOOD HEAD AND NECK RHABDOMYOSARCOMA

R. Schoot[1], E.A.R. Theunissen[2], O. Slater[3], M. Lopez Yurda[4], C.L. Zuur[2], M.N. Gaze[5], Y.-C. Chang[5], H.C. Mandeville[6], J.E. Gains[5], K. Rajput[7], B.R. Pieters[8], R. Davila Fajardo[8], R. Talwar[9], H.N. Caron[1], A.J.M. Balm[2], W.A. Dreschler[10], J.H.M. Merks[1]

[1]Department of Paediatric Oncology, Emma Children's Hospital Academic Medical Centre Amsterdam, Amsterdam, Netherlands; [2]Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute, Amsterdam, Netherlands; [3]Department of Paediatric Oncology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [4]Department of Epidemiology and Biostatistics, The Netherlands Cancer Institute, Amsterdam, Netherlands; [5]Department of Oncology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; [6]Department of Radiotherapy, The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; [7]Department of Audiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [8]Department of Radiation Oncology, Academic Medical Centre, Amsterdam, Netherlands; [9]Department of Otorhinolaryngology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom; [10]Department of Audiology, Academic Medical Centre, Amsterdam, Netherlands

Objectives: The majority of children with head and neck rhabdomyosarcoma (HNRMS) need radiotherapy to achieve and maintain local control. However, radiotherapy to this region can cause significant adverse events, especially in young patients. The prevalence of hearing loss as an adverse event in this population of survivors is unknown. Therefore we assessed the hearing status of HNRMS survivors in a long-term follow-up clinic. Furthermore, we compared hearing loss between survivors with external beam radiotherapy (EBRT) -based local treatment with survivors with AMORE-based local treatment. AMORE is an innovative multi-disciplinary local treatment and consists of: Ablative surgery, MOld technique afterloading brachytherapy and surgical REconstruction (AMORE).
Methods: A prospective analysis was conducted of hearing thresholds at low and high frequencies obtained by long-term pure tone audiometry. The difference between hearing thresholds between treatment groups was assessed using repeated measurement linear regression analyses. Clinically relevant hearing loss was defined as a deterioration of ≥20 dB at PTA 0.5-1-2 kHz or at 4 kHz.
Results: Seventy-three out of 80 survivors were included (median follow-up 11 years). We found clinically relevant hearing loss in 19% (14/73) of the survivors at Pure Tone Average 0.5-1-2 kHz; 13/14 (93%) had a conductive or mixed type of hearing loss. Fewer survivors experienced clinically relevant hearing loss after AMORE-based treatment compared with EBRT-based treatment: 15% versus 26% ($p = 0.26$). Multivariable regression analysis showed that survivors treated with EBRT-based treatment and those with parameningeal tumors had significantly more hearing impairment post-treatment when compared to survivors with AMORE-based treatment and non-parameningeal tumors
Conclusions: We found clinically relevant hearing loss in 19% of all HNRMS survivors. Furthermore, this study shows a trend towards less radiation-induced hearing loss after AMORE-based treatment compared to local treatment with EBRT in HNRMS survivors.

EP-256

IMPAIRMENT OF BONE HEALTH IN CHILDREN AFTER TREATMENT WITH POLYCHEMOTHERAPY FOR RETINOBLASTOMA IN EARLY CHILDHOOD IS SUBTLE

M.M. Schündeln[1], P.K. Hauffa[1], S.C. Goretzki[1], J. Bauer[1], W. Sauerwein[2], N. Bornfeld[3], B.P. Hauffa[4], C. Grasemann[4]

[1]Pediatric Hematology and Oncology, University Hospital Essen, Essen, Germany; [2]Radiotherapy, University Hospital Essen, Essen, Germany; [3]Ophtalmology, University Hospital Essen, Essen, Germany; [4]Pediatric Endocrinology and Diabetology, University Hospital Essen, Essen, Germany

Objectives: Impairment of bone health in survivors of childhood cancer occurs frequently. Retinoblastoma (RB) is a malignant eye tumor in very young children. Enucleation is usually curative. However chemoreduction, as an eye sparing treatment attempt is being applied increasingly. Chemotherapy is commonly combined with local treatment modalities. We conducted a cross sectional study to analyze the impact of chemotherapy for retinoblastoma on bone health.
Methods: The study (DRKS00003636) was approved by the local ethics committee. 33 Patients (12 female, age at diagnosis 0.75+ 0.67) were recruited at regular visits to the Essen University-Hospital. Of these, 14 patients had unilateral, 19 bilateral RB. Patients underwent polychemotherapy (33) and either enucleation (21), intra-arterial melphalan (2), thermo-chemotherapy (12), brachytherapy (10), percutaneous radiation (10) or a combination of therapies. Polychemotherapy consisted of cyclophosphamide (4800 mg/m2), etoposide (1800 mg/m2), vincristine (9mg/m2) and carboplatin (1200mg/m2). Clinical and biochemical parameters of growth, pubertal development and bone health were obtained. The history of fractures and bone pain were assessed. Age dependent parameters were calculated as SDS (height, weight, BMI, pubertal stage, IGF-1) or assessed using age appropriate norms (Bone specific alkaline Phosphatase (BAP), osteocalcin (OC).
Results: Mean chronological age: 4.4 + 3.8 (0.69-15.8) y, height SDS -0.5 + 0.92 (−2.92 - 1.21), BMI SDS 0.46 + 0.81 (−1.41 – 2.28). SDS for testicular volume/breast development: -0.02 (−1.3 – 1.41). 25 OH-vitamin D deficiency (VD: 23.2 + 13.6 (8–73.8) ng/ml) was observed in 52%. Hyperparathyroidism (PTH 37.4 + 22 (14.5–100) pg/ml) in 15% of patients. BAP was elevated in 16%. 7% reported bone pain. 9% experienced fractures.
Conclusions: Impairment of bone health after treatment with chemotherapy for RB was only subtle. However, some children presented with bone pain and altered parameters of bone health. Since identification of children at risk is difficult, we recommend long term monitoring and supplementation of vitamin D.

EP-257

LATE MORBIDITY AMONG SURVIVORS OF CHILDHOOD CANCERS: EXPERIENCE AT TERTIARY CARE CANCER HOSPITAL

N. Shaheen[1], F. Naz[1], S. Raiz[1], M.S. Khan[1], M. Ahmed[1]

[1]Paediatric Oncology, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan

Objectives:
1. To study the cohort characteristics and late effects of various treatment modalities in childhood cancer survivors at our center.
2. To organize exposure-based health screening guidelines among childhood cancer survivors.

Methods: All children under the age of 18 years with diagnosis of cancer during Jan 1995 to Dec 2008 at SKMCH, who fulfilled the following inclusion criteria were enrolled in the study:

1. Treatment at our center with chemotherapy and/or radiation and/or surgery
2. Five years or more post primary diagnosis and followed in long term follow up clinic (LTF). Data were analyzed retrospectively to determine each candidate's clinical, demographic characteristics and details of treatment. Toxicity evaluations were tailored according to specific therapeutic exposures. Frequency of toxicities attributed to chemoradiation agents was calculated.

Results: Three hundred patients were studied. Male to female ratio was 2.7:1. At the time of diagnosis 20% were under 4 years, 44% between 5-9 years, 26% between 10-14 years and 10% were above 15 years of age. Current median age was 18 years (range 10 -32 years). Hodgkin lymphoma was the most common diagnosis (49.6%) followed by acute leukemia (17%), NHL (13.4%), GCT (9.7%), retinoblastoma (5%) respectively. Duration of survival was more than 10 years in 69% and less than 10 years in 31% of patients. Regarding treatment modalities, 57% received chemotherapy, 23%-chemo and XRT, 15% chemo and surgery, 3% chemo, surgery and radiation and 2% surgery only. On toxicity evaluation, azospermia was the most common late effect (49%) followed by oligospermia (15%); 13.5% of our patients had hypothyroidism, 6.5% develop ototoxicity, 4.6% had impaired DLCO, 4% low bone density and 2.4% had cardiomyopathy.
Conclusions: Our study confirms high prevalence of persisting end-organ toxicities from chemoradiation exposure among survivors of childhood cancers. There is need to implement risk based and exposure related guidelines for life long follow up of cancer survivors.

EP-258

LONG TERM RISK OF CARDIAC MORBIDITY AFTER CRANIO-SPINAL IRRADIATION

A. Sharma[1], B. Sarkar[1], S. Agrawal[1], N. Hazarika[2], T. Ganesh[1], A. Munshi[1], B.K. Mohanti[1]

[1]Radiation Onclogy, Fortis Memorial Research Institute, Gurgaon, India; [2]Paediatric Onclogy, Fortis Memorial Research Institute, Gurgaon, India

Objectives: To evaluate long term risk of cardiac morbidity in patients treated with cranio-spinal radiotherapy (CSI). Approx Odds ratio of development of cardiac morbidity for non radiated medulloblastomas is 2.3.
Methods: The study included six medulloblastoma patients that were simulated in supine position after immobilization using thermoplastic cast. Target delineation included CTV_brain that encompassed whole of the brain tissue CTV_spine included entire spinal canal that extended caudally till the lower end of thecal sac, CTV_Boost encompassed posterior fossa. Additional 7 mm margin generated respective PTV. CSI dose was 23.4 Gy/13#/2.5 wks for low risk disease and 35Gy/21#/4.1wks for high risk disease, posterior fossa boosted to a dose of 54-55Gy. Organs at risk delineated included heart, lungs, thyroid, esophagus, eyes, cochlea, hypothalamic-pituitary axis kidney and liver. Patients were planned either by 3DCRT, IMRT, VMAT either in Xio V4.80.00.7 or Moanco V 3.03.01. All patients were planned in SAD technique. 3DCRT was planned using a systematic junction shift where IMRT/VMAT using a junction dose gradient technique. For evaluation of late cardiac morbidity D_{max}, D_{mean} and volume of heart was recorded in all patients. Odds radio for development of late long term cardiac morbidity was calculated by the formula $OR = 1 + \alpha_1 D + \alpha_2 D^2$ where D is mean dose received by heart and value of $\alpha_1 = 0.19$ and $\alpha_2 = 0.002$ were used in the equation.
Results: Median age of presentation was 12.5 years (range2-26 yrs). Four patients were standard risk medullblastoma whereas two were in high risk category. Median volume of heart was 367cc (range 213-577cc). D_{max} for heart was 32.03 Gy (range 21.06-33.47Gy) whereas D_{mean} received by the heart was 12.77Gy (range 8.36-14.67Gy). Odds radio for development of late long term cardiac morbidity after CSI was 3.75 (range 2.59-4.21).
Conclusions: Risk of late long term cardiac morbidity after CSI is higher than non-radiated medulloblastoma patients.

EP-260

FOLLOW-UP CARE AND CANCER RELATED COMMUNICATION WITH PROVIDERS AMONG YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER AFTER TRANSFER TO ADULT CARE

D. Szalda[1], W. Hobbie[1], J. Ginsberg[1], L. Brumley[1], M. Wasik[1], L. Schwartz[1]

[1]Oncology, Children's Hospital of Philadelphia, Philadelphia, USA

Objectives: Approximately 30% of childhood cancer survivors receive cancer-focused follow-up care as recommended. However, no study has assessed engagement in and perceived quality of adult survivorship care following formal transfer from pediatric to adult care. This study describes: (1) rates of and satisfaction with follow-up care of transferred young adult survivors (YAS) and (2) patient-reported cancer-related communication from adult primary care providers (PCPs).
Methods: YAS transferred from a Survivorship Program to adult providers within 1 - 5 years completed online measures. Data collection is ongoing; final N $\sim$ 90 by conference.
Results: Participants (N = 66) were 23-36 yo (M = 27.5), 48% male and 93% Caucasian. 95% of patients reported seeing a healthcare provider in the past year. 23% (n = 15) reported attending an adult survivorship clinic and 30% (n = 20) reported seeing a PCP for survivorship care in the past year. Quality of cancer care was perceived as good to excellent for 80% of patients attending survivorship clinic and 65% of patients attending primary care. YAS who saw PCPs for survivorship care reported discussions regarding (% who endorsed): prior diagnosis (45%), treatment (35%), risk for late effects (25%), and screening for late effects (35%). Of patients who reported they had not received survivorship care, 38% (n = 26) saw PCPs for non-cancer-related reasons. In those cases, the following% of survivors reported discussions about: prior diagnosis (38%), treatment (23%), risk for late effects (16%), and screening for late effects (21%).
Conclusions: Almost half of transferred YAS did not seek cancer-related follow-up care in the past year. YAS receiving "survivorship care" from a PCP reported only marginally better rates of survivorship-focused communication than those seeking care from a PCP for other reasons. Results highlight the need to better understand barriers of seeking adult survivorship care and improve the competence of PCPs to provide optimal survivorship care.

EP-261

RELATIONSHIP BETWEEN CISPLATIN ADMINISTRATION AND THE DEVELOPMENT OF OTOTOXICITY

G. Tokuc[1]

[1]Pediatric Hamatology and Oncology, Marmara University, Istanbul, Turkey

Objectives: Cisplatin-induced ototoxicity is an important dose-limiting side effect. Our purpose is to determine the audiologic toxicity associated with cisplatin in pediatric oncology patients.
Methods: We performed an audiometric analysis of 58 pediatric oncology patients who received cisplatin therapy between January 1998 and January 2014, who were treated with cisplatin with the diagnosis of neuroblastoma, medulloblastoma, osteosarcoma, germ cell tumour, and hepatoblastoma.
Results: The median age at the time of diagnosis was 9.7 (range 3.4–16.9) years. There were 26 males and 32 females. The underlying diseases were neuroblastoma (18 cases), medulloblastoma (18 cases), osteosarcoma (11 cases), germ cell tumors (9 cases), and hepatoblastoma (2 case). The median individual dose was 100 mg/m2/cycle (56-200). The median cumulative dose was 480 mg/m2 (200-1,200). Sixteen patients received cranial radiotherapy. Of the 58 patients, 24 developed hearing loss, leading to an overall incidence of 42%. Logistic regression analyses showed that the age at treatment (P = 0.02) and cumulative dose of cisplatin (P = 0.005) were the significant risk factors in predicting hearing loss in children treated with cisplatin. There was neither improvement nor aggravation during the follow-up in all of the patients who had hearing loss (3–68 months).
Conclusions: The cumulative dose of cisplatin (>500 mg/m2) and the younger age at treatment (<12 years) were 2 mainly important risk factors for ototoxicity in patients treated with cisplatin. Serial audiometric evaluations are needed in the patients with risk factors during and after cisplatin treatment.

EP-262

THYROID DYSFUNCTION FOLLOWING TREATMENT FOR HODGKIN'S DISEASE

G. Tokuc[1]

[1]Pediatric Hamatology and Oncology, Marmara University, Istanbul, Turkey

Objectives: Thyroid dysfunction is an important morbidity of therapy for Hodgkin's disease, which should be well recognized by the doctors of these patients. Our aim is to investigate the thyroid dysfunction incidence among our Hodgkin lymphoma patients after treatment
Methods: Forty eight pediatric patients (less than 18 years old at diagnosis), who were treated with chemotherapy and radiotherapy with the diagnosis of Hodgkin disease between 1995 and 2013, were periodically evaluated thereafter. Twenty-nine of the patients were irradiated to the neck and the others were irradiated to the other regions according to the involvement of the disease at the first diagnosis.
Results: The median age at diagnosis was 11 years, and the median duration of follow up was 10 years. 18 patients, out of 38 who were irradiated to the neck region, developed biochemical hypothyroidism. The median time to the development of hypothyroidism was 5 years. Transient hyperthyroidism developed in two patients, 6 and 11 months after treatment for Hodgkin's disease. Among the 10 patients who were irradiated to the regions other than neck, none developed thyroid disfunction. Four patients, although with normal thyroid functions, had hypoechoic nodule diagnosed at thyroid ultrasonography. The nodules showed histological multinodular goiter (3), and single colloid nodule (1).

Conclusions: There is a high risk of thyroid disease development following neck radiation therapy for Hodgkin's disease, reinforcing the importance and need for continued clinical and biochemical evaluation of those patients during follow up.

EP-263

ELECTROEJACULATION AS A METHOD OF FERTILITY PRESERVATION IN BOYS DIANGOSED WITH CANCER: A SINGLE-CENTRE EXPERIENCE AND REVIEW OF THE LITERATURE

M.C. Adank[1], W. van Dorp[2], M. Smit[3], N.J. van Casteren[3], J.S.E. Laven[4], R. Pieters[1], M.M. van den Heuvel-Eibrink[1]

[1]Paediatric Oncology and Haematology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Paediatric Oncology and Haematology and Obstetrics and Gynaecology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [3]Urology, Erasmus University Medical Center, Rotterdam, Netherlands; [4]Obstetrics and Gynaecology, Erasmus University Medical Center, Rotterdam, Netherlands

Objectives: To evaluate the feasibility of electroejaculation to perform semen cryopreservation in pubertal males before gonadotoxic therapy, and to review literature on this topic.
Methods: We performed a retrospective cohort study and review of the literature. The retrospective single-centre study was performed in an academic children's hospital and included males diagnosed with cancer to whom sperm cryopreservation was offered before start of gonadotoxic therapy. We studied the outcome of electroejaculation, including patients' characteristics, hormone levels, and pre-treatment semen parameters.
Results: Pre-treatment semen samples were obtained by masturbation in 106/114 males with cancer, of which 78/106 were adequate for preservation. In 11 males electroejaculation was offered, of which 3/11 appeared adequate for preservation. Reviewing all reported electroejaculation cases in children with cancer in the literature, 13/29 (45%) cases were successful. Testosterone levels were higher in patients with successful sperm yield obtained by electroejaculation (testosterone: median 8.3 nmol/l (5.2-42.4) in successful versus median 1.7 nmol/l (0.01-17.9) in unsuccessful harvests).
Conclusions: Semen cryopreservation should be offered to all pubertal males. If masturbation fails, electroejaculation can be considered as a useful option for semen cryopreservation, and leads to adequate material for cryopreservation in about half of the cases.

EP-264

SLIPPED CAPITAL FEMORAL EPIPHYSIS AFTER TOTAL BODY IRRADIATION

A. Vedi[1], K. Neville[2], D. Saravanja[3], K. Johnston[1], R.J. Cohn[1]

[1]Kids Cancer Centre, Sydney Children's Hospital, Sydney, Australia; [2]Endocrine Department, Sydney Children's Hospital, Sydney, Australia; [3]Orthopaedics Department, Sydney Children's Hospital, Sydney, Australia

Objectives: A significantly increased risk of slipped capital femoral epiphysis (SCFE) has recently been identified in survivors of childhood cancer treated with recombinant growth hormone (rhGH) after receiving total body irradiation (TBI) conditioning for hematopoietic stem cell transplantation (HSCT)[1].
Methods: We identified 4 cases (1 female) of SCFE in our cohort of 104 children who received TBI conditioning prior to HSCT over the past 30 years, of which 3 were rhGH ***naïve*** at the time of presentation.
Results: The children presented 4.8-10.3 years after 12Gy TBI conditioning for autologous HSCT. Presentation was atypical compared to idiopathic SCFE[2]: younger age (6.9-12.2 years), all prepubertal and only one overweight (BMI z-score -2.4 to 1.7). Two were bilateral at presentation, and three of the four patients presented with the uncommon valgus variant of SCFE. Overall time from symptom onset to radiological diagnosis was 5-27 months. The only child presenting with SCFE (unilateral) whilst on rhGH was a 12.2 year old female with unreplaced hypogonadism. She was diagnosed 11 months after commencing rhGH though had experienced x-ray 'negative' transient hip pain 7 months prior. Upon review of her original radiographs, by Yngve's criteria[3], there was subtle evidence of valgus slip.
Conclusions: We conclude that TBI alone is a significant risk factor for SCFE, with delays in diagnosis due to the atypical clinical and radiological presentation being common[4]. Valgus slips are frequently subacute in presentation with standard radiology inadequate. Yngve's criteria are a more sensitive method of screening initial radiographs in children with hip symptoms. However, if standard radiological techniques are negative or equivocal, other modalities such as ultrasound and/or MRI must be considered and early orthopaedic referral mandatory. Furthermore, rhGH therapy is frequently considered in this population. The risk of developing SCFE must be carefully considered by clinicians and clearly discussed with families before embarking on rhGH therapy.

EP-265

LATE-EFFECTS IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH NON-CNS GERM CELL TUMORS TREATED WITH PEB CHOMOTHERAPY REGIMEN

M. Vervaeke[1], Y. Gosiengfiao[2], B. Lockart[2], D. Walterhouse[2], J. Reichek[2], K. Danner-Koptik[2], K. Dilley[2], J. Toia[2], J. Woodman[2]

[1]Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, USA; [2]Hematology Oncology and Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, USA

Objectives: The incidence and severity of the cisplatin-etoposide-bleomycin (PEB) regimen have not been reported in children treated for non-CNS germ cell tumors (GCT). The purpose of this study was to evaluate the incidence and severity of audiologic, reproductive, renal, and pulmonary toxicity in pediatric and young adult patients with non-CNS GCT patients treated with PEB.
Methods: We performed a retrospective chart review of the audiologic, renal, pulmonary, and reproductive toxicity in patients $\leq$ 20 years of age with non-CNS GCT diagnosed and treated at Ann & Robert H. Lurie Children's Hospital of Chicago from January 1991 to December 2007. Patients who received radiation or other chemotherapy agents were excluded.
Results: Twenty-six patients who received 3-4 cycles of PEB had a median follow-up of 82.3 months. 50% had no measureable hearing loss, 23% had CTCAE grades 1-2 hearing loss and 8% required hearing aids following treatment. The 2 patients who required hearing aids received 800 mg/m2 of cisplatin, while all others with hearing loss received standard dose. Of 23 patients with data available to assess kidney function, 70% had normal kidney function, and 30% had stage 2 chronic kidney disease (CKD) with a GFR 60-90 mL/min/1.73m^2. None required electrolyte supplementation. 11 patients had pulmonary function tests performed after treatment. All were normal, excluding 1 patient who had obstructive disease prior to and after treatment. 4 out of 5 patients tested had normal FSH, LH, estradiol or testosterone values. One became pregnant during follow-up.
Conclusions: Our series suggests that a significant proportion of pediatric patients who receive PEB for non-CNS GCT do not have audiologic, renal, pulmonary, or reproductive toxicity. Hearing loss, usually not requiring hearing aids, and reduced GFR, qualifying as stage 2 CKD, were the most frequent late-effects.

EP-266

ESTABLISHING PAEDIATRIC LONG TERM FOLLOW-UP TRANSITION CLINICS IN THE TERTIARY ADULT HEALTH CARE SECTOR

S. Skinner[1], R. Harrap[1], K. Egan[1], J. Williamson[2], P. Downie[1]

[1]Long Term Follow Up Program, Paediatric Integrated Cancer Service, Melbourne, Australia; [2]Paediatric Integrated Cancer Service, Paediatric Integrated Cancer Service, Melbourne, Australia

Objectives: The number of new patients referred to the Paediatric Long Term Follow-up (LTF) Program, in addition to existing LTF patients requiring ongoing review, exceeds current clinic capacity.
Methods: The Long Term Follow-up Program (LTFP) has collaboratively established transition clinics with two tertiary adult health care providers to support the process of transition and to enhance transfer of adolescent/young adults (AYA) to the tertiary adult health care sector.
Results: In the three years (36 months) prior to June 2012, 14 patients were transitioned to tertiary adult health care providers (an average of 4.6 patients per year). Transition clinics were implemented in July 2012. In the period July 2012 to December 2013 (18 months) a total of 28 patients have been transitioned to tertiary adult health care providers (an average of 18.7 patients per year). An additional 15 patients are planned for transition by June 2014 (an average of 21.5 patients per year).
Conclusions: Following the implementation of formalised transition clinics, transition of AYA's to tertiary adult health services has increased to 7% of all patients referred to the LTFP. Transition has increased from 5 patients per year to 22 patients per year, creating capacity within the LTFP for new referrals and reducing waiting list times. The implementation of formalised transition clinics supports AYA patients receiving a personalised and supported transition, reduces the numbers of AYA patients 'bouncing back' to the paediatric sector, and provides the opportunity for the adult health care sector to receive an in-depth 'face to face' hand over of these complex patients.

EP-267

OPTIMISING FOLLOW UP FOR CHILDREN WITH BRAIN TUMOURS

A. Wong[1], D. Williams[1], H. Greene[1], L. Salisbury[1]

[1]Department of Paediatric Haematology/Oncology, Cambridge University Hospitals NHS Foundation Trust Addenbrookes Hospital, Cambridge, United Kingdom

Objectives: The aim of this project was to optimise the follow up for children with brain tumours recognising that this group of children often have multiple sequelae of their disease or treatment, including growth, endocrine, neurological and neuropsychological sequelae, with ongoing rehabilitation needs. Attending multiple appointments interferes with their schooling and their parents' work commitments, and comprehensive management plans are often difficult to achieve.

Methods: We identified the patients who have been attending both oncology-endocrine and neurosurgical-oncology clinics, many of whom had additional ongoing rehabilitation needs. We produced a clinic proforma summarising the diagnosis, treatment given and complications, and included prompts to address all medical issues, schooling, neuropsychological needs and potential transition plans. In September 2013 the Oncological-Neurosurgical-Endocrine (ONE) clinic was established to bring all the multiprofessional teams together to provide a holistic review of these children. A pre-clinic multi-disciplinary team meeting was established to fully discuss each patient, including their rehabilitation issues. Families move through rooms with the same key worker, one of the Clinical Nurse Specialist team, to ensure all aspects are addressed but not repeated unnecessarily. After each clinic, a comprehensive clinic letter is produced, summarising the medical needs, rehabilitation review, schooling and future management plan for the patients and carers, their local shared care hospital, allied health professionals and their general practitioner.
Results: Three clinics have been run so far. Patient and staff feedback has been very positive particularly in relation to fewer appointments and the more holistic approach to the review.
Conclusions: Children with brain tumours who have multiple sequelae of their disease or treatment benefit from dedicated specialist clinics which address all their medical and holistic needs in a one stop clinic. This also provides an opportunity for patient/parent education around medical, neurological and neuropsychological issues using a variety of different tools.

EP-268

THE FUNCTIONAL IMPACT OF PERIPHERAL NEUROPATHY IN CHILDREN AND YOUTH TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA: MULTIDIMENSIONAL ASSESSMENT

M. Wright[1], D. Twose[2], J. Gorter[1]

[1]Pediatrics, McMaster Children's Hospital/McMaster University, Hamilton, Canada; [2]Pediatrics, McMaster Children's Hospital, Hamilton, Canada

Objectives: To describe a multi-dimensional functional assessment of chemotherapy induced peripheral neuropathy (CIPN) and related impairments, activity limitations, and participation restrictions in children/youth treated for acute lymphoblastic leukemia (ALL).
Methods: Participants were a purposeful sample of children/youth on or off treatment for ALL with varying degrees of CIPN. Multidimensional assessment as outlined in the results and 3-D instrumented gait analysis were conducted. Analyses were descriptive. Normative values provide context.
Results: Fourteen participants were assessed (median age 7 years, range 5-21), 6 males, 6 receiving maintenance therapy and 8 off treatment (mean time off 28 months, range 1-80). Data is presented as mean (standard deviation) [range]{normative}. Pediatric modified Total Neuropathy Scale:4.9 (2.7) [2-12]{0-4}; 6 minute walk test (metres) :400.3 (113.7) [180.0-586.7]{400-600}; Bruininks-Oseretsky Test of Motor Proficiency Running Speed and Agility subtest (Standard Score): 1.1 (0.5) [1-3]{10-20}; Oxford Foot and Ankle Questionnaire (%) Physical: 46.1 (27.2) [0-75]{100}; School Play: 64.7 (31.6) [6.3-100]{100}; Emotional: 80.2 (24.8) [25.0-100]{100}; Shoe Wear 69.5 (36.7) [0-100]{100}; Gross Motor Function Measure-ALL (%) Standing 88.4 (11.8) [66-100]{100}; Walk, Run, Jump 81.6 (14.2) [50-100]{100}; Pediatric Outcomes Data Collection Instrument Transfers and Basic Mobility: 36.7 (27.2) [-49-53]{50}, Sport and Physical Functioning 24.1 (19.0) [-27.0-42]{50}, Pain and Comfort 33.4 (19.7) [-6-57]{50}; Edinburgh Gait Scale: 6.2 (4.6) [0-14]{0}. Common kinematic gait characteristics included knee hyperextension, decreased dorsiflexion, delayed heelrise, and decreased ankle plantarflexion pre swing in stance; and decreased ankle dorsiflexion with compensatory hip and knee motion in swing. Temporal spatial data showed reduced step length with a corresponding reduction in velocity. Kinetics demonstrated decreased ankle moments/power generation at push off. Tibialis anterior and gastrocnemius electromyography showed timing and amplitude abnormalities.
Conclusions: Multi-dimensional functional assessment in children/youth participants treated for ALL demonstrated variability in impairments, activity limitations, and participations restrictions related to CIPN. These measures have the potential to inform clinical decision making regarding vincristine dosing, exercise, and orthotics; facilitate evaluation over time; and provide tools for further research of the impact of CIPN during and following treatment for ALL.

EP-269

RECALL OF FERTILITY DISCUSSION IN ADOLESCENT FEMALE CANCER PATIENTS

S. Zarnegar[1], Y. Gosiengfiao[2], A. Rademaker[3], R.L. Casey[4], K.H. Albritton[5]

[1]Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, USA; [2]Pediatric Hematology Oncology & Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, USA; [3]Department of Preventive Medicine, Feinberg School of Medicine Northwestern University, Chicago, USA; [4]Pediatrics-Hematology/Oncology, Children's Hospital Colorado, Aurora, USA; [5]Hematology and Oncology, Cook Children's Health Care System, Fort Worth, USA

Objectives: Current clinical guidelines emphasize that oncologists should discuss the risk of treatment-related infertility and preservation options before starting therapy. The purpose of this study was to determine whether female adolescent cancer patients at Ann & Robert H. Lurie Children's Hospital of Chicago remembered a discussion about fertility and preservation options at initial treatment planning and whether they were satisfied with information received.
Methods: We surveyed females who were 13 – 18 years old at cancer diagnosis and were 6 months - 3 years from diagnosis at enrollment regarding initial treatment planning, current feelings including mental health status, and demographics.
Results: Of the 16 subjects surveyed, 10 (A) recalled a discussion of decreased fertility as a potential side effect of therapy while 6 did not (B). 8/10 in A recalled a discussion of preservation options. 100% of subjects in A (9/9, 1 non-respondent) were satisfied with information received at diagnosis, contrasted with 50% satisfaction in B ($p < 0.04$). Presently, 80% of subjects in A (8/10) remain satisfied compared to 50% in B. Half the subjects in A reported making joint medical decisions with their parents compared to only 1/6 in B. More subjects who had looked forward to future pregnancy before cancer diagnosis recalled a discussion of fertility (5/7 = 71%). Overall, more subjects in A now anticipate difficulty in becoming pregnant because of treatment and one woman believes she will not be able to become pregnant.
Conclusions: A majority of subjects recalled a discussion of treatment-related infertility and preservation options. These young women were more satisfied with the information they received than were those who did not recall a discussion about fertility. Shared decision-making may be an important factor in recall of these discussions.

LIVER TUMOURS

EP-270

NON HEPATOBLASTOMA LIVER TUMORS IN CHILDREN - A SINGLE CENTRE EXPERIENCE

M. Bhagat[1], S. Qureshi[1], S. Kembhavi[2], M. Ramadwar[3], S. Desai[3], G. Chinnaswamy[4], T. Vora[4], S. Laskar[5], N. Khanna[5]

[1]Pediatric Surgery Oncology, Tata Memorial Hospital, Mumbai, India; [2]Dept of Radiology, Tata Memorial Hospital, Mumbai, India; [3]Dept of Pathology, Tata Memorial Hospital, Mumbai, India; [4]Pediatric Medical Oncology, Tata Memorial Hospital, Mumbai, India; [5]Radiation Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: The aim of this study was to review the clinical features, management and the outcome of children diagnosed with non hepatoblastoma liver tumors (NHLT).
Methods: All pediatric patients with NHLT managed in our institute from 2006 to 2013 were included in the study. Biopsy was performed if serum tumor markers were normal, radiological features were not suggestive of hepatoblastoma or age was less <6 months or > 3 years. All lesions were staged retrospectively as per the pretext staging system. The clinical findings, imaging, surgical details, intraoperative and postoperative complications, relapse and survival details were analyzed. Chemotherapy or radiotherapy was utilized when indicated.
Results: Of the total 14 liver lesions, 9 were benign: hemangioendothelioma (3), mesenchymal hamartoma (3), hemangioma (1), adenoma (1) and focal nodular (FNH) (1). Primary liver tumors were hepatocellular carcinoma (HCC) (1) and synovial sarcoma (1) and three had metastatic lesions. The primaries in metastatic patients were ovarian germ cell tumor (GCT), pancreaticoblastoma and Wilms tumor. The PRETEXT distribution was: I (5), II (6), III (2), and IV (1). Right hepatectomy was performed in four, left lateral sectorectomy (LLS) in three and non anatomic resections (NAR) in seven. The median blood loss was 250 ml (range 10 to 2100ml) and median intraoperative time was 3.30 hours (range- 2 -8 hours). All patients had negative margins except one with FNH. There were no intraoperative or postoperative complications. At mean follow-up of 30 months there were no local recurrences and all patients are alive and disease free.
Conclusions: NHLT are often low PRETEXT stages. Safe surgery is feasible without morbidity and is associated with good outcome.

EP-271

TREATMENT OUTCOME OF CHILDREN WITH HEPATOBLASTOMA

B. Demirag[1], D. Ince[1], A. Celik[2], A. Erbay[3], M. Hosgor[4], G. Diniz[5], Y. Oymak[1], Y. Yaman[1], G. Ozek[1], C. Vergin[1]

[1]Pediatric Hematology & Oncology Clinic, Dr Behcet Uz Children Hospital, Izmir, Turkey; [2]Pediatric Surgery Dept., Ege University Faculty of Medicine, Izmir, Turkey; [3]Pediatric Hematology & Oncology Dept., Baskent University Faculty of Medicine, Adana, Turkey; [4]Pediatric Surgery Dept., Dr Behcet Uz Children Hospital, Izmir, Turkey; [5]Pathology, Dr Behcet Uz Children Hospital, Izmir, Turkey

Objectives: To evaluate treatment results of patients with hepatoblastoma (HB).
Methods: Medical records of patientswith HB who diagnosed and treated between 1996-2013 were reviewed retrospectively.
Results: There were 18 patients with diagnosis of HB, and 16 of them were eligible. Two patients refused the treatment. Median age of diagnosis was 13 months (3months-10.5yrs), 81%of patients were <2years of age; M/F ratio was 1.0. Stage distribution: PRETEXT-I 12.5% (n:2), PRETEXT-II 12.5% (n:2), PRETEXT-III 62.5% (n:10), PRETEXT-IV 12.5% (n:2). Two patients had pulmonary metastasis. The median AFP level was 8112 ng/mL (53–

148.206). Histopathologic examination revealed epithelial HB in 69%, and HB-NOS in 31%. Primary total resection was performed in four cases who had PRETEXT-I and PRETEXT-II disease. A 10 years-old male had PRETEXT-I-HB and AFP < 100ng/mL; CR was achieved by primary total tumor resection and COG-high risk chemotherapy protocol. Twelve patients received chemotherapy according to the SIOPEL protocol (SIOPEL-2 in four, SIOPEL-4 in 9 patients), then delayed surgery was performed. Dextrazoxan was provided only for three patients who received SIOPEL-4 protocol. Delayed surgery was resulted in microscopic residue in two patients with PRETEXT-III disease. One of these two patients relapsed with pulmonary metastases at the 26th month and the other relapsed at primary tumor site at the 7th month. Liver transplantation was performed in patient who had primary relapse. The median follow-up time was 76months (11months-12years). Survival analysis was done 14 patients who treated according to the SIOPEL protocol. The 2-years EFS rate was 93%, 5 and 10-years EFS rates were 83%; the 5 and 10-years OS rates were 100%. There was no early or late chemotherapy toxicity.
Conclusions: Performing surgery in experienced centers is important for hepatoblastoma treatment. There was no death related to chemotherapy toxicity or surgery. Survival rates were acceptable. SIOPEL protocol was found applicable and successful in our conditions.

EP-272

LIVER MASSES, CLINICAL AND RADIOLOGICAL DIFFERENTIAL DIAGNOSIS – REPORT OF 4 CASES ADMITTED IN A SINGLE MONTH

D. Gasperini[1], E. Boldrini[1], C. Cavalcante[2], N. Suarez[1], E. Silva[3], L.U.I.Z. Lopes[4]

[1]Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Radiologist Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Pathology Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [4]PhD Medical Director, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: In this paper, we report four cases of liver mass in children admitted to our hospital in August of 2013.
Methods: With ages ranging from 3 months to 4 years, all male, with abdominal distension and palpable liver mass as the chief complaint, associated with other signs and symptoms (weight loss, respiratory distress, cough, dyspnea, jaundice, acholic stools and dark urine). Two of them had elevated alpha-fetoprotein (AFP), two had abnormal liver enzymes and one had hyperbilirubinemia. They underwent examination of biopsy: three were malignant (two hepatoblastomas and rhabdomyosarcoma of the biliary tract) and one was mesenchymal hamartoma.
Results: Hepatoblastoma is the most common liver tumor in childhood, most often before the age of three, male to female ratio is 2:1 and is not associated with cirrhosis; the mass is usually large single and most often increases AFP. Biliary rhabdomyosarcoma is a rare tumor (0.8%), which is the most common cause of malignant obstructive jaundice in this age group, occurs around the age of 3, can have jaundice, acholic stools, dark urine, and hepatomegaly. With increased bilirubin and liver enzymes. Mesenchymal hamartomas are more frequent in children under 2 years, they are congenital and benign lesions, presenting as palpable abdominal mass with abdominal distension, painless and without altering liver function or AFP. The most common radiological findings are: hepatoblastoma is well circumscribed and may appear lobulated with septa; rabdomiassarcoma biliary can be present and solid-cystic dilatation of bile and mesenchymal hamartoma pathways appear as cystic liver injury, multilocular with thin internal septa.
Conclusions: The ultrasound is an excellent screening test for suspected liver mass because is no ionizing radiation and no need for sedation. If confirmed hepatic mass, CT scan and MRI should be performed, to guide biopsy or surgery subsequently.

EP-273

HEPATOBLASTOMA: CLINICAL CHARACTERISTICS AND OUTCOME OF 13 PATIENTS

D. Ince[1], K. Mutafoglu[1], E. Buke[1], F. Yenigurbuz[1], M. Kilic[2], M. Olguner[3], C. Arikan[2], E. Ozer[4], H. Guleryuz[5], N. Olgun[6]

[1]Dept. of Pediatric Oncology, Dokuz Eylul University Institute of Oncology, Izmir, Turkey; [2]Liver Transplantation Team, Kent Hospital, Izmir, Turkey; [3]Dept. of Pediatric Surgery, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [4]Dept. of Pathology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [5]Dept. of Radiodiagnostics, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [6]Dept. of Pediatric Oncology, Dokuz Eylul University Insitute of Oncology, Izmir, Turkey

Objectives: To evaluate the clinical features and treatment results of the patients with hepatoblastoma (HB) in our department.
Methods: Medical records of children who diagnosed, and treated with HB were analyzed retrospectively.
Results: There was 13 children with HB. Median diagnosis age was 20months (1.5mos-16.5yrs), M/F ratio was 0.44. Stage distribution: PRETEXT IV in 46%, PRETEXT II in 31%, PRETEXT III in 15% and PRETEXT II in 8% of patients. The median AFP level was 83000ng/mL (320-1129000). Histopathologic examination revealed epithelial HB in 69% (fetal in 46%, mixed fetal+embryonal in 23%), epithelial+mesenchymal HB in 23%, HB not-otherwise specified in 8% of patients. PRETEXT I-II HB (n:5) Primary (n:3), and delayed (n:2) surgery were performed without residue. Chemotherapy was given accordingly to SIOPEL1 in one, SIOPEL3 in four patients. For a 16.5 year-old female who had PRETEXTII-HB relapsed at primary site at the 20th month, and died with progression at the 58th month. Other cases has been followed-up without disease. Median follow-up time was 3yrs (13mos-12.5yrs). PRETEXT III-IV HB (n:8): Patients receivedSIOPEL3 (n:4) and SIOPEL4 (n:4) chemotherapy schema. Delayed surgery was performed in all patients of which liver transplantation was done in six. Surgical magrin was tumor positive in one, and residual tumor thrombus remained in one, both patients relapsed and died with progression. First one had out of primary relapse at the 13th month and died at the 15th month. Second one relapsed at primary site at the 11th month and died at the 14th month. Median follow-up time was 16.5months (9mos-4yrs). Two- and 4-years EFS were 71% and OS were 69%.
Conclusions: The oldest patient had poor outcome despite having PRETEXTII-HB. Residual tumor after liver transplantation had resulted an early relapse and death in two cases. Multidisciplinary treatment and performing surgery in experienced centers are essential in management of HB.

EP-274

MANAGEMENT OF PEDIATRIC HEPATOCELLULAR CARCINOMA: A MULTIMODAL APPROACH

M. Kohorst[1], D.M. Warad[2], D.K. Freese[3], J.M. Matsumoto[4], V. Rodriguez[2], A.A. Nageswara Rao[2]

[1]Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, USA; [2]Pediatric and Adolescent Medicine/Division of Pediatric Hematology/Oncology, Mayo Clinic, Rochester, USA; [3]Pediatric and Adolescent Medicine/Division of Pediatric Gastroenterology, Mayo Clinic, Rochester, USA; [4]Pediatric and Adolescent Medicine/Division of Pediatric Radiology, Mayo Clinic, Rochester, USA

Objectives: Pediatric hepatocellular carcinoma (HCC) is exceedingly rare and accounts for 0.5-1.5% of childhood tumors. Survival rates for primary unresectable HCC have been dismal. Cisplatin and doxorubicin (PLADO) regimen has demonstrated a 5-year event free and overall survival of 17%, and 28%, respectively. Adjunctive sorafenib has shown favorable results in adults with very little, but promising, data in children. Furthermore, hepatic arterial chemoembolization (HACE) has been proven as an effective treatment strategy to achieve resectability with minimal systemic toxicities. Liver transplant may be considered with unresectable HCC. Our objective is to describe a multimodal approach for management of unresectable HCC.
Methods: Case report and literature review.
Results: A 12 year-old female presented with abdominal pain, firm hepatomegaly and elevated alpha-fetoprotein (62,645 ng/mL; range <6). MRI abdomen revealed a large liver mass involving all sections and the left portal vein. Liver biopsy showed poorly differentiated HCC with angiolymphatic invasion and fibrosis. Metastatic work-up was negative. She underwent 5 cycles of PLADO and sorafenib followed by HACE with doxorubicin and mitomycin to further decrease tumor burden. Alpha-fetoprotein levels declined dramatically with reduction in liver size allowing complete tumor resection and orthotopic liver transplant. Explanted liver demonstrated 20-30% tumor viability. Sorafenib was restarted but discontinued after 4 months due to significant hand-foot syndrome. A trial of sirolimus (mTOR inhibitor) for post-transplant immunosuppression was initiated for added benefit of recurrence risk reduction; however development of mild acute rejection resulted in restitution of tacrolimus. She is currently 21 months post-transplant and in remission with a 100% performance score.
Conclusions: Limited pediatric literature exists on HCC management, especially in unresectable cases. Multimodality treatment involving chemotherapy with PLADO and sorafenib, HACE, timely liver transplantation, and mTOR inhibitors in the post-transplant period may help improve outcomes and prolong survival in pediatric patients with unresectable HCC.

EP-275

STUDY ON THE CLINICAL CHARACTERISTICS AND PROGNOSTIC FACTORS IN 15 CASES OF HEPATOBLASTOMA

Z. Lu[1]

[1]Hemotology/Oncology, Shanghai Children's Hospital, Shanghai, China

Objectives: To investigate the clinical characteristics and survival analysis of childhood hepatoblastoma for prognostic factors.
Methods: Between February 2009 to September 2012, 15 cases of hepatoblastoma diagnosed in Shanghai children's hospital were included in this study, with 9 males and 6 females, median age was 19 months (range, 3-51 months). Follow up to December30, 2013, the median follow-up time was 34 months (9-58 months). All patients' staging referred to Pretext staging before operation. Surgery and chemotherapy were used according to different stage. Evaluation of correlation between the survival rate, stage and treatment strategies.
Results: According to Pretext staging, the number of cases in stage II, III and IV was 3 (20%), 10 (66.7%) and 2 (13.3%). The 5-year overall survival (OS) of stage II, III and IV were 100%,

90.0% ± 9.0% and 50.0% ± 35.4% (P = 0.304);and the EFS were 100%, 67.59% ± 20.7% and 0% (P = 0.012). 2 cases received tumor complete excision at first diagnosis both cured. 13 cases received chemotherapy after tumor biopsy, second tumor resection were given when tumor shrinkage. 2 cases of 13 relapsed, 11 cases cured.
Conclusions: Onset age of pediatric hepatoblastoma were younger, Surgical resection combined with preoperative and postoperative chemotherapy was the main way to improve the survival rate. Stage and complete resection may be the risk factors with children hepatoblastoma.

EP-276

PEDIATRIC HEPATOBLASTOMA IN THAILAND: AN 18-YEARS EXPERIENCE IN SINGLE INSTITUTE

K. Phuakpet[1], K. Sanpakit[1], N. Vathana[1], P. Tanaanunmongkol[1], M. Laohapansang[2], T. Chuangsuwanich[3]

[1]Department of Pediatrics, Faculty of Medicine Siriraj Hospital Mahidol University, Bangkok, Thailand; [2]Department of Surgery, Faculty of Medicine Siriraj Hospital Mahidol University, Bangkok, Thailand; [3]Department of Pathology, Faculty of Medicine Siriraj Hospital Mahidol University, Bangkok, Thailand

Objectives: To assess the treatment outcome and disease-free survival (DFS) of children with hepatoblastoma who were treated at our institute.
Methods: We retrospectively reviewed the medical record of hepatoblastoma patients under 15 years old who were diagnosed and treated at Siriraj hospital, Thailand during June 1994 to December 2011. The demographic data, investigation results, treatment approach and treatment outcome were collected and analyzed.
Results: Forty-one patients were diagnosed with hepatoblastoma during the study period, with the median age at diagnosis 1.17 years old (range 0-11.05 years old). Patients had the following Children Oncology Group (COG) stages: I (22%), II (2.4%), III (56.1%), and IV (19.5%). Seven patients (17.1%) had initial lung metastasis. Thirteen patients with resectable tumor underwent upfront surgery followed with adjuvant chemotherapy. The remaining 28 patients received neoadjuvant chemotherapy; 23 of these patients achieved total tumor removal later. The most common chemotherapy regimens were continuous doxorubicin plus either carboplatin or cisplatinum. Eighteen patients (43.9%) had hematologic toxicity; cardiotoxicity was not reported. Thirty-one patients achieved complete remission; 4 patients subsequently had local relapsed at the median duration of 1 year (range 0.25-1.7 years). Eleven patients (26.8%) died of disease. Median follow-up time was 5.1 years (range 0.2-18.4 years). Five-year DFS for COG stage I, II, III, and IV were 77.8%, 100%, 73.9% and 25%, respectively. DFS was significantly better in those who achieved total tumor removal (p = 0.013), and significantly worse in those with metastatic disease (p = 0.002).
Conclusions: Treatment outcome of hepatoblastoma in developing country is comparable to that of developed country. Total tumor removal is the key of the treatment success. Neoadjuvant chemotherapy, rather than attempt surgery, is suggested if complete resection is unlikely at the beginning. Total tumor removal can eventually be achieved in most cases, leading to a more favorable outcome. However, more intensive treatment is needed in metastatic disease.

EP-277

PAPILLARY THYROID CARCINOMA AFTER CHEMOTHERAPY AND LIVING-DONOR LIVER TRANSPLANTATION FOR HEPATOBLASTOMA

K. Watanabe[1], H. HIramatsu[1], K. Umeda[1], S. Okamoto[2], E. Ogawa[2]

[1]Dept. of Pediatrics, Kyoto University, Kyoto, Japan; [2]Dept. of Pediatric Surgery, Kyoto University, Kyoto, Japan

Objectives: Hepatoblastoma is a rare childhood malignancy and may present as a familial cancer such as familial adenomatous polyposis (FAP). However, association of papillary thyroid carcinoma and hepatoblastoma has been rarely reported.
Methods: We describe here a female who had papillary thyroid carcinoma after treatment for hepatoblastoma.
Results: The patient was diagnosed as having non-metastatic PRETEXT III hepatoblastoma at six-month old age, and underwent preoperative chemotherapy (cisplatin/pirarubicin, Ifosfamide/pirarubicin/etoposide/carboplatin) followed by living donor liver transplantation from her mother. She received postoperative three courses of irinotecan. During follow up, chest-abdominal CT scan accidentally revealed thyroid mass, and fine needle aspiration biopsy led to the diagnosis of papillary carcinoma. At nine years old, total thyroidectomy and cervical lymph node dissection was performed and the disease was diagnosed and staged as papillary carcinoma pT3 N1b pEx with lymph node metastasis. Because of extrathyroid extension and lymph node metastasis, radioiodine ablation was performed to prevent recurrence.
Conclusions: Papillary thyroid carcinoma is rare in childhood, and has been reported to be associated with radiation exposure.
Association of hepatoblastoma with papillary thyroid carcinoma might be related to FAP. However, the patient has no history of radiation exposure, no family history suggesting FAP, and pathology of the thyroid cancer was not cribriform pattern that is typical to FAP. FAP mutation analysis was currently underway.

LYMPHOMAS

EP-278

PRIMARY IMMUNODEFICIENCY DISEASES (PID) PRESENTING AS LYMPHOMA AND TREATED WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): DESCRIPTIONS OF 6 PATIENTS

K. Aabideen[1], V. Gupta[1], Z. Nademi[1], M. Slatter[1], S. Hambleton[1], A. Gennery[1], T. Flood[1], M. Abinum[1], A. Cant[1]

[1]Bone Marrow Transplant, Great North Children's Hospital, Newcastle upon Tyne, United Kingdom

Objectives: PIDs are one of the risk factors for lymphoma in children. Management strategies for lymphoma due to PIDs are still evolving. HSCT is the treatment of choice for many PIDs. We present 6 patients who underwent HSCT who presented with lymphoma due to PID
Methods: We retrospectively reviewed clinical details and outcome of six patients with PID who presented with lymphoma.
Results: Patient1: 4 years old male diagnosed as EBV driven lymphoproliferative Disease (LPD) resembling Hodgkin Disease and confirmed as Interleukin 2 inducible T cell Kinase (ITK) deficiency. Patient2: Brother had ITK deficiency. Therefore he was confirmed to have ITK deficiency at birth. While waiting for transplant, he developed EBV driven LPD similar to Diffuse Large B cell Lymphoma (DLBL). Patient3: 12 year old male diagnosed as MALT lymphoma and found to have Combined Immune Deficiency (CID). Patient4: 11 year old male diagnosed as EBV negative DLBL and confirmed as CID. Patient 5: One year old male diagnosed as CID due to T cell activation disorder and developed multiple lymphadenopathies, confirmed as EBV positive LPD. Patient6: 5 year old female with family history of family history of undiagnosed PID and developed Nodular Sclerosing Classical Hodgkin Disease and subsequently confirmed as CID. All patients had successful HSCT. Lymphoma resolved in all patients. All patients are surviving at different post transplant follow up periods. They are 28, 2, 13, 9, 18, and 45 in months respectively in patients 1 to 6.
Conclusions: PID should be ruled out in all atypical, chemotherapy resistant, or relapsed cases of lymphoma. As chemotherapy is unlikely to be effective in lymphoma due to PID and HSCT is the treatment of choice for several PIDs, HSCT can be curative for lymphoma due to PIDs.

EP-279

INTRACARDIAC LYMPHOMA; TREATMENT CHALLENGES AND OUTCOME IN A RESOURCE LIMITED SETTING

O. Adefehinti[1], U.U. Onakpoya[2], A.O. Komolafe[3], O.O. Adeodu[4], M.A. Durosinmi[5]

[1]Paediatric Haemato-Oncology Unit Department of Paediatrics, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria; [2]Cardiothoracic Surgery Unit Department of Surgery, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria; [3]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria; [4]Haemato-Oncology Unit Department of Paediatrics, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria; [5]Department of Haematology and Immunology, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria

Objectives: To highlight the need for early recognition, diagnosis and the challenges involved in the treatment of intracardiac lymphoma.
Methods: Malignant lymphoma presenting as intracardiac mass is rare. Morbidity and mortality may be high if associated with pericardial effusion and cardiac tamponade without timely interventons. A 9-year old female who presented to our Children Emergency Ward with clinical features of pericardial effusion with cardiac tamponade is reported. Echocardiography confirmed massive pericardial effusion with a huge mass attached to the anterior tricuspid valve that impeded diastolic flow into the right ventricle, a dilated right atrium with interatrial shift to the left almost collapsing the left atrial wall. She had emergency pericardiostomy and pericardial biopsy done. Cytology and histology reports of pericardial fluid and biopsy confirmed B-cell Non-Hodgkin lymphoma positive for CD 45 and CD 20, negative for CD 3, CD30 and CD 34 on immunohistochemistry. Peripheral blood and bone marrow were free of blasts. She had pre-phase cylophosphamide, oncovin and prednisolone (COP pre-phase) for one week followed by cylophosphamide, oncovin cytosine arabinoside and prednisolone (COAP) regimen. She received only two of six cycles of COAP for financial reasons. Serial follow up echocardiography at the end of the COP pre-phase and at the end of each cycle of COAP confirmed significant reduction in intracardiac mass. She was alive and well for one year and later became symptomatic and died.
Results: None
Conclusions: Intracardiac lymphoma is rare but life-threatening if associated with pericardial effusion and cardiac tamponade. Cost of treatment is enormous and challenging in resource limited setting.

EP-280

NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMAS. EXPERIENCE IN A SINGLE INSTITUTION IN ARGENTINA

E. Alfaro[1], C. Sanchez La Rosa[1], M. Guitter[1], A. Rose[1], W. Caccavillano[1], L. Galluzzo[1], M. Felice[1], P. Zubizarreta[1]

[1]*Hematology-Oncology, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina*

Objectives: Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL) represents 5% of Hodgkin Lymphoma (HL) and has distinct clinical-pathological features with an overall good prognosis. Treatment strategies have been based on protocols for HL. Selected patients can be treated with surgery alone. Our aim was to describe the clinical characteristics, management and outcome of patients with NLPH.
Methods: Between October-1997 and January 2014, 13 patients (11 M/2 F), median age: 9.8 (range 4.9-14.5) years, were consecutively diagnosed in our institution. Initial chemotherapy schedules were ABVD (Doxorubicin, Bleomycin, Vinblastine and Dacarbazine), COPP/ABVD or AV-PC (Adriamycin/Vincristine/Prednisone/Cyclophosphamide). When response was partial or null, additional chemotherapy was administered, IF-RT, Anti CD20 and/or HDC/ASCT. A watch-and-wait strategy after lymph node complete surgery was used in two cases when this strategy became trustworthy.
Results: Eleven patients (84.6%) showed nodal compromise, cervical localization was the most frequent. Ten patients (77%) presented localized disease (stage IA: 8, stage IIA:2) and 3 (23%) advanced disease (stage IIIA:1, stage IVA:1, IVB:1). One patient had B symptoms. Two IA stage cases (15.3%) had complete node resection. Five patients (38.4%) received 4 cycles of ABVD. One patient (7.7%) received COPP/ABVD. Three patients (23%) received 3 cycles of AV-PC. One patient (8.3%) received 6 cycles of AV-PC plus 4 doses of Rituximab. One patient (8.3%) presented progressive disease after 3 cycles of ABVD, additional chemotherapy was administered and HDC/ASCT. Three (23%) received IF-RT plus chemotherapy. One patient is still on treatment. Response to treatment was: CR 8 pts (66.6%), Partial-response: 2 pts (16.6%), NR: 2 pts (16.6%). Median follow up: 50.5 (range 1-132) months. All patients remain in CR.
Conclusions: Although the management of NLPHL was not uniform in our retrospective analysis, the results were excellent. Tailored therapy according to staging and disease response, seemed to be a good strategy in our setting.

EP-281

3 DIFFERENT TYPES OF MALIGNANCY IN A CHILD DURING DIFFERENT TIME PERIOD OF LIFE

Y.R. Chopra[1], M. Ramzan[1], R. Sharma[1], S. Katewa[1], S. Yadav[1]

[1]*Pediatric Hematology Oncology and Bone Marrow Transplant Unit, Fortis Memorial Research Institute, Gurgaon, India*

Objectives: Cancer survivors have a higher risk of new primary cancer, in the same or in another organ, than the general population. We describe a case of 13 yrs. old male who presented with multiple malignancies at 6, 12 and 13 years of age.
Methods: Pediatric case report
Results: A 5 year old male born to G4 P3 2nd in birth order, non-consanguineous marriage with strong family history of malignancy. His 3 paternal uncles had died of unknown reasons and his elder brother had died of Neuroblastoma Stage IV at 4.5 years of age. His 4th sibling had died of Glioblastoma Multiforme at 1.5 years of age and he had one healthy7 years old female sibling. He was diagnosed as Stage II ileocecal Burkitt's lymphoma which was surgically resected followed by 2 cycle of COPAD chemotherapy. He was asymptomatic till 12 years of age when he had features suggestive of superior vena cava syndrome. CECT chest showed anterior mediastinal mass. CECT abdomen, bone marrow and CSF were normal. Trucut biopsy was suggestive of Unclassifiable lymphoma. He was treated with 2 cycles of CHOP chemotherapy. Repeat CECT after 2 cycles showed marginal shrinkage so he further received 2 cycles of ICE chemotherapy and after that he went in to CR 2. He underwent autologous stem cell transplant following BEAM conditioning regimen. He was asymptomatic till 100 days post-transplant when he had abdominal lump. CECT abdomen revealed diffuse mesenteric lymphadenopathy with conglomerated necrotic mass encasing SMA. Biopsy and flowcytometry of the mass revealed features of T- cell malignant lymphoma. Genetic studies could not be performed due to monitory problems. Unfortunately due to economic constraints parents opted for palliative care.
Conclusions: Three malignancy during childhood is a rare event. Each family member should be scrutinized in details including genetic studies.

EP-282

AVASCULAR NECROSIS IN PEDIATRIC PATIENTS WITH HODGKIN'S DISEASE IN KING HUSSEIN CANCER CENTER

R. Deebajah[1], M. Tawfiq[2], F. Bazzeh[3]

[1]*pediatric, King Hussein Cancer Center, Amman, Jordan;* [2]*nursing, King Hussein Cancer Center, Amman, Jordan;* [3]*pediatrics, King Hussein Cancer Center, Amman, Jordan*

Objectives: There is limited data on the incidence of avascular necrosis (AVN) of bone in adolescents and children with HL. We reviewed our institutional experience were higher incidence of AVN is reported.
Methods: We conducted a retrospective analysis of children (<18 years) with Hodgkin's lymphoma who developed AVN during treatment, presented from December 2008 until June 2013. Patients' characteristics, treatment regimen, steroids cumulative dose and treatment modalities of AVN were analyzed.
Results: We identified 9 patients (7 females) who developed AVN during treatment of HL. the median age at diagnosis was 15 years (range 14 to 17). Eight were treated as high risk with BEACOPP regimen and one as intermediate risk with 4 cycles of ABVD and 2 cycles of COPP. An MRI of the lower limbs was requested during therapy due to symptoms. The cumulative dose of steroids (range 1.2 gm/m2 to 4.8 gm/m2), one patient received radiotherapy with field involving the femoral head. Two patients underwent joint decompression, the rest of the patients (N = 7) were treated with conservative management.
Conclusions: We observed higher than expected number of patients with HL who developed AVN. This may reflect genuinely increased risk in our population or under-diagnosis of this condition by others. Careful clinical follow up is warranted to detect the early signs of AVN in adolescents with HL.

EP-283

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RELAPSED/REFRACTORY LYMPHOMAS IN CHILDHOOD: SINGLE CENTER EXPERIENCE

F. Erbey[1], D. Atay[1], A. Akçay[1], M. Akbiyik[1], G. Öztürk[1]

[1]*Pediatric Hematology/Oncology & Pediatric BMT Unit, Bahcelievler Medicalpark Hospital, Istanbul, Turkey*

Objectives: We evaluated treatment outcome of patients with relapsed/refractory lymphoma receiving autologous stem cell transplantation (ASCT) in childhood.
Methods: We retrospectively analyzed the outcome of 12 patients who were done ASCT, between January 2012 - December 2013.
Results: The median age was 13,5 years (range, 11-16 years), 8 males, 4 females. There were 5 non-Hodgkin lymphomas (NHL), and 7 Hodgkin lymphoma (HL) patients. Seven patients received BEAM (BCNU, etoposide, ara-C, melphalan), and 5 patients received BuMel (busulfan, melphalan) supported with ASCT. At the time of study, 10 patients were alive, 2 patients died due to progressive disease. There was no transplant-related mortality. Overall survival (OS) and disease free survival (DFS) were 83,3% and 75% with a median follow-up of 17 months (range, 2 – 26 months) for all patients, respectively. There was no differences in efficacy between the conditioning regimens were found.
Conclusions: ASCT is an effective treatment for patients with relapsed/refractory lymphoma. No significant differences in outcomes were observed between BEAM and BuMel conditioning regimens.

EP-284

COMPARISON OF TWO TREATMENT REGIMENS IN NON HODGKIN LYMPHOMA PATIENTS; SINGLE INSTITUTION EXPERIENCE AT CHILDREN HOSPITAL, LAHORE

M. Faizan[1], S. Anwar[1], N. Asghar[1], A. Shabbir Ali[2], M. Taj.from PODC CCLG[3]

[1]*Paediatric Hematology/Oncology, The Children Hospital & Institute of Child Health, Lahore, Pakistan;* [2]*Paediatrics, Lahore General Hospital, Lahore, Pakistan;* [3]*Paediatric Hematology/Oncology, Royal Marsden Hospital, London, United Kingdom*

Objectives: The Children Hospital, Lahore is a tertiary care Pediatric Hospital in Pakistan with a 60 bedded Hematology/oncology unit. We report our experience in treating Non Hodgkin Lymphoma (NHL) using 2 regimens, CCLG-NHL guidelines and MCP842 protocol in 50 patients
Methods: Fifty consecutive biopsy proven patients of NHL (Burkitts, Burkitt-like and Diffuse Large B cell Lymphoma) were included in the study. The first 25 patients were treated according to CCLG guidelines (containing High dose Methotrexate,3-6 gm/m2) and the next 25 according to the less intensive MCP842 consisting of cyclophosphamide, adriamycin, vincristine, ara-C, etoposide, ifosfamide & low dose methotrexate (15 mg/m^2).
Results: There were total of 50 patients. Thirty seven (74%) patients were male. Majority 29 (58%) of patients were 5-9 years of age. Majority presented with abdominal symptoms 48 (96%). Abdominal mass 33 (66%), intussusception 9 (18%), and intestinal obstruction was presenting complaint in 6 (12%) patients. One patient each had nasopharyngeal mass and symptoms of obstructive uropathy. Majority 40 (80%) presented in stage III, 10 (20%) in stage IV. None presented in stage I or II. The group that received treatment according to CCLG guidelines, overall survival was 7 (14%) with abandonment and 37% without abandonment,12 (24%) expired, 6 (12%) left against medical advice (LAMA). Cause of mortality was high dose methotrexate (MTX) toxicity in 06 (12%), sepsis in 03 (08%), not documented in chart 3 (6%) Overall survival had been 17 (68%) with abandonment and 85% without abandonment for patients treated with MCP842 protocol, 2 (8%) relapsed, 01 (04%) expired due to sepsis, 05 (20%) LAMA.
Conclusions: High dose MTX toxicity has been a major cause of mortality in patients receiving treatment according to CCLG guidelines. MCP 842 involving low dose MTX was better tolerated in our patients. Therapy was offered mostly on outdoor basis and had better

outcome. In developing countries need is to adopt protocols that demand limited supportive care facilities and are more tolerable.

EP-285

STUDY OF 4 CASES OF PRIMARY BONES OF LYMPHOMA

N. Suarez[1], M. Paula[1], D. Gasperini[1], C. Cavalcante[2], E. Silva[3], L.U.I.Z. Lopes[1]

[1]Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula Da Silva, Barretos, Brazil; [2]Radiology Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula Da Silva, Barretos, Brazil; [3]Pathology Oncology Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula Da Silva, Barretos, Brazil

Objectives: Hodgkin and non-Hodgkin lymphomas represent approximately 10-15% of tumors in children under 15 years. Bone presentation is very rare in children; diffuse large B-cell lymphoma of the most frequent.
Methods: We report 4 cases of lymphoma of bone as a primary site; admitted between December 2010 and February 2014.
Results: There were 2 females and 2 males, aged between 10 and 15 years. All patients had bone pain as the main symptom. Some associated with claudication and paresthesia. The time of onset of symptoms was five months to a year. The diagnoses were confirmed by biopsy. According to histology and clinical aspects they were: 1-lymphoblastic lymphoma B left acetabulum - stage IV; 1-Lymphoblastic Lymphoma T right tibia - stage III; 1-diffuse large B-cell lymphoma in the left humerus - stage III and 1-diffuse large B-cell lymphoma in right iliac bone with involvement of the pubis and ischium body - stage III. Immunohistochemical exam with Ki-67 (90%) in all cases, TdT, CD45, CD20, CD99, CD 79a, CD 43 positive, confirmed the diagnosis.
Conclusions: The clinic, the radiology (bone destruction, lytic areas, sclerotic variables and involvement of the entire bone with extension into the soft tissues) and the histology (diffuse infiltration of small, round cells) are not specific to bone lymphomas. Because of that is mandatory to extend the immunohistochemical panel including CD99, TdT, CD 43 and CD 79a (done for these cases), avoiding possible errors in diagnosis. We conclude that bone lymphomas should be included in the differential diagnosis of bone tumors.

EP-286

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOME OF PEDIATRIC HODGKIN LYMPHOMA AT CHILDREN HOSPITAL BENGHAZI - LIBYA

N. Gheriani[1], L. Ballo[1], A. Alshkteria[2]

[1]Hematology - Oncology Unit, Children Hospital Benghazi, Benghazi, Libya; [2]Community Medicine Department, Benghazi University, Benghazi, Libya

Objectives: Lymphoma is the third most common childhood malignancy. However, little data is available on lymphoma in our developing country. The present work was performed to identify clinical characteristics and treatment outcome of pediatric Hodgkin lymphoma (HL) at our center.
Methods: A retrospective study on 51 patients diagnosed with HL between 1995 and 2012. Used chemotherapeutic regimens were ABVD, COPP. For stage IV BEACOPP (Bleomycin, Etoposid, Adriamycin, Cyclophosphamide, Vincristin, Procarbazine, Prednisolone) and VVAC (Vinblastin, Vp16, AraC, Cisplatin) were added. 30 patients received radiotherapy. Ann Arbor HL staging criteria was applied for staging. Rye system was used for histopathologic examination. Treatment outcome was evaluated using Kaplan-Meier methods. Differences between outcome were tested using Logrank test.
Results: There were 34 males and 17 females. Male to female ratio was 2:1. Median age was 9 years (4-14 years). Bulky disease and B symptoms found in 7 and 27 patients respectively. Stage distributions were 11, 9, 19, and 12 patients in stage I, II, III, and IV respectively, 60.8% patients presented at stage III and IV. Histopathologic subtypes were nodular sclerosis, mixed cellularity, lymphocytic predominance, lymphocytic depletion in 22, 19, 9, and 1 respectively, 80% of death and 60.5% of relapse in mixed cellularity. 84.3% patients had complete remission, 5.9% relapsed then cured, 9.8% relapsed and died. Overall survival (OS) and event-free survival (EFS) rates were 90.2% and 84.3% respectively with median follow up of 5 years. OS rate was 75% with bulky disease and 95.3% without, ($P>0.05$). OS rate was 88.9% with B symptoms and 97.7% without, ($P>0.05$). Histopathology, stage, and relapse had effect on OS rate, ($P < 0.05$, $P < 0.01$, $P < 0.05$) respectively.
Conclusions: Stage, histopathology, and relapse are statistically significant predictive factors for OS rate. Our patients are commonly presented with advanced stages; further studies are required to evaluate causes.

EP-287

PAEDIATRIC PLASMABLASTIC LYMPHOMA: A SINGLE UNIT EXPERIENCE IN KWA-ZULU NATAL, SOUTH AFRICA

Y. Goga[1], R. Thejpal[1], K. Moodley[1], N. Moonsamy[1], B. Neethling[1]

[1]Paediatric Haematology Unit Dept of Paediatrics and Child Health, Nelson R Mandela School of Medicine University of Kwa-Zulu Natal, Durban, South Africa

Objectives: To describe patient characteristics, treatment response and survival of patients with Plasmablastic Lymphoma, at a single centre from 2003 – 2013
Methods: A retrospective chart review of patients with Plasmablastic Lymphoma diagnosed between January 2003 and December 2013
Results:

Sex	Age at Diagnosis	Site	Stage	Treatment	Survival
M	12Y	Jaw, Zygomatic arch, abdominal mass, bone marrow	4	COP x 2 ACOP-BVM x 4	Died after 16m Palliated
M	6Y	maxillary antrum	2	COP x 2 ACOP-BVM x 10	Alive after 5yrs
M	5Y	maxillary antrum	2	COP x 1 COPADM x 3	Died after 12m, Palliated
M	10.5Y	maxillary antrum	2	COP x 1 COPADM x 3 DXT to oral cavity	Alive after 21m
F	11Y	multiple bone lesions	4	COP x 2 COPADM x 3 ongoing	Alive after 4m, on treatment

Five patients were diagnosed with Plasmablastic Lymphoma. There was a male predominance. All 5 patients were Black. Three patients had stage 2 disease, and two patients had stage 4 disease. 4/5 patients presented with maxillary/nasal masses, 1 had abdominal and maxillary disease, and the female patient presented with multiple bony lesions. None of the patients had CNS involvement. All patients were HIV positive and were HAART (highly active anti-retroviral disease) naive at diagnosis. CD4 counts were available in 4 patients. 2 patients had CD4 counts < 100, and the count was 390 and 629 in the other 2 patients. 2 patients were treated with cytoreductive therapy (cyclophospomide, vincristine, prednisone - COP), followed by a hybrid of vincristine, doxorubicin, cyclophosphomide and prednisone alternating with bleomycin, methotrexate and vincristine. 3 patients were treated using a BFM based COPADM protocol.
Conclusions: Plasmablastic Lymphoma is a rare HIV associated malignancy with a predilection for the nasal and maxillary areas. Low CD4 counts are not predictive of survival. Treatment protocols are poorly defined.

EP-288

ROLE OF FDG-PET SCAN IN THE MANAGEMENT OF MATURE B CELL PEDIATRIC NON-HODGKIN'S LYMPHOMA. CCHE EXPERIENCE

H.A.N.Y. Abdelrahman[1], A. Hamoda[1], M. Sedky[2], E.M.A.D. Moussa[3], I.M.A.N. Attia[1], T. Raafat[4], A.Y.D.A. Youssef[4], W. Omar[5], O. Hassanein[1], A.L.A.A. Elhadad[1]

[1]Pediatric Oncology, National Cancer Institute, Cairo University, Fom Elkalig, Cairo, Egypt; [2]Pediatric Oncology, National Research Center, Cairo, Egypt; [3]Pediatric Oncology, Elmounofia University, Cairo, Egypt; [4]radiodiagnosis, National Cancer Institute. Cairo University. Fom Elkalig, Cairo, Egypt; [5]nuclear Medicine, National Cancer Institute. Cairo University. Fom Elkalig, Cairo, Egypt

Objectives: To evaluate the sensitivity, specificity and predictive values of PET scan during management of pediatric Non-Hodgkin's lymphoma (NHL).
Methods: A retrospective study enrolled on pediatric patients with NHL at Children Cancer Hospital of Egypt (CCHE) during the period from July 2007 till end of June 2013 was done. Inclusion criteria included the diagnosis of mature B cell NHL, for whom PET - in addition to conventional CT scan- was done at any stage of the treatment. Blind revision of all PET and CT scans was specifically done for this study.
Results: For 115 pediatric NHL patients, 152 PET and 152 CT scan were done. Median age was 5.7 years (range 1-18 years). They were 85 males (74%) and 30 females (26%). One hundred twenty six scans (82.9%) were done for 100 Burkitt lymphoma patients, while 26 scan (17.1%) done for 15 DLBC. Nineteen examination (12.5%) were done before starting chemotherapy, 107 (70.3%) at time of evaluation while 26 (17.1%) during Follow up. For all patients, sensitivity was 91.6% for PET, while was 70.0% for conventional CT ($p = 0.02$). Specificity was 84.1% for PET and 58.9% for CT ($p < 0.001$
In burkitt lymphoma; sensitivity of PET was 91.6%, while was 66.6% for CT ($p = 0.08$). Specificity was 82.4% and 57.8% for PET and CT respectively ($p =$
Conclusions: PET scan is significantly more sensitive than conventional CT in the management of aggressive mature B cell pediatric NHL.

EP-289

CLINICAL REVIEW OF 18 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD) CASES ARISING IN YOUNG LIVER TRANSPLANT RECIPIENTS

S. Huang[1], K. Chiang[2]

[1]Oncology Department, Beijing Children's Hospital, Beijing, China; [2]oncology Department, Queen Mary Hospital, Hong Kong, Hong Kong China

Objectives: To make the clinicians have a better understanding of PTLD in young children, reduce the delayed diagnosis in early stage, and to explore feasible means for the prophylaxis and treatment.
Methods: Retrospective analysis of clinicopathologic features, and treatment outcome in 18 consecutive cases with PTLD after liver transplant from January 2001 to December 2012. The initial symptoms, delayed diagnosis time, both of the EBV and CMV status, completely blood count, LFTs, pathology results, imaging results, treatment outcome were reviewed respectively.
Results: Six cases were diagnosed clinically, majority of them had the IM-like symptoms, snoring, and deranged LFTs, the median time from initial symptoms onset to PTLD diagnosis was 2 months. 12 cases had the histopathology diagnoses, and the initial symptoms were various among the different pathological subtypes, and T-cell mononorphic LPD cases were more systemic and aggressive. For these 12 cases, the interval between initial symptoms onset and the final diagnosis were also various, 12 out of 18 had a delayed diagnosis due to the extra-nodal/graft organ involvement or the especial clinical manifestations. PTLD treatment consisted of reducing or stopping the immunosuppressant, followed by rituximab and chemotherapy if required. 16 cases were in remission (CR = 15, PR = 1) and two died of PTLD related multiple organ failure. The episode of liver rejection post-PTLD was in 2 cases. Two-year OS and EFS were 75% and 88.9%, respectively.
Conclusions: The delayed diagnosis of PTLD in young children was common due to the various clinical manifestations among different pathological subtypes. The timely diagnosis and treatment were very essential to the prognosis. Rituximab was an efficacious drug for PTLD. Since the high incidence of PTLD after liver transplant, the rejection episodes post-PTLD was few, and relapse of disease was possible, it was always essential to keep low dose immunosuppressant if possible. Monitor the patients during and after treatment of PTLD are necessary.

EP-290

CLINICAL REVIEW OF MEDIASTINAL T-LYMPHOBLASTIC LYMPHOMA (T-LBL) IN PEDIATRIC PATIENTS - A SINGLE CENTER EXPERIENCE FROM CHINA

S. Huang[1], Y. Zhang[1], L. Jin[1]

[1]Oncology Department, Beijing Children's Hospital, Beijing, China

Objectives: The clinical features and the treatment outcome of mediastinal T-LBL in Beijing Children' s Hospital were studied.
Methods: We retrospectively examined the clinical features and treatment outcome of 54patients with mediastinal T-LBL, within the period of Jan.2003to December 2009 (18 cases did not have the bone marrow involvement, 6 cases were <25% bone marrow involvement, the rest 30 cases had >25% bone marrow involvement). We used the modified BFM 90 LBL protocol.
Results: 1) In 72 newly diagnosed T-LBL cases, with a median age of 7.9 years, 18 patients (25%) had "B" symptoms, 54 (75%) had bulky mediastinal mass (diameter >10 cm), and 15 cases (27.7%) had superior vena cava syndrome (SVCS), 9 cases (16.7%) had the upper airway obstruction symptom,5 cases had the acute tumor lysis syndrome (ATLS). 2) Among the 54cases, the median time from initial symptoms onset to the final diagnosis was 34d. 3) In our study group (n = 54), stage III n = 24, stage IV n = 30. 11 cases had elevated uric acid (UA), and 44cases had elevated lactate dehydrogenase (LDH), among the 44 cases,15 cases were>1000U/L,29 cases were>500U/L. 4) 7 cases died during or after chemotherapy (6 was dead as the disease progress or relapse, 1 was dead because of the sever infection). Estimated the 5-year overall survival (OS) and event free survival (EFS) were 84.4%and 80.5% respectively.
Conclusions: Bulky mass was common in T-LBL, which mostly cause SVCS, upper airway obstruction or ATLS, and the advanced disease (stage IV) was common. It was a dependent poor prognostic factor.

EP-292

A SINGLE CENTER CLINICAL ANALYSIS FOR CHILDHOOD NON HODGKIN'S LYMPHOMA

J. Hui[1], Z. Lu[1], J. Yang[1], J. Shao[1], H.O.N.G. Li[1]

[1]Hemotology/Oncology, Shanghai Children's HoapitalShanghai Jiao Tong university, Shanghai, China

Objectives: To retrospectively analyze the clinical efficacy for childhood non Hodgkin's lymphoma (NHL) according to 2008 World Health Organization classification of tumors.
Methods: From January 2000 to December 2012, 58 patients newly diagnosed with NHL verifies by clinic, imaging, cell morphology and immune phenotype, histopathological classification. There were 56 patients in total received treatment, 45 males and 13females. The average age was 6.8 years (ranged from 2 years to 14 years). According to St. Jude staging classification, 6 of 56 cases (10.7%) were divided into stage II, 25 cases (44.6%) into stage III and 25 cases (44.6%) into stage IV. The chemotherapy regimens were based on phenotype, pathologicaly sub-classified and clinical stages. Precursor / lymphoblastic lymphoma received the treatment as acute lymphoblastic leukemia.
Results: 1. Among 56 cases, 25 (44.6%) were Burkitt's/Burkitt's like lymphoma, 13 (23.2%) were anaplastic large cell lymphoma (ALCL), 5 (8.9%) were diffuse large B-cell lymphoma (DLBCL) and 13 (23.2%) were precursor / lymphoblastic lymphoma (11 cases were T cell and 2 cases were B cell).2. The Kaplan-Meier estimates of 5-year event-free survival (EFS) was 83.7% for all patients (figure1) while 96% for Burkitt's/Burkitt's like lymphoma, 58.3% for ALCL, 80% for DLBCL and 84.6% for precursor / lymphoblastic lymphoma (figure2). The difference of 5-year EFS between Burkitt's/Burkitt's like lymphoma and ALCL was significant (P = 0.004), while the difference of ALK positive or not in ALCL was not (P>0.05). 3. 5-year EFS was 100% for stage II, 79.6% for stage III, 83.8% for stage IV (P = 0.245).
Conclusions: Correct cell phenotype and pathologicaly diagnosis of NHL are the key step for the prognosis for NHL. Burkitt's/Burkitt's like lymphoma have good prognosis in child though it is aggressive. Current treatments are effective and safe for childhood NHL.

EP-293

PATTERNS OF FAILURE AND OUTCOME OF PEDIATRIC PATIENTS WITH RELAPSED OR PROGRESSIVE HODGKIN LYMPHOMA

C. Karadeniz[1], A. Oguz[1], A. Okur[1], F.G. Pinarli[1], M. Isik[1], F. Tekkesin[1], N. Akyurek[1], H. Bora[1]

[1]Pediatric Oncology, Gazi University School of Medicine, Ankara, Turkey

Objectives: In this study, we present clinical characteristics, failure patterns and outcomes of pediatric patients with Hodgkin lymphoma (HL) treated with chemotherapy and low- dose involved field radiotherapy (LD-IFRT) in a single institution.
Methods: This retrospective analysis comprise 123 patients with HL treated at our institution from 1990 to 2013 who received four or six cycle of ABVD/COPP alternating chemotherapy based on their stages followed by LD- IFRT (20-25 Gy).
Results: Out of 123 patients nine had recurrence or progression at 1- 58 months after the diagnosis. Median follow-up was 68.6 months (8-152 months) after the progression or recurrence. The mean age at diagnosis was 12.8 ± 3.4 years. Five patients had localized (Stage IIA, IIB) and four patients had advanced disease (stage IIIB, IV) at diagnosis. Two patients had progressive disease during first line chemotherapy: One of them did not respond to high dose chemotherapy (HDCT) and autologous hematopoietic stem cell transplantation (HSCT), and died of disease. The other patient was lost to follow-up with disease. Two patients had early while five patients had late relapse. One patient with early relapse died with disease in 2 months during salvage therapy. The other patient with early relapse received HDCT allogeneic HSCT and is alive at 104 months without disease. Five patients with late relapse achieved complete remission (3 with autologous HSCT, two with second line chemotherapy) and are alive without disease at 14-125 months from recurrence. Three patients had local, two patients had distant, and two patients had both local and distant relapses. The lung parenchyma was the most common extralymphatic site of involvement (44%) in patients with relapsed or progressive disease.
Conclusions: We have seen both local and distant relapses in almost equal number of patients. The outcome of the patients with early relapse or progressive disease was poor.

EP-294

PEDIATRIC T-CELL-RICH LARGE B-CELL LYMPHOMA: CLINICAL FEATURES, TREATMENT, AND OUTCOME

I. Kirov[1], M. Lones[2]

[1]Division of Oncology, CHOC Children's Hospital, Orange California, USA; [2]Department of Pathology and Laboratory Medicine, University of California Los Angeles, Los Angeles California, USA

Objectives: T-cell-rich large B-cell lymphoma (TCRLBCL) is a subtype of diffuse large B-cell lymphoma (DLBCL) characterized by small numbers of scattered large B-cells with numerous reactive T-cells. Pediatric TCRLBCL is uncommon and not well understood. The goal of this preliminary study is to characterize the clinical features of pediatric TCRLBCL at primary diagnosis, treatment, and outcome.
Methods: Three pediatric patients with TCRLBCL were evaluated for clinical features, treatment, response to therapy, and outcome.
Results: Clinical features included: age 14-16 years; male: female 2:1; Murphy stage – I (axilla), II (cervical, tonsil, nasopharynx), III (abdomen, pelvis, spleen, spine/epidural); elevated lactate dehydrogenase 1. Treatment was according to the CCG-5961 protocol with the two patients with stages I and II following arm B1, and the patient with advanced disease (stage III) following arm C1. All patients achieved a complete response (CR), and had no subsequent relapse and remain in remission for more than ten years from diagnosis.
Conclusions: Pediatric TCRLBCL occurs in adolescents, and may present in lymph nodes or extranodal sites as localized or advanced disease. Treatment with a current pediatric B-cell lymphoma regimen in these patients achieved CR with durable remission.

EP-295

LATENT EPSTEIN-BARR INFECTION AND IMMUNOLOGICAL STATUS OF THE HOST IN PEDIATRIC HODGKIN LYMPHOMA. A SINGLE CENTER STUDY

T. Klekawka[1], W. Balwierz[1]

[1]Department of Pediatric Oncology and Hematology, Polish-American Institute of Pediatrics Jagiellonian University Med. Colleg, Krakow, Poland

Objectives: Association between latent Epstein-Barr virus (EBV) infection association and Hodgkin Lymphoma (HL) is well documented. However scanty data on host immunological status in aspect of EBV latent infection of Hodgkin and Reed-Sternberg cells are available for pediatric patients.
Methods: To assess the impact of latent EBV infection on immunological status of the patient an analysis of 61 HL cases (age 2.6-18.0; median: 14,2 years) was performed. HIV infection and inherited immune deficiency syndromes were excluded. EBV status of neoplastic cells was determined by EBER-specific in situ hybridization and by immonohistochemical LMP-1 protein detection (respectively 27 and 14 cases were positive) as well. Serum IgA, IgM and IgG concentration data were collected for 59 cases. Lymphocyte subpopulation studies were available in 47 cases and lymphocyte transformation tests were performed in 16 cases only. Immunological tests results were compared both for LMP-1 expression status and EBER status as well.
Results: No differences between both groups of patients were found for IgA and IgG serum concentration. IgM serum concentration was significantly lower ($p = 0.03$) in LMP-1 positive than in LMP-1 negative group (median: 1.06 and 1.57 g/L respectively). No differences between groups were also found for serum immunoglobulin concentration below and above the reference values. Also a trend towards slightly lower IgM concentration in EBER-positive than in EBER-negative cases ($p = 0.06$) was observed. No difference in CD3, CD4, CD8 and CD19 lymphocyte subpopulations in respect to LMP-1 or EBER status was found. Only a trend towards higher mitogen response index to PWM was observed ($p = 0.07$) in an EBER-positive group. No other differences in lymphocyte transformation tests were found respective to EBER or LMP-1 status.
Conclusions: No relation to EBV status was found except for IgM concentration. Larger group is to be analyzed to identify differences between host immunological status and EBV latency in HL.

EP-296

LIFE-THREATENING CONDITIONS AT THE MOMENT OF DIAGNOSIS OF NON-HODGKIN LYMPHOMAS IN CHILDREN.

L. Maiejka-Kapuscinska[1], M. Kozlowska[1], N. Irga-Jaworska[1], M. Niedzwiecki[1], M. Szalewska[1], E. Adamkiewicz-Drozynska[1], G. Wrobel[2]
[1]Pediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [2]Pediatric Oncology Hematology and Bone Marrow Transplantation, Wroclaw Medical University, Wroclaw, Poland

Objectives: Non-Hodgkin lymphoma (NHL) is the third most common malignancy in children. Although prognosis is good (5 year survival rates of up to 95%), delayed diagnosis may lead to life-threatening conditions without giving the patient chance to react to the treatment. The aim of the study was to show patients with newly diagnosed NHL who presented life-threatening conditions.
Methods: Among 34 patients diagnosed with non-Hodgkin lymphoma in the Department of Pediatrics, Hematology and Oncology Medical University of Gdansk in years 2008-2014, there were 12 patients who presented life-threatening conditions at the moment of the diagnosis (35%).
Results: Among all the patients there were 20 children with B-cell, 3 with pre-B, 8 with T-cell, and 3 with anaplastic NHL. We observed no life-threatening conditions in children with anaplastic NHL. Children with B-cell NHL presented vena cava inferior syndrome (2 patients), cholestasis with pancreatitis (2), ileus (5), and pleural effusion (3). Patients with T-cell malignancy showed vena cava superior syndrome (4 patients), and cardiac tamponade (1). Almost all the patients with T-, pre-B, and B-cell NHL presented acute tumor lysis syndrome (ATLS). 50% of the patients with life-threatening symptoms were successfully treated with chemotherapy before histopathological diagnosis was made due to emergency.
Conclusions: NHL is a very aggressive malignancy because of its high mitotic index. It may lead to life-threatening conditions in a very short time. Life-saving chemotherapy even without histopathological diagnosis may be needed in order to increase the chances of survival.

EP-297

CLINICAL CHARACTERISTIC AND PROGNOSIS OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER: A SINGLE INSTITUTE EXPERIENCE IN JAPAN

T. Miyamura[1], Y. Hashii[1], N. Fukushima[2], M. Minami[3], S. Kogaki[1], T. Ueno[4], H. Kondo[1], H. Yoshida[1], E. Miyashita[1], N. Nakagawa[1], K. Ozono[1]

[1]Department of Pediatrics, Osaka University Graduate School of Medicine, Osaka, Japan; [2]Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine, Osaka, Japan; [3]Department of General Thoracic Surgery, Osaka University Graduate School of Medicine, Osaka, Japan; [4]Department of Pediatric Surgery, Osaka University Graduate School of Medicine, Osaka, Japan

Objectives: Post-transplant lymphoproliferartive disorder (PTLD) caused by Epstein- Barr virus (EBV) recently has been recognized as a serious complication of the various organ transplantation. We investigated clinical features of PTLD retrospectively in a single institute in Japan.
Methods: The evaluation period was from July 2004 to February 2014. Seven patients with PTLD (4 male, 3 female) were diagnosed PTLD by the blood examination, lymph node histology and EBV viral load.
Results: PTLD was associated with various organ transplantation (5 heart, 1 lung, 1 liver). In our institute, we have the follow-up of twenty-eight patients post heart transplantation, six post lung transplantation and fifty patients post liver transplantation. Median age at onset was 3.8 years old (range 2-16). Six patients were alive in remission, and one patient died of toxicity. Median time to onset of PTLD from transplantation was 23 months (range, 7-54). Six patients were EBV-seronegative recipient for EBV-seropositive donor. Abdominal lymph node involvements were detected in all cases, and they had severe abdominal symptoms including intestinal perforation. Bone marrow and CNS invasion was not detected. After the reduction of immunosuppressive agents, the chemotherapy combined with rituximab was performed in 6 patients and resulted in remission. A patient had disappeared the lesion by the discontinuation of the immunosuppressive agents.
Conclusions: Although reduction of immunosuppressive agents may be an effective treatment for PTLD, it is difficult to reduce the dose because of the risk of rejection in many cases. All patients but one were EBV-seronegative status, so it could be one of the factor to develop PTLD. Gastrointestinal lesion was detected in all cases, so it was important to select the treatment carefully. We should establish the appropriate treatment strategy according to the prognostic factor because of the distinctive character of PTLD by accumulating more cases.

EP-298

PEDIATRIC HODGKIN LYMPHOMA: EXPERIENCE AT THE CHILDREN'S CANCER CENTER OF LEBANON OVER TEN YEARS

R. Farhat[1], T. Eid[2], B. Youssef[2], R. Saab[1], H. El-Solh[1], M. Abboud[1], S. Muwakkit[1]

[1]Department of Pediatric and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; [2]Department of Radiation Oncology, American University of Beirut, Beirut, Lebanon

Objectives: We describe our experience with hybrid chemotherapeutic regimen consisting of COPP with ABV in children with Hodgkin lymphoma (HL).
Methods: 65 patients were treated through 2002-2012. Patients were classified into Group 1 (disease stages I and IIA), Group 3 (stage IV), and Group 2 patients not belonging to either.
Results: Median age was 13 years (range, 1-20); M:F was 2:1. 1 (1.5%) patient had non classical HL. 24 (36.9%) patients had bulky disease (BD), 33 (50.7%) had B symptoms, 23 (35.3%) had active disease after 2 cycles and 24 (36.9%) patients had stage IV disease at presentation. 22 (33.8%) patients had Group 1 disease, and were treated with 4 cycles of COPP/ABV, 13 received radiotherapy (RT), and none of them relapsed. 19 (29.2%) had Group 2 disease and received 6 cycles of ABV/COPP, 14 had B symptoms, 10 had BD, 2 had ICR after 2 cycles of chemotherapy, and 15 received RT. 24 (36.9%) patients had stage IV and were treated with 2 courses of intensive chemotherapy, 18 had B symptoms, 10 had BD, 13 had ICR after 2 cycles, and 18 received RT; 7 (29.1%) recurred. Patients who received involved-field RT were 46 (70.7%); 5 (10.8%) relapsed. At 34-month follow-up, 8 patients recurred, 7 had stage IV disease among whom 6 had B symptoms, 5 had ICR after 2 cycles, 3 had bone marrow involvement, and 1 had BD. 1 patient had stage II BD, with B symptoms, achieved CR after 2 cycles and received RT, however recurred outside RT field. OS and EFS were 98.5% and 86%. All 17 pubertal males developed azoospermia after therapy.
Conclusions: Majority of Lebanese children with HL had advanced-stage disease. Despite excellent OS and EFS, this protocol was associated with azoospermia. Patients who did not have stage IV disease, B symptoms, nor bulky disease and who achieved CR after 2 cycles did not recur regardless of RT.

EP-299

BURKITT LYMPHOMA CHALLENGES IN RESOURCE LIMITED RURAL COMMUNITIES

J. Ngwang[1], E. Ngwa[1]

[1]Paediatric Unit, CALMEF Health Centre, Tiko, Cameroon

Objectives: Burkitt lymphoma (BL); the most prevalent children cancers in Cameroon, is lethal if not treated; but 50% curable with lone cyclophosphamide (CPD) therapy or combination with methrotrexate. Huge palliative care responsibilities, challenges and support needs especially for paediatric oncology health professionals exists, compelling a June 2010 -

June 2012 cross-sectional community study to ascertain paediatric palliative care, support needs, challenges and also alternative approach to meeting these needs.
Methods: Survey using questionnaires based on aspects of palliative care in relation to the cultural views and traditional beliefs of the community with special attention on paediatric oncology needs where this care and support is provided to ascertain palliative care needs and possible practical interventions.
Results: Much difference exist between the western palliative care and support approach, to this community because of ther unique super attachment to their cultural views and beliefs; some of which are not compatible with a typical modern approach. Death rates, as much as 50% result from the late diagnosis, lack of health units, inaccessibility of treatment products and more.
Conclusions: Poverty and primitive cultures noted as the main hurdle not only to accessing BL care and treatment; but also to palliative care and support hence our study outcome will guide our new guidelines drafting and implementation. It is difficult to 'copy and paste' a modern approach to palliative care and support though startling study results portray that, reviewing paediatric palliative care and support guidelines with consideration and probably with the improvisation of the guidelines for resource limited communities may be more beneficial and successful in enhancing quality of life for families with cancer requiring palliative care and support.

EP-300

EVALUATION OF FDG-PET/CT AND CONVENTIONAL IMAGING TECHNIQUES IN PEDIATRIC HODGKIN LYMPHOMA PATIENTS IN A SINGLE CENTER

A. Oguz[1], F. Tekkesin[1], F.G. Pinarli[1], C. Karadeniz[1], L.O. Kapucu[2], O. Boyunaga[3], A. Okur[1]

[1]Pediatric Oncology, Gazi University, Ankara, Turkey; [2]Nuclear Medicine, Gazi University, Ankara, Turkey; [3]Radiology, Gazi University, Ankara, Turkey

Objectives: We aimed to evaluate the role of FDG-PET/CT in diagnosis, staging and response to therapy during follow-up in children and adolescents with Hodgkin Lymphoma and to compare them with conventional imaging techniques.
Methods: We retrospectively evaluated the FDG-PET/CT and conventional imaging findings of 46 patients with Hodgkin Lymphoma diagnosed between January 2006-December 2013 at Gazi University, Department of Pediatric Oncology.
Results: The mean age of the patients with Hodgkin Lymphoma at the time of diagnosis was $12,1 \pm 3,5$years (range 5-17) with a F/M ratio of 0,53 (16/30). Primary involvement area was head and neck region in 16 patients, mediastinum in 3, head & neck + mediastinum in 24, axillary region in 1 and bone in 2 patients. All of the patients received alternate COPP/ABVD frontline chemotherapy plus involved field low-dose radiotherapy. Median follow-up time was 46 ± 28 months (range 5-94) for the patients. FDG-PET/CT was performed for 40 patients at the time of diagnosis, interim for 16 patients and at the end of therapy for 38 patients. When FDG-PET/CT and conventional imaging techniques at diagnosis were compared, there was no statistically significant difference in determining the stage ($p = 0,754$). The sensitivity and specificity of FDG-PET/CT for evaluation of advanced stage Hodgkin lymphoma were 75% and 100%, respectively whereas positive predictive value (PPV) and negative predictive value (NPV) were 100% and 80%, respectively. The sensitivity and specificity of conventional imaging techniques were 81%,96% and PPV and NPV were 94%,86%. There were 9 patients who had partial regression at interim PET/CT. One of them had a relapse after 2 months, while the other patient was accepted as refractory. There were 7 patients who had normal interim FDG-PET/CT; only one of them had a relapse after 15 months.
Conclusions: We could find no statistically significant difference between FDG-PET/CT and conventional imaging techniques in our patient group but a larger number of patients is needed for evaluation.

EP-301

CD10 – BCL6 – BCL2 – MUM1 – TCL1 EXPRESSIONS IN CHILDHOOD MATURE B-CELL NON-HODGIN LYMPHOMA

A. Oguz[1], A. Uslan[2], N. Akyurek[3], F. Pinarli[1], C. Karadeniz[1], A. Okur[1]

[1]Pediatric Oncology, Gazi University School of Medicine, Ankara, Turkey; [2]Pediatri, Gazi University School of Medicine, Ankara, Turkey; [3]Pathology, Gazi University School of Medicine, Ankara, Turkey

Objectives: To differentiate germinal center B-cell like (GCB) and non-GCB B-cell non-Hodgkin's lymphomas (NHL) types with immune phenotype analysis, evaluation of amount of TCL1 expression, and their effects on prognosis are the main objectives of this study.
Methods: The paraffin tissue blocks of27 patients (age = 3-16 years) with mature B-cell NHL were examined. CD10, BCL6, BCL2, MUM1 and TCL1 expressions were evaluated with the immunohistochemistry staining methods. C-MYC and BCL-2 translocations were evaluated by FISH.
Results: The expressions of CD10, BCL6, BCL2 and MUM1 in Burkitt Lymphomas (BL, $n = 14$) were 78.6%, 100%, 21.4% and 7.1% respectively. GCB phenotype was present in all cases of BL. In cases of diffuse large B-cell lymphoma (DLBCL, $n = 11$) the expressions of these markers were 27.2%, 45.4%, 36.3%, 72.7% respectively. Three cases of DLBCL (27.3%) were GCB phenotype and other 8 cases (72.7%) were non-GCB phenotype. Although there was no statistically significance ($P > 0.05$) between immune phenotype groups and prognosis of DLBCL, we found that overall (OS) and event free survival (EFS) were higher in GCB patients (GCB phenotype = 100% / 100%; non-GCB phenotype = 71.4% / 71.4%). The expression of TCL1 in BL and DLBCL were 64.3% and 54.5% respectively. While C-MYC translocation was positive in all BL cases, no C-MYC translocation was found in DLBCL. According to these results there was no statistically significant correlation (Pearson's $R = 0.106$, $P > 0.05$) between C-MYC translocation and TCL-1 expression in mature B-cell NHLs.
Conclusions: In this study, no correlation was found between C-MYC translocation and TCL-1 expression in mature B-cell NHLs. There is a need for future studies with a larger number of patients for immune phenotypic classification in order to show the impact on the prognosis.

EP-302

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDERS: EXPERIENCE OF THREE PATIENTS

N. Olgun[1], K. Mutafoglu[1], D. Ince[1], E. Buke[1], D. Kizmazoglu[1], M. Kilic[2], C. Arikan[2], E. Ozer[3], L. Doganay[2], H. Guleryuz[4]

[1]Dept. Pediatric Oncology, Dokuz Eylul University Insitute of Oncology, Izmir, Turkey; [2]Liver transplantation team, Kent Hospital, Izmir, Turkey; [3]Pathology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [4]Radiology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

Objectives: To present our treatment experience in posttransplant lymhoproliferative disorders (PTLD).
Methods: Medical records of the patients with diagnosis of PTLD were reviewed. Oncologic treatment details and treatment responses were summarized.
Results: There were three patients with PTLD after liver transplantation (LT). The cause of LT was biliary atresia in two, and chronic liver disease in one of them.
Case1: 27month-old male. He applied with fever, abdominal pain and distension at 21st month of LT. Multiple abdominal enlarged lymph nodes, hepatic nodules, bilateral renal infiltrations were detected by CT. Bone marrow examination revealed L3 lymphoblasts, EBER was positive. Burkitt-like lymphoma, EBV-related PTLD was diagnosed. Gancyclovir, 5 courses chemotherapy (prednisolon, VCR, CYC, VP-16, DOXO, it MTX) were given. He has been followed without disease for 13 years. Case2: 48 month-old male. He applied with fever, abdominal mass at 39th month of LT. Multiple enlarged abdominal lymph nodes and thickening of the intestinal walls were detected by CT. Gastrointestinal (GIS) endoscopic biopsy revealed B cell PTLD (CD 20+). At admission EBV DNA and CMV DNA were positive. Acyclovir, gancyclovir and 4 courses of chemotherapy (prednisolon, CYC/rituximab) were given. He has been followed without disease for one month. Case3: 28 month old female. She applied with diarrhea at 22nd months of transplantaion. Endoscopic GIS biopsy revealed. PTLD (CD 20+) and H.pylori like microorganisms in stomach. Sirolimus and 3 courses of chemotherapy (prednisolon, CYC/rituximab) were given. She has been followed without disease for 6 months.
Conclusions: PTLD may be related with EBV, CMV, H. Pylori. Endoscopic biopsies may be helpfull in diagnosis and follow-up. Complete remission can be achieved by antiviral treatment and reduced intensity chemotherapy. Rituximab is an effective agent in CD 20+ PTLD. In follow-up of patients undergoing solid organ transplantation, symptoms should be carefully evaluated in terms of PTLD.

EP-303

COMPLEX VIZUALIZATION DIAGNOSIS OF RENAL INVOLVEMENT OF PEDIATRIC NON-HODGKIN LYMPHOMAS

T. Panferova[1], T. Valiev[2], I. Kaminskaya[1], E. Mikchailova[1], N. Koshechkina[1]

[1]Radiology Dpt, Institute Of Pediatric Oncology And Haematology N.n.blokhin Cancer Research Cent, Moscow, Russia; [2]Hematologic Dpt, Institute Of Pediatric Oncology And Haematology N.n.blokhin Cancer Research Cent, Moscow, Russia

Objectives: Renal involvement in children with non-Hodgkin lymphomas (NHL) should be specified. We analyzed and assessed a role of ultrasound (US), computed tomography (CT) and magnetic resonance tomography (MRI) data in children with NHL renal involvement.
Methods: It was analyzed results of complex examination (US, CT, MRI) of 21 pediatric patients (age from 2 to 16 years old) with NHL with renal involvement. Statistics was performed with program SPSS19.
Results: We found the following types of renal lesions, based on ultrasound, computed and magnetic resonance tomography data: infiltrative, small focal, medium focal, and nodular. The most common types were infiltrative and focal -76.2% ($p < 0.05$); medium focal type was associated with Burkitt lymphoma (BL) 62.2% ($p < 0.05$). In patients with T-lymphoblastic lymphoma (T-LL) it was found small focal type of lesions in 80% ($p < 0.05$). Nodular type was found in patients with B-lyhmphoblastic lymphoma and primaryh mediastinal B-cell lymphoma, but not in BL and T-LL ($p < 0.05$).
Conclusions: It was found a correlation between renal lesion type (based on complex visualization diagnosis) and morphologic and immunologic NHL variant.

EP-304

ABVE-PC AND MODIFIED BEACOPP REGIMENS FOR HODGKIN LYMPHOMA IN INDIAN CHILDREN: TOXICITY AND OUTCOME

S. Jayabose[1], K. Rathnam[1], V. Kasi[1], S.R. Vignesh[1], S. Arthi[2], J.X. Scott[2]

[1]*Pediatric Hematology & Hemato Oncology, Meenakshi Mission Hospital & Research Centre, Madurai, India;* [2]*Pediatric Hematology & Hemato Oncology, KanchiKamakoti CHILDS Trust Hospital Chennai India, Chennai, India*

Objectives: To study the usefulness of ABVE-PC (Adriamycin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide) and modified BEACOPP (m-BEACOPP) regimens in the treatment of intermediate risk and high-risk Hodgkin's lymphoma (HL) patients regarding their toxicity and outcome.
Methods: High risk patients received 4 cycles of modified BEACOP (m-BEACOPP): bleomycin, etoposide (100 mg/m^2/day $\times$ 3), doxorubicin, cyclophoshamide, vincristine, procarbazine and prednisone (for 7 days) plus 4 cycles of ABVD. Intermediate risk patients received 4 cycles of ABVE-PC (doxorubicin, bleomycin, vincristine, etoposied, prednisone and cyclophosphamiede) plus 2 cycles of ABVD.
Results: Over a 4-year period, 14 patients received 55 cycles of m-BEACOPP and 8 received 37 cycles of ABVE-PC. In the m-BEACOPP and ABVE-PC courses respectively, thrombocytopenia (<50,000) occurred in 5.4% vs 0%; significant anemia (Hb. <8 gm/dl) in 27.2% vs 8.5%; neutropenia (ANC<500) in 50.9% vs27%; and febrile neutropenia in 34.5% vs. 16.2%. The mean duration of hospitalizations was 4.6 vs 2.9 days respectively. There was one episode of localized infection (hepatic abscess) in the ABVE-PC courses; and none in m-BEACOPP. There were no episodes of bacteremia or sepsis in either regimens. Two of 14 high-risk patients required additional chemotherapy and involved field radiation therapy to achieve complete remission (CR). All 22 patients are in CR and doing well with a median follow-up of 27 months (range 3-35); and there have been no relapses. Thus the relapse free and event free survival are 100%.
Conclusions: m-BEACOPP is more likely to cause cytopenias than ABVE-PC. But both regimens are well tolerated with acceptable toxicity profile in Indian children and thus can be used in most institutions with adequate facilities for optimum supportive care. These two regimens offer a high-rate of remission and relapse free survival in intermediate and high-risk Hodgkin lymphoma patients.

EP-305

CLINICAL PROFILE AND CHEMOTHERAPY RESPONSE IN CHILDREN WITH HODGKIN LYMPHOMA AT A TERTIARY CARE CENTRE

R. Seth[1], P. Singh[1], K. Puri[1], R. Das[1]

[1]*Pediatrics, All India Institute of Medical Sciences, New Delhi, India*

Objectives: Optimal treatment strategy in children with Hodgkin Lymphoma (HL) still remains controversial, especially in advanced disease.
To review the clinical profile of pediatric HL at a tertiary care centre, and to evaluate the efficacy of chemotherapy (CT) alone as a treatment modality in childhood HL.
Methods: Retrospective evaluation of case records of children treated for HL for five years at a teriary center in India was done.
Results: Thirty-five children (31 males, 4 females) with a median age of 8 years (range 3.5 – 13years) were studied. Twenty-four (68.6%) were <10 years old, and 23 (65.7%) had late stage disease (stage III to IV). B-symptoms were present in 21 (60%), bulky mediastinal disease in 9 (25.7%), and spleen involvement in 21 (60%) cases. None had bone marrow involvement. The histological types were: nodular sclerosis in 10 (28.6%), mixed cellularity in 9 (25.7%), lymphocyte predominant in 9 (25.7%), and unclassified in 7 (20%) patients. Most patients received ABVD/COPP or ABVD regimen. Two patients needed BEACOPP due to progressive disease, and 4 patients needed low-dose involved field radiotherapy (RT). At a mean (SD) extended event-free follow-up of 42.7 ($\pm$ 17.1) months, 4 patients relapsed. Of these one was lost to follow-up, while 3 were treated with chemotherapy. No child died due to the disease. Two patients had asymptomatic mild restrictive pulmonary function test pattern, while 1 patient developed hypothyroidism after radiotherapy. There was no association of adverse prognostic factors with survival.
Conclusions: Systemic CT alone is an effective therapy in childhood Hodgkin lymphoma. This avoids potential long-term organ dysfunction or secondary malignancy associated with radiotherapy, which may be used as salvage therapy.

EP-306

CLINICOPATHOLOGICAL STUDY OF PEDIATRIC HODGKINS LYMPHOMA WITH IT TREATMENT OUTCOME - A 5 YEARS EXPERIENCE (2008-2012) AT RESOURCE LIMITED SETTING (BPKMCH), BHARATPUR, CHITWAN, NEPAL

K.S. Sharma[1], S. Mehta[2], D. Misra[3]

[1]*Head Pediatric Oncology Division, B P Koirala Memorial Cancer Hospital, Bharatpur, Nepal;* [2]*Medical Officer Pediatric Oncology Division, B P Koirala Memorial Cancer Hospital, Bharatpur, Nepal;* [3]*Medical officer Pediatric Oncology Division, B P Koirala Memorial Cancer Hospital, Bharatpur, Nepal*

Objectives: To know clinicopathological profile of childhood Hodgkin's lymphoma, chemotherapy effectiveness, outcome and follow up in resource limited setting.
Methods: We analyzed all the patient's records from 2008 to 2012 coming to division of pediatric oncology with the suspicious of lymphoma. We recorded the major clinical details and histopathological reports. Pretreatment assessments were done for staging with hematological, biochemical, radiological and Bone marrow examination. All diagnosed patients were treated with standard chemotherapy Protocol with Doxorubicin, Bleomycin, Vinblastine and Dacarbazine. Radiotherapy was recommended for residual disease and patients were advices for follow up.
Results: There were total 46 Patients diagnosed as Hodgkins Lymphoma during this period. 36 numbers of children started recommended chemotherapy. There were 3 children below 5 years, 24 children between 6 to 12 years of age and 9 children between 13-19 years. 30 out of 36 numbers of patients were male. 89% (32) of children had primary disease in cervical area. Other sites were inguinal, abdominal, waldeyer's ring, axillaries. Forty-two percent patients presented within 2 to 6 month of illness, 25% presented before 2 months and 33% presented beyond 6 months. Histological types were Mixed cellularity (44.40%), lymphocyte predominant 36.10% and 19.40% nodular sclerosis. Children present in stage III were 55.60%, stage II 27.8%, 13.90% in stage I and 2.80% at stage IV. Seventy-five percent of patients completed and cured their primary disease. Twenty-five percent of patients were dropped out due to financial constrain. Only 28% (10/36) childrens were in regular follow up. Organ involvements included Spleen (9/36), Liver (6/36), lungs (1/36) without bone marrow involvement.
Conclusions: Hodgkin Lymphoma was common in male between 6-12 years. Cervical lymphadenopathy was the commonest presentation. 2/3rd presented after 2 months of illness. Mixed cellularity was commonest type. 55.6% presented in stage III. 75% Hodgkin's lymphomas were cured. 28% patient presented for follow up without any significant side effects.

EP-307

NON-HODGKIN LYMPHOMA IN CHILDHOOD: CLINICOPATHOLOGICAL FEATURES AND THERAPY OUTCOME AT TWO EGYPTIAN CENTERS

L. Sherief[1], U. El-Safy[1], E. Abdelkhalek[1], D. Youssef[2], N. Kamal[3]

[1]*Pediatric Hematology And Oncology, Zagazig University, Zagazig, Egypt;* [2]*Pediatric, Zagazig University, Zagazig, Egypt;* [3]*Pediatric, Cairo University, Cairo, Egypt*

Objectives: To describe the epidemiological and clinicopathological characteristics and treatment outcome Non-Hodgkin lymphoma (NHL) treated at two Egyptian centers.
Methods: This was a cross-sectional study. Data were collected by a retrospective review of 142 medical records of children with NHL admitted to the 2 oncology units during the period of February 2004 to February 2012.
Results: Abdominal involvement was the most common presentation 70.3%. Burkitt's lymphoma was the most common NHL subtype (69%). The majority of patients had been diagnosed with advanced disease (Murphy stage III / IV disease) 88.7%. The 5 years OS and EFS for all patients was 88.7% and 85.4% respectively. None of the clinical, epidemiological or pathological characteristics had a significant association with the probability of survival.
Conclusions: NHL occurs in younger age, with a higher incidence of Burkitt's lymphoma and advanced disease. The outcome of NHL in our two centers were satisfactory approaches the international percentage.

EP-308

OUTCOME OF TREATMENT OF KI-1+ ANAPLASTIC LARGE CELL LYMPHOMA (ALCL) BY BFM-NHL 90 PROTOCOL FOR KI-1+ALCL PATIENTS

M. Tawfique[1], T. Islam[2], K. Islam[3]

[1]*Pediatric Hematology & Oncology, Square Hospitals Ltd, Dhaka, Bangladesh;* [2]*Pathology, Square Hospitals Ltd, Dhaka, Bangladesh;* [3]*Pediatric Surgery, Square Hospitals Ltd, Dhaka, Bangladesh*

Objectives: To present the outcome of treatment of CD30+ve (Ki-1+) ALCL by BFM-NHL 90 protocol of chemotherapy.
Methods: This was a series of 4 cases. Cases were included purposively in the series. They were diagnosed clinically as NHL. Histopathology of biopsied tumor mass was suggestive of Anaplastic Large Cell variety of NHL. Immunohistochemistry confirmed the diagnosis of ALCL by having positive stain for CD 3 & 30 along with negative stain for CD 20.
Results: In our short series, all the four cases were diagnosed as ALCL. All of them were found CD30+ve by immunohistochemistry. Two of them presented with systemic manifestations only, two of them had both systemic and cutaneous manifestations. All the cases were treated by BFM-NHL 90 protocol for CD30+ (ki-1+) ALCL. All of them completed their scheduled chemotherapy regime. All of them have already been past their 5 years of event free survival.
Conclusions: BFM-NHL 90 protocol specifically for Ki-1+ cases of ALCL was found very effective in the treatment of Ki-1+ ALCL.

EP-309

ABVD WITHOUT CONSOLIDATION RADIOTHERAPY (RT) AFTER COMPLETE REMISSION (CR) IN PEDIATRIC HODGKIN LYMPHOMA (HL): PRELIMINAY RESULTS OF A PILOT STUDY

M. Terenziani[1], E. Schiavello[1], F. Crippa[2], G. Cefalo[3], L. Gandola[4], E. Pecori[4], M. Casanova[1], A. Ferrari[1], R. Luksch[1], C. Meazza[1], D. Polastri[1], F. Spreafico[1], S. Catania[1], V. Biassoni[1], M. Podda[1], S. Chiaravalli[1], N. Puma[1], M. Massimino[1]

[1]Pediatric Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Department of Nuclear Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [3]Department of Pediatrics, Ospedale San Paolo, Milan, Italy; [4]Radiotherapy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Objectives: Children with HL have a good survival but treatments bring on appreciable morbidity. To minimize sequelae, we designed a study with ABVD, for stages 1-3, including B symptoms, without RT in CR patients and reduced RT volumes and doses for PR patients.
Methods: From 1998 onwards 69 consecutive children with HL (median-age 13 yrs; stage I/12; II/40, III/17; B symptoms 30%) were treated. Chemotherapy consisted of 4-6 courses of ABVD followed by RT for patients in PR (25 Gy on PR sites). CR was defined on the basis of clinical and imaging. After 2008, to assess early response, we regularly performed PET2 after 2nd ABVD.
Results: Fourtyfive/69 pts achieved CR after CT (12 stage I, 24 stage II, 9 stage III). 18 children were irradiated, only one after introduction of PET2. The number of irradiated patients did not differ between stages I-II and III (p = ns) and presence of B symptoms. 56/69 patients are in CCR at a median follow up of 7 years. Seven patients relapsed (median time 12 months): 2 after CT only (1 in previously uninvolved and 1 in involved nodes), 5 after CT+RT (3 within RT field, 2 outside). Three primary refractory were intensified. Six out of 10 relapsing-refractory patients are in CR (5 in 2nd,1 in 3rd); three pts died, 1 is alive with disease. We observed two second malignancies: one osteosarcoma outside RT-field and one lung synovial-sarcoma adjacent to the radiation field, at 81 and 89 months after diagnosis. With a median follow-up of 7 years PFS, EFS and OS were 83.4%, 81.5% and 96.2%, respectively.
Conclusions: A significant number of pts (69%) could be cured without RT in any stage. Those poor responders may deserve an intensified treatment. The systematic use of PET has improved response evaluation and reduced the number of irradiated patients.

EP-310

TREATING HODGKIN DISEASE IN A RESOURCE POOR SETTING: PROBLEMS AND OUTCOME

N. Verma[1], A. Kumar[1], N. Moulik[1]

[1]Pediatrics, King George Medical University, Lucknow, India

Objectives: To assess the problems encountered in managing children with Hodgkin disease (HD) in a resource poor Indian setting and to describe the clinical profile and outcome of these children.
Methods: Case records of 184 previously untreated children (age 0-18yr) diagnosed to have HD at our center between 1994 and 2012 were reviewed. 148 children consented to take treatment at our center (16 refused treatment; 20 abandoned treatment). The clinical characteristics, treatments offered and outcomes of these children were analyzed.
Results: There were 130 males and 18 females with a median age of 8yrs. Sixty-two percent of children came from rural areas. 60% children were malnourished, 66% had anemia and 69% had hypoalbuminemia. Median duration of symptoms prior to treatment was 12 months (range 1-96 months). 82% children had advanced disease (stage IIb-IV) at presentation. Mixed cellularity was the most common histological subtype (46%). Ninety-one children (61%) experienced complications during treatment (deranged liver function in 49, fever in 33, anemia in 20). 41 children acquired hepatitis B and 7 hepatitis C during treatment; 22 children died during treatment (12 deaths due to chemotherapy related toxicity, 9 due to advanced disease, and 1 unrelated death due to CNS Tuberculosis); 126 children completed treatment, out of which 20 relapsed. 36 children experienced delays in chemotherapy due to various reasons (deranged liver function-25, fever-5, neutropenia-2, social-4); 118 children (80%) were surviving free of disease with a median follow up of 3.3yrs (range 0.3-19.3yrs).
Conclusions: Children with HD coming to our center tend to have a delayed presentation with advanced disease. Abandonment rates are high. Over one-third of these children get infected with hepatitis B or C during the course of treatment. Complications are common during treatment, leading to therapy delays. These factors are responsible for a poor outcome as compared to developed countries.

EP-311

RITUXIMAB IN CHILDHOOD MATURE B-CELL LYMPHOMA: REPORT FROM A SINGLE CENTER OF CHINA

H. Wang[1], X. Zhai[1], F. Lu[1], L. Hu[1], J. Li[1], H. Miao[1], X. Qian[1], X. Zhu[1], Y. Yu[1]

[1]Hematology, Children's Hospital of Fudan University, Shanghai, China

Objectives: To evaluate the efficacy and safety of Rituximab in childhood mature B-cell lymphoma.
Methods: We treated 22 children with progressive B-cell lymphoma with in combination with Rituximab. Data on patients' were analyzed.
Results: Fourteen were stage III; 8 were stage IV. Sixteen patients were diagnosed with Burkitt's lymphoma, 3 were DLBL and the rest were B cell lymphoma. Seventeen patients were initially treated with Rituximab and the rest were treated in replaced. Among patients with Rituximab as initial therapy 15 had LDH>1000U/L, 1 had LDH>500 U/L, 1 < 500U/L. Three patients experienced relapse and died. The mean follow up duration were 18.5 month with EFS 82.4%. All five Patients with relapsed lymphoma died. Deaths in our studied cohort were not related to Rituximab treatment.
Conclusions: No serious adverse effects were observed. Initial therapy with Rituximab might improve the prognosis of B-cell lymphoma in children with heavy tumor load.

MYELOID LEUKEMIAS, MYELODYSPLASTIC SYNDROMES, MYELOPROLIFERATIVE SYNDROMES

EP-312

SIMULTANEOUS PRESENTATION OF ACUTE MYELOID LEUKEMIA AND BURKITT LYMPHOMA. CASE REPORT AND REVIEW OF THE LITERATURE

F. Arreguin[1], V. Flores[2], L. Merino[2], J. Trejo[2]

[1]Pediatric Oncology, Centro Medico Nacional "20 de Noviembre " ISSSTE, Mexico City, Mexico; [2]Pediatric Hematology, Centro Medico Nacional "20 de Noviembre " ISSSTE, Mexico City, Mexico

Objectives: To perform a case report and review of the literatura of a simultaneous presentation of two hematologic malignancies: Burkitt lymphoma and acute myeloid leukemia in a child in the Pediatric Oncology-Hematology Service of Centro Medico Nacional 20 de Noviembre ISSSTE in Mexico city.
Methods: All the pathological, flow citometric, cytogenetic and assays were performed in certified clinical laboratorios using standard techniques. Inmunohistochemistry was performed with antibodies to CD18, CD54, LFA-1, Ki-67, CD45, BCL-6, CD10, CD20, CD22, CD79a, sIgM, TdT.
Results: This paper reports a 6 year old child with Burkitt lymphoma Stage III. No cytogenetic abnormalities were found and VEB infection was discarded. He received COPADM scheme and after four months of treatment, he presented leukocytosis, cephalea and bilateral proptosis. The bone marrow aspiration showed 86% of myloblasts, with CNS infiltration with involvement of the optic neve and meninges. He received treatment according to the Acute Myeloid Leukemia high risk protocol, achieving complete remission. We did not find donos for the bone marrow transplantation. After 3 months, he relapsed of Burkitt's lymphoma. He finally died.
Conclusions: This case shows a patient with acute myeloid leukemia and Burkitt lymphoma. This patient had a short response to treatment with early relapse and poor prognosis.

EP-313

PEDIATRIC MYELODYSPLASTIC SYNDROME: EXPERIENCE FROM A SINGLE CENTER

M. Cetin[1], S. Unal[1], T. Bayhan[1], S. Aytac[1], B. Kuskonmaz[1], B. Tavil[1], D. Uckan-Cetinkaya[1], M. Tuncer[1], F. Gumruk[1]

[1]Division of Pediatric Hematology, Hacettepe University Medical School, Ankara, Turkey

Objectives: Pediatric myelodysplastic syndrome (MDS) is a group of heterogeneous clonal disorder with lesser frequency compared to adults. Additionally, there is much rare data in pediatric age group in relation to presentational findings and treatment.
Methods: The clinical and laboratory data, in addition to therapeutic interventions and outcomes of 47 patients in a single who were diagnosed between 2001-2014 were summarized.
Results: Median age of the study group was 2.8 years (0.1-16.8). The most common complaints at presentation included fever (27%), fatigue (17%), bleeding (15%), abdominal distention (13%), in addition to other rare presentational complaints including pallor, rash, vomiting, irritability, jaundice, stridor, abdominal pain and easy bruising. The underlying disorder was established as: neurofibromatosis in 5, Down syndrome in 3, secondary to prior chemotherapy in 2 (ALL and PNET), Fanconi anemia in 1, Jacobsen syndrome in 1, Klinefelter in 1. Final diagnosis was MDS in 22, JMML in 19, hypoplastic MDS in 4 and chemotherapy related MDS in 2. Median Hb, WBC, thrombocyte counts at presentation were 8.7 g/dl (4.1-12.7), 10.3×10^9/L (1.3-117) and 55×10^9/L (4-1515), respectively. Of the mutations studied related to MDS in 22 of the patients, k-ras positivity was the most common (23%). The most common cytogenetic abnormality was chromosome 7 related abnormalities (25%). Of the patients, 21 (45%) are alive and of these alive patients 62% are alive subsequent to hematpoietic stem cell transplantation (HSCT).
Conclusions: The patients with pediatric MDS may present with various complaints and they may have underlying genetic diseases causing propensity for MDS. The survival is better among patients who underwent HSCT.

EP-314

SUCCESSFUL MANAGEMENT OF CASE OF GRANULOCYTIC SARCOMA WITH CONCURRENT HEMOPHAGOCYTIC LYMPHO HISTIOCYTOSIS

Y.R. Chopra[1], M. Ramzan[1], S. Katewa[1], S. Yadav[1]

[1]Pediatric Hematology Oncology and Bone Marrow Transplant Unit, Fortis Memorial Research Institute, Gurgaon, India

Objectives: Granulocytic sarcoma (GS) is rare extra medullary tumor usually associated with Acute Myelogenous leukaemia (AML M2). Hemophagocytic Lympho Histiocytosis (HLH) has rarely been reported in a child presenting with GS. We describe a successful management of GS concurrent with HLH in a 6-year-old.
Methods: Medical records from our institute were reviewed
Results: A 6 year old admitted to us with complaints of pain in her right frontal region with swelling of the right eye. She received oral antibiotics for a week from an ophthalmologist, thought to be peri-orbital cellulitis and in view of no improvement, was evaluated further and found to have a mass visible through the right nasal cavity. MRI brain with paranasal sinuses was done which revealed a mass in the posterior aspect of the nasal cavity extending into the nasal choana. Biopsy of the mass was suggestive of GS. Subsequent BMA and flow cytometry was consistent with diagnosis of AML-M2 with 34% blast and AML-ETO (translocation 8:21) positivity. She was treated as per modified UK AMLXII protocol. She had a seizure after first lumbar puncture for which no cause was found. After first induction she developed persistent fever and was diagnosed with HLH. No other cause for HLH could be identified. We meticulously treated her with chemotherapy for AML and dexamethaone for HLH.
Conclusions: High suspicion is necessary to diagnose GS in children. Early diagnosis and immediate initiation of treatment are mandatory to overcome this condition. Further clinical data describing the clinical course and the management of children with MAHS are warranted.

EP-315

CYTOGENETICS OF PEDIATRIC ACUTE MYELOID LEUKEMIA: A SINGLE CENTRE EXPERIENCE

M. Chowdhry[1], R.N. Makroo[1], S. Sharma[1], S. Priyanka[1], M. Mishra[1], Y. Thakur[1], M. Singh[1], A. Mahajan[1]

[1]Molecular Biology & Transplant Immunology, Indraprastha Apollo Hospital Delhi, Delhi, India

Objectives: Acute myeloid leukemia (AML) is a clinically and genetically heterogeneous disease and accounts for 15-20% of all childhood leukemias. The current WHO classification for hematology malignancies has defined distinct entities of myeloid disorders based on the presence of recurrent cytogenetic abnormalities. The cytogenetic abnormalities are divided into following three prognostic groups used in risk stratification for treatment: favorable risk: t (8;21) (q22;q22), t (15;17) (q22;q21), and inv (16) (p13q22); adverse risk: monosomy 5/ deletions of the long arm of chromosome 5 [del (5q)], monosomy 7, abnormalities of 3q, and complex karyotypes; and intermediate risk: other changes. Because AML is rare in children, the true prognostic significance of individual chromosomal abnormalities in this age group remains unclear. The present study was undertaken to determine the cytogenetic abnormalities in pediatric AML and their prognostic significance.
Methods: Bone marrow samples collected from 52 pediatric AML patients, cultured for 24 hours without any stimulating agent. The samples were treated with colcemid followed by hypotonic treatment and fixation. The karyotypes were analyzed using the GTG banding technique, described according to International System for Human Cytogenetic Nomenclature 2009.
Results: Out of 52 AML patients, 33 (63.4%) were male and 19 (36.5%) were female. The median age of patients was 14.5 years. Cytogenetics abnormalaties were detected in 31 (59.6%) patient while 21 (40.3%) had a normal karyotype. In the favorable prognostic category, there were 20 (64.5%) cases with t (8;21) (q22;q22) and 3 (9.6%) cases with t (15;17) (q22;q21). Out of 20 t (8;21) cases, 12 had only t (8;21) with no accompanying structural abnormality, where as 8 had either loss of sex chromosome or other structural abnormality. In the unfavourable prognostic category, Trisomy 8 was found in 1 (3.2%) case, hyperdiploidy in 1 (3.2%) and complex karyotype in 6 (19.3%).
Conclusions: Larger studies of this kind may provide more information about prognostic significance of cytogenetic abnormality in pediatric AML.

EP-316

MAINTAINENCE THERAPY IN ACUTE MYELOID LEUKEMIA: EXPERIENCE FROM A DEVELOPING COUNTRY

K. Jain[1], S. Udgire[1], S. Mudaliar[1], A. Swami[1], N. Shah[1], M. Desai[1], B. Agarwal[1]

[1]Oncology, B.J. Wadia Hospital for Children, Mumbai, India

Objectives: The objective of this study is to determine if the addition of maintainence therapy (MT) would improve the survival of children with acute myeloid leukemia (AML) when compared with those treated without MT.
Methods: Retrospective analysis of cases with AML,0-15 years, diagnosed from 2000-2013, with patient demographics and therapy details.2001-2007, a regimen of induction with 7+3 and 5+2 followed by Denver protocol was used.2008 onwards to current, patients are treated with 7+3,5+2 followed by 3cycles of high dose cytarabine with additional MT.
Results: Of total 88 patients with AML,50 patients were diagnosed between 2000-07 and 38 from 2008-13.28/88-recieved complete therapy,3/88-currently on medication,5/88-relapsed on therapy,6/88-refractory,16/88-expired during treatment (secondary to infection), 17/88-lost to follow up and 13/88-refused treatment.14/38 patients received MT in 2008-13.10/14 patients are surviving and 4/14 have relapsed. Remission period in the survivors is 1month to 2.9years (median:2years), 3children had WBC >1lac/cumm,3 had unfavourable cytogenetics (1-complex,1-5q deletion), 1 patient did not achieve complete remission (CR) after 1st induction. Of the 4 which relapsed,1 had WBC>1lac/cumm,2 had unfavourable (complex) cytogenetics.2patients did not achieve CR after 1st induction, of which 1 had dysplastic changes in the bone marrow. They probably needed bone marrow transplant. 14/50 children were treated without MT from 2000-2007.12/14 relapsed and 2/14 surviving until their last follow up. Median remission period in the relapsed patients is 5months. Of them,1-complex cytogenetics;1-WBC>1lac/cumm,1-did not achieve CR after 1st induction. For the 2 survivors, followup is 1-3.5years and 2nd-6years.1 had WBC>1lac/cumm, both had achieved CR. Cytogenetic analysis was not done in both.
Conclusions: While there has been impressive progress in the treatment of AML, majority of patients still die from this disease. As compared to before, the disease free remission period for AML has improved at our centre with the use of MT. However the initial chemotherapy (induction and consolidation), supportive care and financial help are also better now, which may have been an added factor for the improvement.

EP-317

USE OF MODIFIED MRC-10 PROTOCOL FOR ACUTE MYELOBLASTIC LEUKEMIA IN INDIAN CHILDREN

S. Jayabose[1], T. Kasi Viswanathan[1], S.R. Vignesh[1], R. Priya[1], K. Rathnam[1]

[1]Pediatric Hematology-Oncology, Meenakshi Mission Hospital & Research Centre, Madurai, India

Objectives: To analyze the results of treatment of AML with modified MRC-10 protocol; and to assess the toxicity of this regimen
Methods: This study is a retrospective analysis of 39 consecutive AML patients treated over a period of 4 years (2010-2014). Male: female ratio, 19:20. Median follow-up for living patients is 29 months (3-46). Thirty-four patients had denovo AML and 5 patients had a pre-leukemi MDS phase. (MDS-AML). Two patients had acute promyelocytic leukemia. Six had t (8;21) and one had inversion 16. Eight patients had chloromas- two of them with no evidence of AML in bone marrow. The modifications of MRC -10 protocol included reduced number (14 instead of 20) of cytarabine doses and etoposide doses (3 instead of 5) during induction; and only 3 doses of mitoxantrone instead of 4 during intensification. All patients received 3 cycles of oral maintenance therapy with 6-TG 40 mg/m^2 and etoposide 50 mg/m^2 daily x 3 weeks—given every 28 days. All patients received above treatment without risk stratification.
Results: Six of 39 (15.3%) patients died of infectious complications during induction. Five patients (12.8%) failed induction; 28 patients (71.8%) achieved complete remission. Four of 5 patients who failed induction therapy had MDS-AML. Seven patients died in remission-due to sepsis in 5 and other infections in 2. Six of 28 patients (21.4%) relapsed in 3 to 13 months. Two of the 6 relapsed patients are alive, 4-5 months from relapse. Three patients developed significant cardiac dysfunction; all three died of infectious complications in remission. The 3-yr estimated overall survival is 47.5%; and the 3-yr event-free survival 40%.
Conclusions: The modified MRC-10 regimen is poorly tolerated by Indian children, The unacceptably high mortality during induction and in remission requires reduction of treatment intensity during induction and consolidation, especially for good-risk patients.

EP-318

CYTOGENETIC PROFILE OF ACUTE MYELOBLASTIC LEUKEMIA IN CHILDREN AND ADOLESCENTS: ABOUT 119 CASES

N. Khoubila[1], M. Lamchahab[1], N. Hda[1], S. Cherkaoui[1], A. Madani[1], S. Benchekroun[1], A. Quessar[1]

[1]Department of hematology-pediatric oncology, Hospital 20 August 1953, Casablanca, Morocco

Objectives: Determine the cytogenetic profile of children and adolescents with AML and evaluate the prognostic impact of cytogenetic abnormalities.
Methods: We conducted a retrospective study between March 2004 and March 2009, including patients with de novo AML, aged 0 to 20 years. The diagnosis is confirmed by cytology by FAB classification +/- immunophenotyping. All children treated with Moroccan protocol AML-MA03 (2 induction+2consolidation).
The karyotype was performed at diagnosis on samples from bone marrow. The cytogenetic study was made RHG band after 24 hours of culture. The cytogenetic abnormalities found were classified into 3 prognostic groups: favorable, intermediate and unfavorable.
Results: 125 cases of AML were diagnosed, the karyotype was performed in 119 patients (95%) including 2 culture failures (1.6%). These 58 males and 61 females (sex ratio M/

F = 0.95). The median age is 15 years (7months - 20 years). The cytological type was the most common type M2 (45%). Of the 119 karyotypes performed, 87 patients (74.5%) had acquired clonal abnormalities. We noted 2 cases of culture failure (1.6%).103 patients (84%) were treated by the national protocol AML-MA 03, the continuous complete remission (MCR) for groups favorable, intermediate and unfavorable was respectively 41%, 25% and 10% with a decline of 24 months. The distribution of prognostic groups is as follows:- Favorable group: 34 (29%) patients with 31 (26.5%) cases of t (8;21), 2 cases of inversion of chromosome 16 and one case of t (15; 17).- Intermediate Group: 64 (54.5%) patients. 30 (25.5%) had a normal karyotype and 3 cases had a deletion of band 11q23.- Unfavorable group: 19 (16.5%) patients had 3 or more abnormalities in karyotype, monosomy 7 in one patient (1%).
Conclusions: These results enabled us to identify the cytogenetic profile of our patients and to guide our therapeutic strategy including better management.

EP-319

A PEDIATRIC CASE OF DNMT3A GENE MUTATION-POSITIVE ACUTE MYELOID LEUKEMIA

W. Lin[1], X.U.A.N. Zhou[1], M. Wu[1], W. Li[1]

[1]Hematology/Oncology Center, Beijing Children's Hospital, Beijing, China

Objectives: Recent reports have revealed that epigenetic changes (such as DNA methylation) are important causes of leukemia. Although mutation in *DNMT3A* is very rare in pediatric AML patients, it remains an important diagnostic and prognostic factor for which patients are commonly screened. Here, we report a pediatric case of AML that was positive for the *DNMT3A* gene mutation at onset of diagnosis.
Methods: A two-year-old male first presented with a scalp lump that, upon examination, suggested myeloid sarcoma. The lump disappeared after anti-infection treatment, and there was no other evidence to suggest the presence of leukemia, except *DNMT3A* gene mutation-positive. Five months later, the male presented with testicular swelling, which resulted in a diagnosis of AML.
Results: Eventually, the patient was diagnosed with acute monocytic leukemia, testicular leukemia, and central nervous system leukemia. Chemotherapy successfully eliminated *DNMT3A* mutant-positive bone marrow cells. Although the child also received hematopoietic stem cell transplantation, he had a relapse of testicular leukemia for which he received radiotherapy.
Conclusions: The *DNMT3A* gene mutation is important for both prognosis and early diagnosis of pediatric AML.

EP-320

A PRELIMINARY REPORT OF A DIAGNOSTIC STUDY WITH (18) F-FDG-PET (PET) FOR DETECTION OF EXTRAMEDULLARY DISEASE (EMD) IN PEDIATRIC ACUTE MYELOID LEUKEMIA (AML)

M. Matsui[1], J. Yamanaka[1], H. Uryu[1], N. Sato[1], K. Kubota[2], T. Matsushita[1]

[1]pediatrics, National Center for Global Health and Medicine, Shinjyuku, Japan; [2]Radiologist, National Center for Global Health and Medicine, Shinjyuku, Japan

Objectives: The primary purpose of the study is to assess the diagnostic usefulness of PET for detection of EMD in pediatric AML at diagnosis. The secondary purposes include assessing usefulness to evaluate remission status after induction therapy and to analyze relationship between the findings of PET and clinical outcome. During the study, we consecutively experienced 2 children with AML with PET-detectable EMD. Considering significant importance of the findings, we decided to present as a selective case report of the 2 cases.
Methods: Patients enrolled in this study undergo PET scan immediately after the diagnosis, prior to starting induction therapy. The prevalence of EMD detected by PET scans and by conventional assessments are compared. The second scan is performed prior to consolidation therapy to evaluate the response to chemotherapy judged by FDG uptake change in EMD area and bone marrow (BM). Correlation between PET findings and clinical outcome will be analysed after accumulation of the data of all cases.
Results: The first case is an 8-month-old male diagnosed AML (FAB M4) with inv (16) and CBFB-MYH11 fusion gene. The second case is a 9-year-old male diagnosed AML (FAB M4) with t (8;21) and AML1-ETO fusion gene. The first PET demonstrated 2 EMD lesions in the case 1 and 4 in the case 2, while standard diagnostic examination detected only 1 lesion in each case. Both of them achieved complete remission (CR) after the induction therapy by conventional criteria. The second scan could confirm CR by reduced uptake of FDP in EMD and BM in both of the patients.
Conclusions: We present two cases of childhood AML with EMD who were performed PET scan. These cases demonstrate the usefulness of PET for diagnoses of EMD and assessing treatment responses of EMD and BM.

EP-321

CYTOGENETIC AND MOLECULAR GENETIC ABNORMALITIES EVALUATION IN PEDIATRIC ACUTE MYELOBLASTIC LEUKEMIA

A. Mehrvar[1], M. Tashvighi[1], A.A. Hedayati Asl[1], M. Faranoush[1], J. Sabery Nejad[2], A. Ramyar[3], N. Mehrvar[4], L. Kuchakzadeh[3], F. Kompany[3], M.S. Rahiminejad[3]

[1]Oncology, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran; [2]Pediatric, Children Center Hospital, Tehran, Iran; [3]Pediatric, Children Center Hospital, Tehran, Iran; [4]Research, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran

Objectives: Genetic abberations underlying Acute Myeloblastic Leukemia (AML), is the importance landmark for better managing the pathogenesis of disease. Two main referral centers for childhood malignancies in Tehran (capital city of Iran) are MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) and Children Center Hospital. Children less than 15 years old with all kind of childhood malignancies will admitted in these two centers for diagnosis and therapy. Patients from all parts of Iran can refer there.
The main goal of this study was to evaluate genetical abnormalities in patients with AML for better managing this disease in future.
Methods: Enrolled Patients have been referred from all parts of Iran to two referral childhood malignancy centers in Tehran, Iran (MPCTRC, Children Center Hospital) during April 2007 to April 2013. There was a unique check list for all patients than implied basic data about sex, age, date of dead. Bone marrow aspirates of 104 pediatric AML cases were analyzed by G-banding technique, karyotyping and Real Time-PCR for translocations. Finally data analysed by SPSS version 19.
Results: There were 57 males (54.81%) out of 104 enrolled patients. The mean age of patients were 6.9 ± 0.43 years. Immunophenotyping results showed the M4 (n = 20, 19.2%) and non-M3 (n = 19, 18.3%) groups as the majority phenotypes respectively. Twenty out of 104 patients (19.2%) had genetic abnormalities; t (15;17) (n = 6, 30%), inversion (n = 5, 25%), mosaicism with deletion (n = 2, 10%), t (8;21), t (6;11), hyperdiploidy, mosaicism with translocation, mosaicism with monosomy, trisomy 8 and gene deletion (n = 1, 5%). Fourthy-four patients died (42.3%) during this study. The three-years survival rate was 88%.
Conclusions: Analysis and literature reviews revealed that t (15;17) was the most prevalence abnormalities. Authors suggestion is comprehensive studies with larger patients series to confirm these evaluation. Focusing on cytogenetic abnormalities will consider prognostic significances of patients with AML that can affect treatment planning.

EP-322

IMATINIB MESYLATE INDUCED BONE MARROW APLASIA: NEED EXTRA VIGILANCE FOR A RARE COMPLICATION

R. Mohammed[1], C. Yogiraj[1], S. Rajat[1], K. Satyendra[1], C. Ritu[2], Y. Satya Prakash[1]

[1]Pediatrics Hematology Oncolgy and BMT Unit, Fortis Memorial Research Institute, Gurgaon, India; [2]Department of Pathology, Fortis Memorial Research Institute, Gurgaon, India

Objectives: Imatinib mesylate, a signal transduction inhibitor molecule, has revolutionized the management ofchronic phase of chronic myelogenousleukemia (CML). The drug is generally well tolerated. Severebone marrow (BM) aplasia has rarely been reported.
Methods: A 6-year-old male child presented in November 2013 with a history of low-grade fever for 15 days and fatigue. On examination he hadgood general condition with mild pallor without organomegaly. The rest of the systemic examinationwas within normal limits. Haemoglobin (Hb) was 7.9 g/dl, whiteblood cell count (WBC) 126 x 10^9/l and platelets1979 x 10^9/l. Differential counts and bone marrow studies confirmed the diagnosis of chronic phase CML. Cytogenetic studies revealed 100% Ph-positive metaphases.
Results: He was started on 400 mg/day on 21 November 2013, with weekly monitoring of counts. He tolerated the drug welland did not require any dose modification. On 20December 2014, during a follow-up visit, he was foundto have pancytopenia. Hbwas 8.5 g/dl, WBC 435 x 10^9/l, and platelet count 95 x 10^9/l. BCR-ABL by quantitative method was 13.37. Repeat CBC on 24 January 2014 showed Hb was 8.3 g/dl, WBC 351 x 10^9/l, andplatelet count 79 x 10^9/l. His Imatinib was discontinued. The Bone marrow aspiration was hemodiluted, biopsy showed severely hypoplastic marrow (10-15% cellularity) with no increasein blasts with a mild increase in fibrosis on reticulin stain. CBC on 13 Feb and 26 Feb 2014 showed Hb 8.9/8.8, WBC 599/617 $\times$ 10^9/l, and platelet count 150/230 x 10^9/l respectively. His BCR-ABL by quantitative method was zero. He was restarted on low dose imatinib (200mg/day).
Conclusions: Imatinib induced severe bone marrow aplasia is a rare complication. CML patients on imatinib therapy need close monitoring.

EP-323

ACUTE ERYTHROLEUKEMIA IN A CHILD-IMMUNOPHENOTYPIC AND CYTOGENETIC FEATURES

E. Papakonstantinou[1], A. Taparkou[1], N. Gompakis[1], F. Vadikolia[1], A. Athanasiadou[1], P. Anagnostopoulou[1], D. Athanasiadis[1], O. Vrani[1], M. Kourti[1], D.E. Koliouskas[1]

[1]Paediatric Oncology, Hippokration General Hospital, Thessaloniki, Greece

Objectives: Erythroleukemia is a rare disorder characterized by uncontrolled proliferation of erythroblasts and myeloblasts comprising 2-7% of all acute myeloid leukemias. The French

American British (FAB) classification of these leukemias is AML M6. They are generally seen in old age. Very few cases of pediatric erythroleukemia have been reported in literature, comprising less than 1% of pediatric leukemias.
Methods: One rare de novo case is presented of pediatric erythroleukemia, AML-M6 in a 2-year-old patient who presented to our department. The clinical, morphologic, immunophenotypic and cytogenetic features of the patient are reviewed. The purpose of this study is to correlate the bone marrow morphology with the immunophenotype and the karyotypes of the neoplastic cells.
Results: The patient was presented with thrombopenia. The peripheral blood examination showed anemia (Hb 8g/L), thrombocytopenia (26 x 10 (9)/L) and 7% blasts. Multiple cervical lymph nodes were present, measuring 1-2 cm, which were free and mobile. There were multiple purpuric spots present all over the body. Bone marrow (BM) aspirates showed predominantly erythroid population with scant to moderate amount of pale blue cytoplasm, round or oval nuclei and many coalescent vacuoles. Erythroblasts showed positivity for periodic acid Schiff (PAS). Myeloperoxidase (MPO) was negative. Flow cytometry demonstrated blast population 28% expressing myeloid markers (CD33, CD13, CD117). The blasts do not express monocytic markers (CD34, HLADR, CD64, CD14, CD15, CD11b, CD56, CD4) or megakaryocytic markers (CD61, CD41). Immunophenotypes of the pretreatment bone marrow showed CD36, CD71, CD235 (glycophorin-A). Chromosomal analysis revealed an abnormal karyotype, 46, XY, t (5;16) (q13:p11.2) [11]/48,+19,+21. Our patient is in first complete remission after 2 cycles of AML-BFM protocol under search for compatible donor for bone marrow transplantation (BMT).
Conclusions: The prognosis of erythroleukemia is very poor. Our patient was good responder to AML induction regimen and long-term survival could be achieved with BMT in first complete remission.

EP-324

RELATION OF HLA-A, -B, -DRB1 ALLELES AND HAPLOTYPES IN PATIENTS WITH ACUTE MYELOBLASTIC LEUKEMIA

T. Patiroglu[1], H.H. Akar[2]

[1]Department of Pediatric Hematology and Oncology, Erciyes University Faculty of Medicine, Kayseri, Turkey; [2]Department of Pediatric Immmunolgy, Erciyes University Faculty of Medicine, Kayseri, Turkey

Objectives: Previous studies have demonstrated some significant differences in HLA allele frequencies in leukemic patients and normal subjects. The purpose of this study is to evaluate the frequencies of HLA class I (A, B) and class II (DRB1) alleles in acute myeloblastic leukemia and compare with unrelated healthy controls.
Methods: We investigated the relation of the HLA alleles in 32 acute myeloblasticleukemia (AML) patients and 126 unrelated normal subjects by PCR-SSOP method using Luminex technology.
Results: Allele frequencies of HLA-A*03and HLA-A*11 were higher in patients with AML compared with the controls ($p = 0.007$ and $p = 0.041$). On the contrary, HLA-B*13 allele frequency lower than controls ($p = 0.017$).
Conclusions: These results suggest that HLA-A*03 and HLA-A*11 alleles may play a presumptive predisposing factor in AML. In addition, HLA-B*13 allele has been found to be negatively associated with AML.

EP-325

INTENSIVE CONSOLIDATION COMPARED WITH LOW-INTENSITY CONSOLIDATION AND MAINTENANCE THERAPY FOR ADOLESCENTS AND YOUNG ADULTS WITH ACUTE MYELOID LEUKEMIA

S. Semochkin[1], T.N. Tolstykh[2], S.S. Kulikova[1], E.G. Arshanskaya[3], V.V. Lunin[3], A.I. Lukina[2], A.G. Rumiantsev[4]

[1]Pediatric Oncology Hematology and Radiation Therapy, Pirogov Russian National Research Medical University, Moscow, Russia; [2]Adolescents and Young Adults Hematology, Federal Scientific and Clinical Centre of Pediatric Hematology Oncology and Immunology, Moscow, Russia; [3]Hematology, City Clinical Hospital n.a. S.P. Botkin, Moscow, Russia; [4]Director of the Centre, Federal Scientific and Clinical Centre of Pediatric Hematology Oncology and Immunology, Moscow, Russia

Objectives: To examine the efficacy of intensive consolidation without maintenance versus low-intensity consolidation plus maintenance therapy for adolescents and young adults with acute myeloid leukemia (AML).
Methods: A total of 108 patients with median age 29.9 years (range, 15-45) with de novo AML were enrolled in this non randomly trial. Of these, 50 patients were assigned to receive 2 cycles of induction '3+7' (daunorubicin 45 mg/m^2 on days 1-3; cytarabine 100 mg/m^2 every 12 hours [q12h] on days 1-7) and consolidation of 3 cycles '1+5' following by maintenance chemotherapy also cycles for 2 years. Other 58 patients were treated 2 cycles of induction '3+7' or '3+7' plus HAM (cytarabine 3 g/m^2 per q12h on days 1-3; mitoxantrone 10 mg/m^2 on days 3-5) if the complete response (CR) was not documented after the first cycle. Then there were 4 cycles of consolidation HiDAC (3 g/m^2 per q12h on days 1-3) without following by maintenance.
Results: CR was documented for 74.0% (intensive consolidation) and 62.1% (low-intensity consolidation followed by maintenance therapy) patients. Median of overall survival (OS) was 2.03 years versus 0.87 years (HR 0.61; 95% CI 0.37-1.02; $P = 0.056$). The median of follow-up for surviving patients was 9.4 and 3.1 years respectively. Two-years OS was $52.0 \pm 7.1\%$ vs. $33.8 \pm 6.3\%$ ($P = 0.052$ by log-rank test). However, the 5-years OS rate was the same ($31.1 \pm 6.7\%$ vs. $26.5 \pm 7.1\%$; $P = 0.184$) due to the high frequency of late relapses for longer tracked by time group (26.0% vs. 8.6%; $P = 0.035$). Intensive consolidation compared with low-intensity consolidation accompanied by a higher frequency of adverse events III/IV degrees, including neutropenia (100.0% vs. 68.9%; P
Conclusions: Both the concept of post-remission therapy for adolescents and young adults with AML was demonstrated an equivalent clinical efficacy.

EP-326

ACUTE MYELOID LEUKEMIA IN CHILDREN: EXPERIENCE FROM A TERTIARY CARE FACILITY IN INDIA

R. Seth[1], R. Seth[1], A. Singh[1], S. Seth[2]

[1]Pediatrics, ALl India Institute of Medical Sciences, Delhi, India; [2]Cardiology, ALl India Institute of Medical Sciences, Delhi, India

Objectives: To document the demographic profile and outcome of children with acute Myeloid Leukemia (AML) treated at a tertiary center in India.
Methods: Retrospective review of case records of children diagnosed and treated for AML was done. Fifty-one patients were diagnosed in two years.
Results: The average age at presentation was7.74 ± 2.75years.64.6% were males. The most common presenting features were fever and pallor followed by bleeding. Hyperleukocytosis was seen in 4 patients. CNS disease was present in 1 patient The cytogenetics profile will be presented.10 patients declined treatment at diagnosis / soon after initiation of treatment. Of the 41 patients 21 patients are undergoing treatment/completed treatment. Average duration of follow up ranges between 7-12 months. The reasons for expiry include febrile neutropenia and myocardial dysfunction. Fungal sepsis emerged as an important cause of febrile neutropenia.
Conclusions: Outcome of pediatric AML is inferior to that seen in some western countries. However patients are more receptive to initiation of treatment of AML now. Mortality is high. There is a need for sensitization towards importance of supportive care and infection control in management of childhood AML.

EP-327

IMPROVING SURVIVAL RATES OF ACUTE MYELOID LEUKEMIA IN DEVELOPING COUNTRIES USING AML_15 PROTOCOL

S. Siddaiahgari[1], B. Jillella[1], A. Manikyam[1]

[1]Pediatric Hematology-Oncology, Rainbow Childrens Hospital, Hyderabad, India

Objectives: To look at the outcome of children with Acute Myeloid Leukemia (AML) using AML 15 protocol
Methods: A 2.1 years prospective and 1.9yrs retrospective observational study done in teritiary care center, in 6 months to 15years children from January 2009 to December 2012.
Results: Total 32 children identified. Most of them below 5 years (14/32). 19/32 are females. Common presenting symptom is fever and organomegaly22 and 21 respectively. 2 had subcutaneous deposits & one had Leukemia cutis. Severe anemia <7 gm% noticed in 15 cases. Six out of 32 had Hyperleucocytosis. 24 cases had platelets less than 50,000cells/mm^3. Most of them (29/32) had blasts in peripheral blood. Most common type of AML is AML M5 (13/32). Acute promyelocytic leukemia (APML) was noticed in 6. M1and M4 are 2 each. M2 and M7 were 6 and 3 respectively. Cytogenetics performed in all. All APML's, t (15,17) positive; 3 were t (8,21) (one M1, one M2, one M5); 2 were Inv 16 (one M5 and one M4), 2 had t (9,22) (one M5, one M7) and 1 case is MLL (M7) positive. Karyotype t (x,3) was noted in one case. 3 were CNS positive (1 Facial nerve palsy, 1 CSF positive and 1 Cerebral deposits). All received chemotherapy as per UK AML 15 protocol,30/32 went into remission after induction except 2 AML- M7 cases. Post treatment 5 had relapse, all within 6 months off treatment and all died with progressive disease. Out of 5 relapses one was M5 with t (9,22), one M5 with normal genetics, one was M1 with CNS positive disease, One M7 with t (X,3) & one M2 with normal genetics. Two expired with febrile neutropenia. Overall 23/32 (71.87%) are alive&well. Out of 23, 13 are 2.5 to 3.6 years off treatment & 10 are 1 to 2 years.
Conclusions: With good supportive care overall survival rates of AML can improve even in developing countries.

EP-328

ORBITAL MYELOID SARCOMA IN ACUTE MYELOID LEUKEMIA: EXPERIENCE OF A TERTIARY CARE CENTRE IN INDIA

J. Srirambhatla[1], T. Kannan[1], S. Sinha[1], R. Parimkayala[1]

[1]Medical Oncology, MNJ Institute of Oncology, RCC, Hyderabad, India

Objectives: Orbital myeloid sarcoma is a rare pediatric malignancy. We woould like to review the clinico epidemiological profile of children presenting with orbital myeloid sarcoma at diagnosis or antedating a leukemia.
Methods: The clinico epidemiological data of children with a diagnosis of orbital myeloid sarcoma registered in our centre from jan 2012 to dec 2012 was collected retrospectively.
Results: There were 8children with orbital myeloid sarcoma amongst the 50 new cases of acute myeloid leukemia. Leukocytosis (>50,000) was noted in 6 (75%). Acute myeloid leukemia (AML) occurred concurrently in 6 (75%) and antedated in 2 (25%). AML M2 in 4 (50%), AML M1 and AML M4 in one each and AML undifferentiated in 2 (25%) were noted. Complete remission was achieved in 6 (75%) while progression was noted in 2 (25%). Relapse of the leukemia was noted in 2 children within 6m. At the end of 1y 4 (50%) children are alive.
Conclusions: AML M2 is commonly associated with orbital myeloid sarcoma in children.

EP-329

OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKEMIA IN MALAYSIA

K.H. Teh[1], E.J. Abdul Rahman[1], B. Menon[1], H. Mohd Ibrahim[1], M. Mohamed[1]

[1]Paediatrics, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia

Objectives: The aim of this study was to review the treatment outcome of children diagnosed with Acute Myeloid Leukemia (AML) treated with a modified UK MRC AML 12 protocol in a middle income country.
Methods: A retrospective review of all patients diagnosed with AML between 2000 till 2011 treated in Hospital Kuala Lumpur was made. Patients less than 1 year old were excluded. Patients with Down Syndrome, chronic myeloid leukemia in acute myeloid blast crisis, transient myelodysplasia of Down Syndrome and juvenile myelomonocytic leukemia were excluded.
Results: 154 patients were identified. One patient refused treatment. Four patients died of severe bleeding before treatment. One patient abandoned treatment and defaulted follow up after the first course. Of the 149 patients who received treatment, 117 (79%) achieved remission. Ten patients (7%) died within 30 days of diagnosis - six due to severe sepsis and four due to uncontrolled bleeding. Fifteen patients (13%) died of sepsis in remission. There were 36 relapses (31%). The estimated 10 year event free survival (EFS) & overall survival (OS) was 31.7 +/- 5% and 50.3 +/- 5% respectively. Segregation of patients into 3 different time periods (2000 – 2004 [period A], 2004 – 2008 [period B], 2009 – 2011 [period C]) showed an improvement in EFS with the introduction of Amsacrine in period C. The estimated 2 year EFS were 35 +/- 6.3% [period A], 30.7 +/- 6.1% [period B] and 67.9 +/- 11.2% [period C] respectively. These differences were only partially explained by the differences in septic death (21% [period A], 10% [period B], 4% [period C]. Autologous / allogeneic haematopoietic stem cell transplantation (HSCT) performed on 34 patients enhances their survival.
Conclusions: Survival of children with AML had improved following adoption of regimes used in developed countries and improvement in supportive care.

EP-331

RESULTS OF AIDA-BASED TREATMENT FOR CHILDREN WITH NEWLY DIAGNOSED ACUTE PROMYELOCYTIC LEUKEMIA - A SINGLE BRAZILIAN-CENTER EXPERIENCE

R.A.P. Teixeira[1], V.M.G. Jardini[1], W.O. Sanglard[1], C.R. Costa[1], T.A. Teles[1], M.M. Silva[1]

[1]Pediatria, Centro de Tratamento Infantojuvenil Fabiana Macedo de Morais (CTFM-GACC), São José dos Campos, Brazil

Objectives: To describe the results of AIDA-based treatment for children with newly diagnosed Acute Promyelocytic leukemia.
Methods: Twenty newly diagnosed children with Acute Promylocytic Leukemia (APL) were treated at *Centro de Tratamento Infanto Juvenil Fabiana Macedo de Moraes* (CTFM-GACC) from December/2001 to January/2013 (13M:7F, median age 111.5 months). 20/20 were analyzed by PCR or cytogenetics regarding the presence of *PML-RARA/t (15;17)*, 18/20 (82%) being positive, and two negative but with isochromosome 17. All of them, were initially treated with all-tran-retinoic acid (ATRA) 45mg/m^2/day from the first day maintained throughout the initial 90 days+ Idarrubicin (IDA) 5 mg/m^2 (4 doses), being added when fibrinogen level became stable without any hemorrhagic manifestation Intensification with IDA and Mitoxantrone plus an additional year of maintenance with 6 mercaptopurine/ Methotrexate backbone and ATRA, every 3 months.
Results: Median leukocyte count at diagnosis was 3,550/mm^3 (1,400 - 43,500/mm^3) and median platelets count 18,500/mm^3 (6,000-70,000/mm^3), 5/20 were high risk patients (leukocyte >10,000/mm^3 and platelets < 40,000/mm^3). 6/20 died, 2 with early hemorrhagic events, one with thromboembolic complications at diagnosis, 2 due to refractory leukemia and one after an early relapse; 3/6 of deaths were in the high risk group. The two patients with isochromosome 17 treated initially with ATRA, did not respond to it. Only one PM/RARA positive patient had no response to ATRA+ IDA and was resistant even with the use of Arsenic Trioxide (ATO), dying of sepsis and pulmonary bleeding.
Conclusions: Hemorrhagic disturbances remain a particular adverse event during the initial treatment of APL. Patients with a high leucocyte count and a low platelet level had the worse prognosis; prompt introduction of ATRA at any APL suspicion is crucial for a better outcome and, finally, we want to point out that the two patients who had isochromosome 17q and PML/RARA negative gene fusion did not respond to ATRA.

EP-332

INDUCTION TREATMENT RESULTS WITH THE NATIONAL PROTOCOL IN ACUTE MYELOID LEUKEMIA AT NATIONAL INSTITUTE OF PEDIATRICS IN MEXICO

R. Cárdenas-Cardós[1], M. Zapata-Tarrés[1], L. Velasco-Hidalgo[1], R. Rivera-Luna[1]

[1]Oncology, Instituto Nacional de Pediatría, Mexico City, Mexico

Objectives: Results of treatment of children with acute myeloid leukemia (AML) is a challenge. In low income countries toxicity of these regimens is the main cause of death. We present promising results of a cohort of patients under 18 treated in a single institution.
Methods: A longitudinal clinical study was performed from January 2005 to September 2013. Nineteen cases of patients with AML were included. All patients received ADE as induction therapy (cytarabine 100mg/m2 q12h for 20 doses, daunorubicin 50mg/m2 days 1,3,5 and etoposide 100mg/m2 over days 1 to 5 and Medical Research Council (MRC) maintenance with four cycles. M3 AML were treated with ATRA and MRC protocol.
Results: Median age was 124 months (21-210). 10.5% were M0, 15.5% M2, 21.1% M3, 26.3% M4, 10.5% M5, 15.8% M7. Two patients had inv16, two t (15;17), two t (8;21) and one 11q23. 42.1% had extramedular infiltration at diagnosis. Three patients needed one cycle for remission, ten needed two cycles and 5 three. The remission rate was 100%. Patients had between one and 9 infectious events, none fatal. One patient abandoned two die of hemorrhage and one of septic shock. Four patients had bone marrow relapse and were rescued with progenitor cell transplantation. Analyzing non-M3 patients overall survival was 77.4% at 100 months.
Conclusions: As an oncology department we have a selection bias with almost half of patients with extramedular infiltration. However, ADE induction therapy showed improved results in overall survival compared with other standard regimens. This regimen can be useful in other developing countries.

EP-333

DIFFERENCES OF SOMATIC MUTATIONS AND GENE EXPRESSION IN BLASTS OF TRANSIENT LEUKEMIA AND ACUTE MYELOID LEUKEMIA OF DOWN SYNDROME

J. Chen[1], F. Yousif[2], T. Beck[2], J. McPherson[2], J. Hitzler[3]

[1]The Developmental & Stem Cell Biology, The Hospital for Sick Children, Toronto, Canada; [2]Informatics and Bio-computing, Ontario Institute of Cancer Research, Toronto, Canada; [3]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada

Objective: Transient leukemia (TL) occurs in 30% of newborns with Down syndrome (DS) and typically resolves spontaneously. Approximately 20% of infants with TL go on to develop acute myeloid leukemia of DS (DS-AML) within the first four years of life. The blasts of both TL and DS-AML harbour somatic mutations of *GATA1*. The objective of this study was to identify genetic events associated with the progression of TL to DS-AML.
Methods: Leukemic blasts of TL and DS-AML and normal T lymphocytes were sorted from blood and bone marrow samples of five patients who successively developed both disorders. In addition, blasts of one patient with subsequent relapse of DS-AML were analyzed. Gene expression and mutational spectrum were determined by RNASeq and exome sequencing.
Results: TL blasts harbored fewer mutations than those of DS-AML. Mutations of cohesin and RAS pathway genes were identified in a subset of DS-AML but not TL. In the patient with relapse, different cohesin gene mutations were detected at initial diagnosis of AML and relapse; a minor clone present at initial diagnosis of AML emerged as the predominant clone at relapse. Differential gene expression was predominantly higher in TL blasts compared to DS-AML. It included genes encoding chemokines and related to IL1 and TGF(signaling. The latter result is consistent with the occurrence of frequently fatal organ fibrosis in TL.
Conclusions: The pathogenic sequence culminating in DS-AML is initiated by a unique event in children with DS (somatic mutation of *GATA1*). In contrast, events associated with the transformation of TL to DS-AML resemble progression factors also found in non-DS AML.

NEUROBLASTOMA

EP-334

ACETYL L CARNITINE INTERFERES WITH ANTITUMOR EFFECT OF CISPLATIN

S. Aktas[1], Z. Altun[1], A. Pamukoglu[1], E. Kolatan[1], P. Ercetin[1], D. Dursun[1], E. Serinan[1], B. Demir[1], O. Yilmaz[2], N. Olgun[1]

[1]Institute of Oncology, Dokuz Eylul University, Izmir, Turkey; [2]Institute of Health Sciences, Dokuz Eylul University, Izmir, Turkey

Objectives: Acetyl-L-carnitine (ALCAR) is a well known antioxidant. In our previous studies, we showed protective effects of ALCAR against cisplatin induced neuro, oto and nephrotoxicities in vitro and in vivo experimental models. The aim of this study is to investigate whether ALCAR interferes with antitumor effect of cisplatin against neuroblastoma.
Methods: Atymic male nude mice, 20 gram 6 week of age (7 animals per group), were subcutaneously injected with 10 million C1300 neuroblastoma cells. The study consisted of four groups: Control, ALCAR, Cisplatin, ALCAR+Cisplatin group). Tumor size reached 1-2 cm in 10 days. Intraperitoneal injection of isotonic solution in control group, 16mg/kg Cisplatin, 100 mg/kg ALCAR and combination at the same time were applied. Animals were sacrified at day 10. Antitumor activity was evaluated by gross measurement of tumor, microscobic evaluation of tumor necrobiyosis and apoptosis evaluation.
Results: In control and ALCAR tumor group with no agent given, tumor cells were alive with minimal necrosis and apoptosis. There was prominent mitosis. In cisplatin group, tumor showed prominent necrosis and necrobiosis with prominent apoptosis. In ALCAR+cisplatin group, tumor showed lesser necrosis compared with cisplatin group.
Conclusions: In this animal model in vivo study, we showed that ALCAR given at the same time with cisplatin interferes with its antitumor activity against neuroblastoma. Using ALCAR as a protective agent against cisplatin induced toxicities should be very well questioned.
Acknowledgement: This study was supported by Turkish Society of Pediatric Oncology.

EP-335

MOLECULAR PROFILE OF NEUROBLASTOMA IN TURKEY ON BEHALF OF THE TURKISH SOCIETY OF PEDIATRIC ONCOLOGY

S. Aktas[1], B. Demir[1], P. Ercetin[1], Z. Altun[1], N. Olgun[1]

[1]Institute of Oncology, Dokuz Eylul University, Izmir, Turkey

Objectives: Neuroblastoma is the most common pediatric neuroendocrine tumor arising from the neural crest of sympathetic nervous system. Neuroblastic tumors exhibit extreme heterogeneity, which affects the outcome of the therapy differently. Neuroblastoma is mainly categorized into three risk levels as low, intemediate and high. The molecular evaluation has come into prominence for the determination of the risk categories of patients. In this study, the results of the molecular analysis performed within the scope of the TPOG (Turkish Society of Pediatric Oncology) protocol were evaluated.
Methods: We compiled molecular analysis of 189 patients diagnosed/pre-diagnosed with Neuroblastoma from oncology centers of Turkey's various government, university and private hospitals. We have analysed Nmyc amplification, 1p LOH, 11q del and 17q gain status for these patients with real-time PCR analysis and DNA ploidy index with flow cytometer.
Results: Molecular analysis of the 189 patients were evaluated. The age interval of these patients were between 1- 168 months. The average age was 36.34 ± 34.75. The percentage of N-myc positivity was 14.9%, while for 1p LOH, 11q del and 17q gain the percentage of positivity were 36%, 16.9% and 39.2%, respectively. DNA ploidy index was DPI >1 for 21.4% of the analysed samples. Positive correlation between Nmyc amplification and 1p LOH were found ($p = 0.001$), while no correlation was found among 11q deletion, 17q gain and Nmyc amplification. 67 samples out of 189 were negative for all of the four genetic parameters.
Conclusions: Our results show that, there exists a positive correlation between Nmyc amplification and 1p LOH, which is consistent with several previous studies. Almost 40% of 189 samples were shown to be positive for 17q25 gain, which is the mostly seen abberation among the samples evaluated.

EP-336

SURGICAL COMPLICATIONS AND LONG-TERM OUTCOME OF PERI-VASCULAR ABDOMINAL NEUROBLASTOMAS: A SINGLE INSTITUTION STUDY

L. Ali[1], F. Guérin[1], S. Branchereau[1], G. De Lambert[1], C. Baujard[2], L. Chevret[2], F. Gauthier[1], H. Martelli[1]

[1]Pediatric Surgery, Bicetre Hospital, Paris, France; [2]Anesthesia, Bicetre Hospital, Paris, France

Objectives: Because of their anatomic relations, surgical excision of peri-vascular abdominal neuroblastomas (PVAN) is a challenging procedure. The aim of our study is to evaluate complications and long-term outcome of patients operated on for such tumours in a single institution.
Methods: From 1997 to 2012, 45 patients were operated on for neuroblastoma encasing abdominal aorta, main abdominal arteries and renal pedicle. Preoperative chemotherapy was given to all patients according to current ongoing protocols. According to the International Neuroblastoma Risk Group (INRG) classification, 21 patients were L2 (46%), 21 were metastatic M (46%) and 3 were Ms (7%). We assessed perioperative and long-term outcome.
Results: Median age at surgery was 4 years (5.5months-15years). Two patients underwent staged procedures. Excision was complete for 25 (56%) patients. We performed 13 planned nephrectomies. Operative complications consisted in 8 vascular adverse events in 8 patients, including: 1 accidental injury of superior (SMA) and 1 of inferior mesenteric artery, 3 spasms and 1 injury of renal artery, 1 spasm of hepatic artery, and 1 injury of renal vein. Post-operative complications occurred in 3 patients: 1 died of mesenteric ischemia (after accidental injury of the SMA), 1 patient had kidney atrophy and 1 patient with thrombosis of the celiac trunk and renal vein, responsible for hemodynamic instability, acute liver ischemic necrosis and renal insufficiency finally recovered without any sequelae. Five patients developed a temporary ascitis and 2 had bowel obstruction. At a median follow-up of 27 months [5months-12years] 31 patients (69%) were alive, 9 patients died of local recurrence (in 5, initial resection was macroscopically incomplete) and 4 died of metastatic recurrence.
Conclusions: Surgery for perivascular abdominal neuroblastoma is challenging and bears potential life threatening complications, mainly vascular. Most of them could be prevented and/or reversed by an appropriate peri and post-operative management of hemodynamic changes.

EP-337

HINGE LAMINOPLASTY IS A USEFUL TECHNIQUE FOR URGENT DECOMPRESSION OF NEUROBLASTOMA CAUSING SPINAL CORD COMPRESSION IN APPROPRIATELY SELECTED CASES

H. Bishop[1], G. Anichini[2], R. Vashu[2], P. Bhatt[2]

[1]Paediatric Oncology, Royal Aberdeen Childrens Hospital, Aberdeen, United Kingdom; [2]Neurosurgery, Aberdeen Royal Infirmary, Aberdeen, United Kingdom

Objectives: To highlight the utility and safety of hinge laminoplasty as a technique for urgent decompression of Neuroblastoma causing spinal cord compression (SCC), in appropriately selected cases.
Methods: In a 12 month period, 3 children presented to the paediatric oncology service of Royal Aberdeen Children's Hospital with a diagnosis of Neuroblastoma with SCC. The first, aged 16 months, with a 4 month history of grade 4 weakness of the lower limbs, had urgent hinge laminoplasty, with high dose Dexamethasone and then emergency Carboplatin and Etoposide. The second, aged 8 months, with a 10 day history of grade 4 weakness of the lower limbs and constipation, had emergency Carboplatin and Etoposide with Dexamethasone, followed by urgent hinge laminoplasty the following day. The third, aged 8 weeks, presented with an abdominal mass, and MRI revealed SCC. There was constipation but no weakness and treatment was with emergency Carboplatin and Etoposide with Dexamethasone.
Results: The first patient, 14 months after diagnosis, is in remission and walks with a frame, with power 4/5 in the lower limbs. The second, 8 months after diagnosis, is in remission with no neurological deficit. The third, 2 months from diagnosis, remains on treatment, with no neurological deficit.
Conclusions: Neuroblastoma with SCC is associated with a relatively good prognosis oncologically, but neurological prognosis varies with severity of motor deficit at presentation[1]. Concerns about symptomatic deterioration, scoliosis, and compromised ability to deliver chemotherapy have caused early decompression to fall out of favour. We show that, in appropriately selected cases, hinge laminoplasty can be an effective approach to urgent decompression, and need not compromise, nor be compromised by, chemotherapy delivery. It also carries a smaller risk of scoliosis[2].
References
1. Thorsten S *et al*. **Dev Med Chil Neurol.** 2012;54 (4) :347-52.
2. Amhaz HH *et al*. **Pediatr Neurosurg.** 2009;45 (2) :151-4.

EP-338

A ROLE FOR INTERLEUKIN-7 IN HUMAN NEUROBLASTOMA TUMOURIGENESIS

L. Prasad[1], A. Roberts[2], T. Chowdhury[2], L. Lau[2], A. Charlton[1], T. Henwood[1], N. Graf[1], S. Arbuckle[1], D. Catchpoole[2]

[1]Histopathology Department, The Children's Hospital at Westmead, Westmead, Australia; [2]Tumour Bank - Children's Cancer Research Unit, The Children's Hospital at Westmead, Westmead, Australia

Objectives: Interleukin-7 (IL7) is a cytokine that has neurotrophic effects during development of embryonic nerve cells leading to neuronal differentiation (Michaelson etal Developmental Biology, 179, 251-263, 1996). IL7R(sequence variations are pathogenic for the neurological disorder, multiple sclerosis (MS). Neuroblastoma (NB), the most common extracranial childhood solid tumour, shows remarkable heterogeneity with respect to neuronal differentiation. Microarray studies indicate IL7 has significantly increased expression in good prognosis NB tumours with treatment outcomes. We present several other lines of evidence that implicate altered IL7 signalling in NB development.
Methods: The expression of IL7, IL7 receptor (IL7R() and its downstream signalling proteins JAK1, JAK3, STAT5 were analysed using immunohistochemistry in 100 stroma poor NB tumours and 24 with stroma rich ganglioneuroma (GN). Their expression was correlated to the level of S100 (stromal marker), NB84 (neuroblast marker) and CD99 (negative marker).
Results: IL7 protein expression was positive exclusively in Schwannian stroma in favourable and unfavourable histology tumours. Specialised digital image analysis determined the expression of IL7, IL7R(, JAK1, STAT5 and pSTAT5 were all increased in GNs compared to NBs. Expression of pStat5 was found to be significantly reduced (t-test, $p = 0.00013$) in stroma poor NB compared to GN. Like the undifferentiated tumours, a NB cell line panel

demonstrated uniform expression of IL7R(, very low expression of Stat5 and the absence of pStat5. The IL7R(partner, IL2R(was depleted in two cells lines. Ion Torrent next generation sequencing of the coding regions of 10 key IL7 signalling pathway genes in 13 NB cell lines identified non-synonymous sequence variations in IL7R(that are known to be associated with MS (eg T244I) (Zhang *etal* Molecular Biology Report, 38:5079-5084, 2011).
Conclusions: Our findings implicate IL7 within the Schwannian stroma of the tumour architecture as having a paracrine signalling effect on neighbouring neuroblasts, which in turn have varying capacity to differentiate in response.

EP-339

IN VIVO EFFECT OF SANGUINARINE ON NEUROBLASTOMA

E. Cecen[1], S. Aktas[2], A. Pamukoglu[2], E. Kolatan[3], P. Ercetin[2], B. Demir[2], O. Yilmaz[3], N. Olgun[4]

[1]Pediatric Oncology, Adnan Menderes University School of Medicine, Aydin, Turkey; [2]Basic Oncology, Dokuz Eylul University Institute of Oncology, Izmir, Turkey; [3]Laboratory Animal Science, Dokuz Eylul University School of Medicine, Izmir, Turkey; [4]Pediatric Oncology, Dokuz Eylul University Institute of Oncology, Izmir, Turkey

Objectives: Neuroblastoma is among the most common extracranial solid cancer in children and originated from primordial crest. Approximately half all patients with neuroblastoma are diagnosed with high-risk poor prognosis disease, and novel therapies are needed.
Sanguinarine is a benzophenanthridine alkaloid and has anti-microbial, anti-oxidant and anti-inflammatory properties. We had previously showed antitumor effect of sanguinarine against neuroblastoma in cell culture studies. The aim of this study is to determine *in vivo* effect of sanguinarine against neuroblastoma.
Methods: Atymic male nude mice, with a mean weight of 20 ± 3 g and 6 weeks of age (7 animals per group), were subcutaneously injected with 10 million C1300 neuroblastoma cells. The study consisted of three groups: Control, sanguinarine and cisplatin). Tumor size reached 1-2 cm in 10 days. Intraperitoneal injection of isotonic solution in control group, 16mg/kg cisplatin, 15 mg/kg sanguinarine were applied. Animals were sacrified at day 10. Antitumor activity was evaluated by gross measurement of tumor, microscobic evaluation of tumor necrobiosis and apoptosis evaluation.
Results: In control tumor group with no agent given, tumor cells were alive with minimal necrosis and apoptosis. There was prominent mitosis. In cisplatin group, tumor showed prominent necrosis and necrobiosis with prominent apoptosis. In sanguinarine group, tumor revealed necrosis and apoptosis as much as prominent compared with cisplatin group.
Conclusions: In this animal model *in vivo* study, we demonstrated that sanguinarine compared with with cisplatin has antitumor activity against neuroblastoma. Further studies are needed to determine the inhibitory effects of sanguinarine on tumor growth in experimental tumor models. Our study suggest that sanguinarine is a likely candidate for further evaluation in neuroblastoma treatment.

EP-340

THE ROLE OF NAMPT-NAD-SIRTUIN PATHWAY IN NEUROBLASTOMA CHEMORESISTANCE

B. Cuglievan[1], F. Hernandez[2], G. De Angulo[3], S. Vanni[4], R. Graham[5]

[1]Pediatrics, Miami Children's hospital, Miami, USA; [2]Pediatric Hematology Oncology, MD Anderson Cancer Center, Houston, USA; [3]Pediatric Hematology Oncology, Miami Children's Hospital, Miami, USA; [4]Neurosurgery Department, University of Miami, Miami, USA; [5]Neurosurgery Department-Neruoblastoma, University of Miami, Miami, USA

Objectives: Chemoresistance is a major obstacle in the successful treatment of high-risk neuroblastoma (NB). Sirtuins (SIRTs) are NAD^+ dependent deacetylases which are activated during periods of stress leading to cellular protection. In cancer, the activity of SIRTs is largely dependent on the NAD+ salvalge pathway, of which Nampt is a key enzyme. Inhibiting NAD+ metabolism or downstream targets may represent a novel way to enhance cancer chemotherapeutics.
Our objective is to determine the therapeutic potential of SIRT and NAMPT inhibition as a novel method to increase NB chemosensitivity to AKT pathway inhibition.
Methods: Cell viability was determined by MTS and LDH assay and cell signaling pathways were evaluated by western blot analysis. NB cells were treated with perifosine and everolimus to inhibit the PI3K/AKT/MTOR pathway.
Results: Both sirtinol (SIRT1 and 2 inhibitor) and APO866 (Nampt inhibitor) induced dose dependent NB cell death. Combined SIRT and AKT pathway inhibition induced PARP cleavage and NB1691 cell death (viability; vehicle $= 100 \pm 1.9\%$, sirtinol $= 70 \pm 1.9\%$, perifosine $= 76 \pm 1.9\%$, sirtinol+perifosine $= 28 \pm 0.9\%$, everolimus $= 87 \pm 3.2\%$, sirtinol+everolimus $= 23 \pm 2.2\%$). Inhibiting SIRTs by targeting NAD production with APO866 (10nM) also significantly increased NB cell death in response to AKT pathway inhibitors.
Conclusions: Our data indicates that SIRTs regulate cell survival following chemotherapeutic insult. Most SIRT inhibitors are in pre-clinical trials, however Nampt inhibitors are in clinical trials and could potentially be used to inhibit SIRTs thereby enhancing the therapeutic effect of AKT pathway inhibitors as well as other chemotherapeutic agents. Here we provide novel insights in role of SIRTs in NB and suggest a new therapeutic regimen for a cancer with minimal survival.

EP-341

PERSISTENT IODINE-123 (123I) METAIODOBENZYLGUANIDINE (MIBG) SPOT IN LONG TERM FOLLOW-UP METASTATIC NEUROBLASTOMA OVER YEAR OF AGE

M.A. De Ioris[1], M.C. Garganese[2], M.D. De Pasquale[1], M. Pizzoferro[2], A. Crocoli[3], F. Del Bufalo[1], A. Serra[1], A. Mastronuzzi[1], A. Castellano[1], F. Locatelli[1]

[1]Hematology/Oncology, Pediatric Hospital Bambino Gesu', Roma, Italy; [2]Nuclear Medicine, Pediatric Hospital Bambino Gesu', Roma, Italy; [3]Surgery, Pediatric Hospital Bambino Gesu', Roma, Italy

Objectives: The iodine-123 (^{123}I) metaiodobenzylguanidine (MIBG) scintigraphy is a useful tool for diagnosis, staging and evaluation of response to treatment in neuroblastoma (NB). Aim of this study is to report on features and implications of a residual ^{123}I-MIBG uptake in metastatic NB long-term survivors.
Methods: We retrospectively reviewed a series of metastatic NB over 1 year of age enrolled in two consecutive local protocols with at least 3 years follow-up. Medical records were reviewed to check patients with persistent MIBG spots. All MIBG scans were reviewed.
Results: 58 metastatic NB patients treated between July 1996 and August 2009 were enrolled in this study. All but one had ^{123}I-MIBG positive disease at diagnosis. Out of 17 survivors, 3 patients presented a persistent and stable ^{123}I-MIBG uptake at 195, 130 and 129 months since diagnosis, respectively. All three patients were younger than 24 months at diagnosis, none had MYCN amplification and all achieved a partial response/very good partial response at the end of the induction phase and before high dose chemotherapy.
Conclusions: A residual and persistent MIBG uptake is reported in few metastatic NB patients younger than 24 months and without MYCN amplification with no impact on survival. These spots may reflect a residual differentiating disease. Further analyses on large series are needed to clarify the implication of residual uptake in a sub-group of metastatic NB, both to modulate treatment and MIBG timing.

EP-342

TREATMENT OF NEUROBLASTOMA WITH AN TOPOTECAN REGIMEN

K. Dong[1], X. Cui[1], K.A.I. Li[1], X. Xiao[1], L.I.A.N. Chen[2]

[1]Surgery, Children's Hospital of Fudan University, Shanghai, China; [2]Pathology, Children's Hospital of Fudan University, Shanghai, China

Objectives: To summarize our experience on the treatment of neuroblastoma with an topotecan regimen.
Methods: Sixty-eight newly diagnosed patients with neuroblastoma were included in this study from January 2007 to December 2012. The age of the patients was from 4 days to 108 months. The diagnosis was made by imageology, bone marrow biopsy and postoperative pathological diagnosis. The staging of patients was determined by INSS system as follows: 7 cases in stage I (10.3%), 14 in stage II (20.6%), 11 in stageIII (16.2%), 23 in stage IV (33.8%) and in stage IVs (19.1%). The treatment scheme was according to a protocol of topotecan regimen.
Results: The remission rate after the new assistant chemotherapy was 60.7% (17/28). Gross total resection rate of this group was 71.7%. The overall survival rates of 2 and 5 years in this group were 75.6% and 62.1% respectively. The overall survival rates of 2 and 5 years in patients with gross total resection were 83.3% and 70.2% respectively. 2 years event-free survival rate is 67.3%, 5 years event-free survival rate is 57.4%. Age of EFS (Event-Free Survival) ROC (receiver operating characteristic) curve analysis showed the best discrimination threshold was 867 day. The sensitivity and specificity were 75.00% and 66.67% respectively. Area under the curve was 0.713.

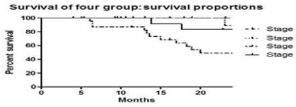


FIGURE 1 Two-year overall suivival rate of the patients according to the tumor stages.

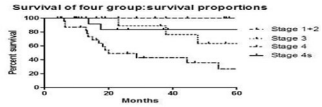


FIGURE 2 Five-year overall suivival rate of the patients according to the tumor stages.

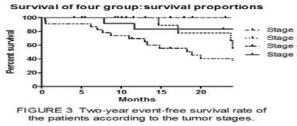


FIGURE 3 Two-year event-free survival rate of the patients according to the tumor stages.

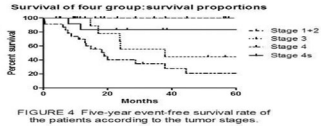


FIGURE 4 Five-year event-free survival rate of the patients according to the tumor stages.

Conclusions: This study showed the treatment of neuroblastoma according to the America COG protocol is better than that of the Japanese Study Group Protocol. Patients in the low risk group with no MYCN amplification can undergo surgery alone, and achieve a favorable prognosis. Through the 68 cases of patients with age of EFS ROC curve analysis, we obtain the best discrimination threshold, 867 day, is much longer than the data we used before.

EP-343

STAGE IV NEUROBLASTOMA: EXPERIENCE FROM A TERTIARY CARE CENTER IN INDIA

T. Durugappa[1], N.I.T.A. Radhakrishnan[1], D. Thakkar[1], S. Aggarwal[1], M. Kalra[1], A. Sachdeva[1]

[1]Pediatric Hematology Oncology, Sir Gangaram Hospital, New Delhi, India

Objectives: Stage IV neuroblastoma is a systemic disease that requires multimodal intensive treatmentour objective was to study the clinical profile and outcome of Stage IV neuroblastoma diagnosed at our institution.
Methods: Retrospective analysis of data of patients diagnosed with Stage IV neuroblastoma over a period of 10 years (2003-2013). All patients were treated on uniform induction protocol consisting of 8 cycles OPEC/OJEC chemotherapy. After 4 cycles, if there was no evidence of metastatic disease and the primary was surgically amenable, resection/debulking of the was attempted. At the end of induction therapy, myeloablative chemotherapy with autologous stem cell rescue followed by local therapy was given. Cis-retinoic acid was given to few patients at completion of treatment.
Results: Total of 27 patients had stage IV neuroblastoma out of 40 patients diagnosed. Majority were males (n = 18, 66.6%) and mean age at diagnosis was 3.5 years (range 0.17 to 7.2). Fever and abdominal distension were the most common (21/27) presenting symptoms. 16 of the patients had primary tumour in suprarenal region, 4 in retroperitoneal region, 2 in posterior mediastinum. Skin involvement seen in 2 patients. Bone marrow was the most common metastatic site (15/27) followed by liver (11/27) and Bone (9/27). Urinary VMA was elevated in 20 patients (74%). N myc done in 4 patients, MIBG scan done in 5, PET CT done in 10. 5 children underwent ABMT of which one expired during therapy, 2 had CNS relapse and expired. Total of 14 children expired, 8 lost to follow up and 4 children abandoned treatment, 3 children are receiving treatment at present.
Conclusions: The survival of patients with stage IV neuroblastoma is dismal. Stem cell rescue has improved survival in recent times which is yet to be supported by strong evidence in Indian scenario. Indian data on Neuroblastoma stage IV outcome is lacking and needs further study.

EP-344

NEURONAL LEUCINE RICH REPEAT PROTEIN1 (NLRR1) SUPPRESSES NGF/TRKA SIGNAL IN NEUROBLASTOMA

M. Fukuda[1], A. Takatori[1], Y. Nakamura[2], A. Nakagawara[1]

[1]Children's Cancer Research Center, Chiba Cancer Center Research Institute, Chiba, Japan; [2]Division of Innovative Cancer Therapeutics, Chiba Cancer Center Research Institute, Chiba, Japan

Objectives: NLRR1, a type 1 transmembrane protein, is highly expressed in unfavorable neuroblastoma (NB). Previously we reported that NLRR1 accelerated EGF and IGF signals and enhanced cell proliferation in NB. However, the functional role in other receptor tyrosine kinases including TrkA was elusive. TrkA is associated with favorable outcomes of NB and enhances cell survival and differentiation upon nerve growth factor (NGF) treatment in NB cells. In the present study, we investigated the functional interactions between NLRR1 and TrkA.
Methods: The mRNA expression of NLRR1 and TrkA was evaluated by quantitative real-time PCR (qPCR) in primary NB samples. NGF/TrkA signal was investigated by western blot analysis in NLRR1-expressing NB cells.
Results: In NB clinical samples, we found that the mRNA expression of *TrkA* was inversely correlated with the expression of *NLRR1* (chi-square test, $p = 0.04$). In TrkA-stably expressing SH-SY5Y cells, the cell growth in NGF-containing medium was reduced compared to control cells. Upon NGF treatments, levels of phosphorylated TrkA and ERK, one of the downstream molecules of TrkA, decreased in NLRR1 expressing cells.
Conclusions: Our data suggest that NLRR1 and TrkA show the mutually exclusive expression pattern in NB clinical samples and that NLRR1 contribute to aggressiveness of NB in part by suppressing TrkA signals.

EP-345

DECREASE TREATMENT OF NEUROBLASTOMA AND MULTIDISCIPLINARY CARE

H. Halalsheh[1], T. Ismael[1], K. Ghandour[2], M. Alboheisi[3], I. Sultan[1]

[1]Pediatric, King Hussein Cancer Center, Amman, Jordan; [2]Pediatric surgery, King Hussein Cancer Center, Amman, Jordan; [3]Nursing, King Hussein Cancer Center, Amman, Jordan

Objectives: The treatment of low and intermediate risk (L/IR) neuroblastoma needs judicious use of different modalities. This group of patients is typically over treated when their care is scattered. We report our experience with emphasis on the role of multidisciplinary care. We also propose an algorithm for management in countries with limited resources.
Methods: We conducted a retrospective analysis of children with L/IR NB who presented from Jan2003 until Dec2009. Patients' characteristics, treatment modalities and outcome were analyzed. All cases were discussed in multidisciplinary clinic that included at least a pediatric oncologist, a radiologist, a pediatric surgeon and a radiation oncologist
Results: We identified 40 patients (21 males) who presented with L/IR NB to our center (25 LR). The median age at diagnosis was 9 months (range, 2 to 48). Stage distribution was as follows: stage I, 8; stage II, 14; stage III, 7 and stage IVs, 10 patients. MYCN was amplified in 3 patients with stage I. Gross macroscopic resection was achieved in 21patients (out of 26 who had surgery). Chemotherapy was given to 20 patients (50%) with most of them (15 patients) receiving $\leq$4 cycles. The 5-year EFS was $92 \pm 4.4\%$ and the 5-year OS was $98 \pm 2.5\%$. Three patients died; two relapsed 15 and 39 months after diagnosis and died of disease; the third patient died of hemorrhage and renal shut down after surgery. Another patient developed progression of the residual mass 47 months after diagnosis and was lost for follow up.
Conclusions: For children with non-high risk neuroblastoma in developing countries there is a possibility for treatment reduction with good outcome. Treatment can be modified through multidisciplinary team discussion. We propose that in countries with limited resources, minimal treatment is provided to all patients with neuroblastoma unless more advanced therapies are available, including stem cell transplantation and immunotherapy.

EP-346

SYNERGISTIC ANTITUMOR INTERACTIONS BETWEEN MK-1775 AND PANOBINOSTAT IN HIGH-RISK NEUROBLASTOMA CELLS

S. Hanmod[1], G. Wang[2], H. Edwards[3], S. Buck[1], Y. Ge[3], J. Taub[2], Z. Wang[2]

[1]Division of Pediatric Hematology Oncology, Children's Hospital of Michigan, Detroit, USA; [2]Department of Pediatrics, Wayne State University School of Medicine, Detroit, USA; [3]Department of Oncology, Wayne State University School of Medicine, Detroit, USA

Objectives: Despite recent advances in treatment regimens, patients with high-risk neuroblastoma have long-term survival rates of <40%. Resistance to the current anti-neoplastic agents continues to be one of the main reasons for treatment failure and progressive disease among this group of patients. Therefore, new agents are urgently needed to improve treatment outcomes for patients with high-risk neuroblastoma. In this study, we utilize the Wee1 inhibitor MK-1775 in combination with panobinostat to determine the antitumor interactions and the underlying molecular mechanisms.
Methods: In vitro cytotoxicities of panobinostat and MK-1775 at clinically achievable concentrations, either alone or in combination, were evaluated in SK-N-AS, SK-N-DZ, and SK-N-BE (2) high-risk neuroblastoma cell lines using MTT assays. The mechanism of antitumor activity was investigated using propidium iodide (PI) staining and flow cytometry analysis to determine apoptosis, as well as Western blotting to assess expression of phosphorylated CDK1/2, CHK1, and H2AX.
Results: Treatment of neuroblastoma cell lines with 500 nM MK-1775 caused growth arrest and apoptosis in SK-N-DZ and SK-N-AS, while it had minimal effect on the SK-N-BE (2) cell line. The combination of panobinostat and MK-1775 resulted in synergistic antitumor interactions in all three of the cell lines tested. MK-1775 treatment in SK-N-BE (2) cells induced increased levels of p-CHK1^{S345}, which could be decreased by the addition of panobinostat. This was accompanied by increased DNA damage and apoptosis. CHK1 selective inhibitor, LY2603618 potently and synergistically enhanced MK-1775-induced proliferation inhibition in the SK-N-BE (2) cells, supporting that CHK1 plays an important role in mediating the synergistic antitumor interactions between MK-1775 and panobinostat.
Conclusions: The combination of panobinostat and MK-1775 has synergistic antitumor activity against high-risk neuroblastoma cell lines and holds promise as a potential effective treatment strategy for the management of high-risk neuroblastoma patients.

EP-347

ADHERENCE TO UK CHILDREN'S CANCER & LEUKAEMIA GROUP GUIDELINES FOR THE MANAGEMENT OF LOW AND INTERMEDIATE RISK NEUROBLASTOMA, 2011-2013

F. Herd[1], K. Wheeler[2], D.A. Morgenstern[3], D.A. Tweddle[4]

[1]Department of Paediatric Oncology, Great North Children's Hospital, Newcastle, United Kingdom; [2]Paediatric Oncology, Oxford Children's Hospital, Oxford, United Kingdom; [3]Department of Paediatric Oncology, Great Ormond Street Hospital, London, United Kingdom; [4]Department of Paediatric Oncology, Northern Institute for Cancer Research Newcastle University, Newcastle, United Kingdom

Objectives: To evaluate how UK children with low (LR) and intermediate risk (IR) Neuroblastoma are managed compared with national CCLG guidelines (v1 August 2011) based on SIOPEN low and intermediate risk Neuroblastoma (LINES) trial.
Methods: CCLG centres were asked if they followed guidelines for LR and IR Neuroblastoma between August 2011-2013. Patient numbers, genetic testing including MYCN and segmental chromosomal abnormalities (SCA), and outcome data for specific subgroups were collected.
Results: All 21 CCLG centres replied describing 80 cases (53 LR, 27 IR). Principally all centres adhered to the guidelines. 74/80 cases were tested for MYCN amplification and SCA either locally or via the central reference facility in Newcastle. LR-:6 LR patients were not biopsied due to co-morbidity, need for emergency chemotherapy, primary surgery or antenatally diagnosed adrenal masses. 38% LR tumours had SCA, 17q gain was the

commonest (13/20). 8 patients had 4s disease without life threatening symptoms, 4 with SCA but 6 received 4-6 cycles of chemotherapy. 12 patients were < 18 months of age with localised, unresectable (L2) tumours and no SCAs, 10 had chemotherapy followed by surgery in 4 cases, and one surgery alone. 11 patients are alive, and one died from disease progression. IR:67% IR tumours had SCA, the commonest was 17q gain (11/17). 12 patients were > 18 months old with L2, undifferentiated tumours, 9 with SCA. All 12 received chemotherapy, but 7/12 surgery, 9/12 radiotherapy and 7/12 retinoic acid. One child is still on treatment, one progressed and died and the remainder are in first remission.
Conclusions: This study shows that all CCLG centres are broadly following the guidelines, but in depth analysis of specific subgroups shows variable adherence. It is important to capture this data as currently the LINES trial is not open in the UK.

EP-348

TUMOR HISTOLOGY FOLLOWING INDUCTION CHEMOTHERAPY AND/OR HIGH-DOSE CHEMOTHERAPY AND ITS IMPACT ON THE OUTCOME OF PATIENTS WITH HIGH-RISK NEUROBLASTOMA

T. Hishiki[1], H. Horie[2], Y. Higashimoto[1], K. Yotsumoto[1], S. Komatsu[1], Y. Okimoto[3], H. Kakuda[3], Y. Taneyamai[3], H. Yoshida[4], J. Iwai[1]

[1]Department of Pediatric Surgery, Chiba Children's Hospital, Chiba, Japan; [2]Department of Pathology, Chiba Children's Hospital, Chiba, Japan; [3]Department of Hematology and Oncology, Chiba Children's Hospital, Chiba, Japan; [4]Department of Pediatric Surgery, Chiba University Graduate School of Medicine, Chiba, Japan

Objectives: In the recent years in Japan, an increasing number of patients with neuroblastoma (NB) are being treated by the "delayed local treatment (DL) " policy, undergoing surgery after the completion of high-dose chemotherapy with hematopoietic stem cell rescue (HDC). We reviewed the histopathological findings of second-look operations, including those of patients treated with DL.
Methods: From 1998 to 2013, 26 patients with high-risk NB underwent second look operation following chemotherapy. Surgery was performed after induction chemotherapy in 17 cases (STD), whereas 9 cases completed induction chemotherapy and HDC before undergoing tumor resection (DL). Treatment effect was measured by the amount of necrosis. The degree of differentiation was assessed according to the international neuroblastoma pathology classification INPC.
Results: Eighty-eight percent of the tumors showed necrosis in more than 1/3 of the specimen. Two DL cases showed complete disappearance of viable tumor cells. Contrarily, seven contained viable neuroblasts at various proportions. However, the amount of necrosis did not affect the prognosis of the patient within the entire cohort. On the other hand, the degree of differentiation within the viable tumor component, evaluated with INPC, had impact on the survival of the patient. Tumors with immature phenotypes (*i.e*. undifferentiated and poorly differentiated NB) at second-look operation had an extremely poor outcome.
Conclusions: Our results support the previous reports advocating that tumors that sustained unfavorable histology after chemotherapy behave aggressively thereafter. To our knowledge, this is the first report focusing on the histological characteristic of tumors resected after the completion of high-dose chemotherapy with hematopoietic stem cell transplantation.

EP-349

THE RESULTS OF APPLYING THE STRATEGY «SEE AND WAIT» IN CHILDREN WITH SUSPECTED NEUROGENIC TUMOR

A. Hizhnikov[1], A. Kazantsev[1], P. Kerimov[1], M. Rubansky[1], O. Kapkova[1], M. Rubanskaya[1], D. Rybakova[1]

[1]Pediatric Oncology, N. N. Blokhin Cancer Research Center Russian Academy of Medical Sciences, Moscow, Russia

Objectives: To determine the role of dynamic monitoring of children with suspected neurogenic tumor
Methods: From 2011 to 2012 8 patients aged 0 to 9 months were monitored with «see and wait» strategy at the Research Institute of Pediatric Oncology and Hematology. In 6 of 8 children neoplasm was localized in the adrenal gland, in the 1 child in the posterior mediastinum, and 1 child in the pelvis. 7 of 8 patients had MIBG-positive tumor. 1 child had MIBG-negative neoplasm, neoplasm was found in the prenatal period, now this child is alive without evidence of disease progression. In 7 children progression of the disease noted by the increase of tumor size between 2 to 6 months from the start of observation.
Results: 7 of 8 children underwent surgical treatment due to disease progression, they are all alive at the momment without evidence of disease progression, the observation period is from 14 to 17 months. 5 adrenalectomies, 1 tumor removal of the posterior mediastinum and 1 tumor removal pelvis were performed. All the children who received surgical treatment, morphologically and molecular genetically proven low-risk neuroblastoma.
Conclusions: For all children with suspected neurogenic tumors at any location, we recommend to perform surgery to determine the diagnosis and strategy for further treatment.

EP-350

GENETIC PREDISPOSITION SYNDROMES IN CHILDREN WITH NEUROBLASTOMA

D. Kachanov[1], G. Muftahova[1], T. Shamanskaya[1], D. Shevcov[1], Y. Olshanskaya[2], N. Semenova[3], G. Novichkova[4], S. Varfolomeeva[4]

[1]Clinical Oncology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [2]Laboratory of Cytogenetics, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [3]genetics, City Clinical Hospital City Clinical Hospital of Pediatrics named after Nil Filatov, Moscow, Russia; [4]Clinical Oncology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia

Objectives: The etiology of neuroblastoma (NB) is not fully understood. The aim of the study was to analyze the incidence and nature of cancer predisposition syndromes in a cohort of patients with neuroblastoma
Methods: During the period from 01.2012 to 01.2014 (25 months) 177 children with NB were treated. Diagnosis of NB were made according to the international criteria. Patients were stratified into risk groups and treated according to NB2004 protocol. Cytogenetic analyses tumor tissue was done by FISH for *MYCN*, 1p and 11q status. Karyotyping was performed for all infants < 1 year. Patient's and familial history were collected. All patients were clinically examined for search of clinical abnormalities. Patients with clinical abnormalities were consulted by medical genetic, chromosomal microarray analysis was done if necessary.
Results: Cancer predisposition syndromes was diagnosed in 3 (1.7%) patients. Case 1: 7-month-old female with left adrenal neuroblastoma, stage 4S had Turner syndrome. The diagnosis was confirmed by karyotyping (45XO). Case 2: 2-month old male with right adrenal neuroblastoma, stage 1 was diagnosed with 1q21.1 microdeletion syndrome. Malformations include heart abnormalities and deafness. Case 3: 38-month-old male was diagnosed with left adrenal neuroblastoma, stage 1 and Sotos syndrome. At the age of 7 days the child was operated because of congenital sacroccocygeal teratoma. Multiple malformations were observed including heart abnormalities, hydrohephalus and myotonic syndrome. In case 2 and 3 the cancer predisposition syndromes were confirmed by chromosomal microarray analyses. FISH analyses showed no unfavorable abnormalities. All patients had phenotypic features typical for the each syndrome. In all cases the presence of genetic syndrome was suspected after the diagnosis of cancer had been done.
Conclusions: Genetic predisposition to neuroblastoma is rare. Genetic consultation including karyotyping and chromosomal microarray analysis is indicated to all patients with malformations.

EP-351

BILATERAL ADRENAL NEUROBLASTOMA: SINGLE CENTER EXPERIENCE

D. Kachanov[1], G. Muftahova[1], T. Shamanskaya[1], R. Moiseenko[1], A. Usychkina[1], Y. Olshanskaya[2], E. Andreev[3], G. Tereschenko[4], V. Roschin[5], Y. Likar[6], S. Varfolomeeva[1]

[1]Clinical Oncology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [2]Laboratory of Cytogenetics, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [3]Surgery, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [4]Radiology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [5]Pathology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [6]Nuclear Medicine, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia

Objectives: Bilateral adrenal involvement in neuroblastoma (NB) is a rare event. Extent of the surgical procedure is a matter of debate. The purpose of the study was to analyses clinical features and outcomes of the cohort of patients treated in single center in Russia.
Methods: During the period 01.2012-01.2014 (25 months) 177 children with NB were treated. The diagnosis was confirmed according to the international criteria. Stage was assigned according to INSS. Patients were stratified into risk groups and treated according to NB2004 protocol. Cytogenetic analyses of tumor tissue was done by FISH for *MYCN*, 1p and 11q status. Morphologic verification was recommended in patients aged 3 months or older.
Results: Bilateral adrenal involvement was diagnosed in 7 (4%) patients. Median age was 1.6 months (range 0.5 -8.8). Male to female ratio was 2.5:1. Initial diagnosis was based on clinical data in 5 (71%) and histology in 2 (29%) patients. Stage distribution: stage 4S – 5 (71%), stage 2 – 1 (14%), stage 1 – 1 (14%). Site of distant metastasis included liver in 4 patients (57%) and liver and bone marrow – 1 (14%). 2 (29%) patients were operated at the age of 3 months. Cytogenetic analysis showed lack of unfavorable abnormalities in all 4 studied cases. 5/6 (83%) patients had MIBG-positive primary tumor, 2/4 had MIBG-positive liver metastasis. Extent of the surgical procedure was gross total resection (1/4), subtotal resection (1/4) and biopsy (2/4). No patients had bilateral adrenalectomy. 3/7 patients received chemotherapy, 1 patient abdominal irradiation. 2/7 patients were observed and showed tumor regression. Median follow-up was 5.8 months (range 1.5-21.9). Outcomes: 6 patients alive (3 archived complete response), 1 patients with stage 4S died due to massive hepatomegaly.
Conclusions: Our data confirmed favorable features of neuroblastoma in patients with bilateral involvement and association with stage 4S. Aggressive surgery is not warranted in such cases.

EP-352

CONCURRENT EXTRARENAL NEPHROBLASTOMA AND NEUROBLASTOMA IN AN INFANT

R. Kebudi[1], C. Buyukunal[2], B. Oflaz Sozmen[3], I. Karaca[4], S. Kurugoglu[5], S. Dervisoglu[6]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and American Hospital, Istanbul, Turkey; [2]Pediatric Surgery, Istanbul University Cerrahpasa Medical Faculty and American Hospital, Istanbul, Turkey; [3]Pediatric Hematology-Oncology, Koc University and American Hospital, Istanbul, Turkey; [4]Pediatric Surgery, Izmir University School of Medicine, Izmir, Turkey; [5]Radiology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [6]Pathology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey

Objectives: Nephroblastoma is the most common malignant renal tumor in children. Extrarenal nephroblastoma is rare. Concurrent extrarenal nephroblastoma and neuroblastoma is extremely rare. We report a 9 month old female with extrarenal nephroblastoma presenting with inguinal mass who was a surrenal mass during investigations for nephroblastoma.
Methods: Case report
Results: A previously healthy9 month oldinfant, born after in vitro fertilization was referred to us after being diagnosed with extrarenal nephroblastoma. She was in good health until 7 months of age when parents noticed a left sided inguinal mass. The ultrasound showed a 39X24X26 mm solid mass. Her AFP, B-HCG, ferritin, LDH levels and CBC were within normal limits. She was seen by a pediatric surgeon at another medical center and and underwent a total resection. The pathology was consistent with nephroblastoma, with no anaplasia. The computed tomography of the chest and abdomen showed no lung metastasis, no lesion arising from kidneys but a left suprarenal mass. The NSE was slightly elevated. She then underwent a total excisional of the suprarenal mass with lymph node sampling at our instituition. The pathology revelaed neuroblastoma with no lymphatic involvement. The bone scan and the bone marrow biopsy showed no metastatic disease. She was diagnosed with totally excised stage 1 neuroblastoma and stage 1, favorable histology extrarenal nephroblastoma. She was started on chemotherapy as per NWTS-5 EE-4A protocol 3 days after the second surgery.
Conclusions: The co-existence of extrarenal nephroblastoma and neuroblastoma is extremely rare. During the diagnostic and metastatic workup for a rare tumor, in caseof co-existence of another mass, detailed investigations should be done in order to stage properly before deciding on further therapy. The correlation, if there is one, of in vitro fertilization and co-existence of the two tumors should also be studied in a larger population of infants.

EP-353

PROGNOSTIC SIGNIFICANCE OF 1P36, 17P DELETIONS, MDM2 GENE EXPRESSION IN NEUROBLASTOMA WITH NEGATIVE MYCN GENE STATUS

N. Khranovska[1], G. Klymnyuk[2], N. Svergun[1], O. Skachkova[1], E. Shaida[2], S. Pavlyk[2], M. Inomistova[1], N. Ionkina[1]

[1]Research Laboratory of Experimental Oncology, National Cancer Institute MPH of Ukraine, Kiev, Ukraine; [2]Research Department of Pediatric Oncology, National Cancer Institute MPH of Ukraine, Kiev, Ukraine

Objectives: The high clinical heterogeneity of neuroblastoma reflects the complexity of genomic abnormalities characterized these tumors. The role of *MYCN* gene amplification in neuroblastoma pathogenesis was first established in the early 1980s due to its association with high risk tumors and low patients survival. Currently prognostic significance of several other genetic abnormalities in neuroblastoma are under consideration. The purpose of our study is to determine the prognostic significance of 1p36, 17p deletions, *MDM2* gene expression in neuroblastoma with negative *MYCN* gene status.
Methods: Seventy two children diagnosed with II-IV stage neuroblastoma, aged 6 months to 12 years were enrolled in our study. Patients were assigned to treatment on the basis of age, tumor *MYCN* status, and tumor cell ploidy. The investigations of 1p36 and 17p deletions and *MYCN* gene amplification in tumor cells were performed by FISH method. The *MDM2* gene expression study was performed by the real-time RT-PCR, tumor cell ploidy study - using flow cytometry.
Results: It has been shown that the negative status of the MYCN found in 66% of neuroblastoma cases with unfavorable disease course. No chromosome 17p loss has been found in these tumors. Assumed that in these tumor cases transcriptional function of *TP53* are under control of MDM2 protein. High MDM2 gene expression level in tumors is associated with poor response to chemotherapy, regardless of the gene *MYCN* status. We have revealed that deletion of chromosome 1p36 in tumor cells occurs in 22% of all investigated neuroblastoma tumors and in 50% of cases associated with *MYCN* gene amplification. In 30% of patients with negative status of *MYCN* gene, deletion of chromosome 1p36 associated with disease progression.
Conclusions: Deletions of 1p36 and 17p and elevated levels of *MDM2* gene expression are important for prognosis in neuroblastoma and could be recommended for the replenishment of the genetic component of the risk grouping stratification complex.

EP-354

TREATMENT OF STANDARD AND HIGH RISK PATIENTS GROUP WITH NEUROBLASTOMA. ONE CENTRE EXPIRIENCE

S. Pavlyk[1], G. Klymnyuk[1], E. Shaida[1]

[1]Pediatric, National Cancer Institute of Ukraine, Kiev, Ukraine

Objectives: Historically, high-risk neuroblastoma patients have had long-term survival probabilities of less than 15%. With the advent of comprehensive treatment approaches that include intensive induction chemotherapy, myeloablative consolidation therapy with stem cell rescue and targeted therapy, OS rates have improved. However, the current survival rates remain unacceptable and have come at the expense of substantial immediate and long-term morbidity
Methods: In 2007-2013, 182 patients with neuroblastoma: 87 standard-risk (SR) patients and 95 high-risk (HR) patients received treatment in the Science Research Department of Pediatric Oncology at the National Cancer Institute. All enrolled patients received treatment according to NB-2004 and HR-NBL-1/ESIOP protocols. 54 HR patients were cured high-dose chemotherapy (HDCT) with autologous stem cell support, of these, 13 patients were cured with tandem HDCT
Results: The 5-year overall survival (OS) was 67% for SR patients and 30.4% for HR patients. The following unfavorable prognostic factors for neuroblastoma were used in our study: the child's age at the time of making a diagnosis, stage, N-myc amplification. Depending on the child's age: the OS was 58.8% for patients under 1 year of age, while the OS was 19.2% for patients aged 1 year or over. We also analyzed the survival rate of HR patients based on whether the patient has N-myc amplification. The OS was 49.8% for N-myc negative subjects and 24.3% for N-myc positive subjects. Currently, the OS is 69.2% for patients who were treated with tandem HDHT with autologous stem cell support
Conclusions: Depending on the therapeutic program used, the OS were 22.7% (NB-2004) and 38.9% (HR-NBL-1/ESIOP) for HR patients. The results of treatment of HR patients with receive tandem HDHT with autologous steam cell support are encouraging.

EP-355

TANDEM PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN CHILDREN WITH NEUROBLASTOMA

G. Klymnyuk[1], S. Pavlyk[1], E. Shayda[1], N. Khranovska[2]

[1]Pediatric, National Cancer Institute of Ukraine, Kiev, Ukraine; [2]Experimental oncology, National Cancer Institute of Ukraine, Kiev, Ukraine

Objectives: Based on the results recent of investigations, application of autologous stem cell tandem transplantation (TT) could improve the treatment results of patients with some malignant solid tumors. Nowadays TT is investigated for medulloblastoma, germ cell tumor and high-risk neuroblastoma. Nevertheless effectiveness convincing results haven't been obtained.
Methods: During the 2012 year the Department of Pediatric Oncology at the National Cancer Institute have been carried out 13 tandem transplantations in children with high-risk of neuroblastoma. Patient's age was 1–14 years. 10 pts. with primary neuroblastoma got TT after chemotherapy on HR-NBL-1/ESIOP protocol, 3 pts. as a consolidation of relapse second-line therapy. The first part of tandem chemotherapy was BuMel in all patients. Ten patients had topotecan-based regimens as the second part of tandem transplantation and three patients had CEM regimen. A time interval between parts of tandem was 1 - 3 months. For autologous transplantation have been used only peripheral stem cells. All patients received 13-cis retinoic acid after of conventional treatment.
Results: All patients successfully completed first high-dose chemotherapy. WBC count recovered more then 500/(L on +10-15 day, PLT count recovered on +13-28 day after PBSC. In one patient was observed neurotoxicity like short clonic and tonic seizures after second high-dose chemotherapy. Chemotherapy was cancelled immediately (patient received 2/3 doses of cyclophosphamide and topotecan full dose). There were neutropenia and thrombocytopenia 4th rate, oral mucositis with different degrees of severity in all patients. WBC count recovered more then 500/(L on +9-14 day, PLT count recovered on +12-22 day. Currently, 5 of 13 patients are in CR, 4 patients had early relapse and continue treatment, 4 died of PD. The follow-up period after accomplishment of TT is 2 - 14 months.
Conclusions: Application of TT in children with high-risk neuroblastoma resulted to two-year disease-free survival rate of about 38% and the overall three-year survival rate to 47%.

EP-356

SURGICAL APPROACH TO THORACIC INLET TUMORS ARISING FROM THE SYMPHATHETIC CHAIN IN CHILDREN - A SINGLE INSTITUTION'S EXPERIENCE

Q.W. Lee[1], H.Y. Chua[1]

[1]Department of Pediatric Surgery, Kandang Kerbau Women's and Children's Hospital, Singapore, Singapore

Objectives: Neuroblastoma (NB) is the commonest extra-cranial pediatric solid tumor in Singapore. NBs arising at the thoracic inlet may carry a better prognosis despite the challenging surgical access to this area. We examine our center's experience with these tumors.
Methods: With IRB approval, clinical charts of patient with thoracic inlet tumors fulfilling ICD-O-3 (International Classification of Diseases for Oncology) 95003 (neuroblastoma); 94903 (ganglioneuroblastoma); and 94900 (ganglioneuroma), managed in our center between 2007 and 2013, were reviewed.
Results: There were 4 females and 1 male with median age of 32 months old (10 months – 60 months) of age. Three patients had neuroblastoma, one had ganglioneuroblastoma and one had a ganglioneuroma. Amongst those with neuroblastomas, 1 had stage 4 disease with bony metastases, the other 2 had stage 3 and 2b disease; with an enlarging neck mass in one and a neck abscess in the other. Following chemotherapy, anterior trap-door thoracotomies were performed for the first 2 patients while thoracoscopic assisted resection was performed in one. Upfront thoracoscopic-assisted resection was performed for the ganglioneuroblastoma and resection using the Da Vinci robot was performed for the ganglioneuroma. All patients had post-operative Horner's syndrome which improved over time. One patient had phrenic nerve-praxia that resolved. Aside for the child with stage 4 NB, all patients are well with no residual disease at a mean follow-up of 24.8 months (4 months – 75 months). One child succumbed to refractory bone marrow disease.
Conclusions: While the thoracic inlet poses challenges for resection of NBs at this site, mature elements in these tumors may lend themselves to a favourable prognosis. Minimally invasive approaches allowed superior visualization of the anatomy while anterior trap-door thoracotomies facilitate dissection around critical structures.

EP-357

THREE CASES REPORT OF PEDIATRIC ATYPICAL NEUROBLASTOMA

Y. Li[1], L. Liu[1]

[1]Pediatric Hematology/Oncology, Sun Yat-Sen Memorial Hospital Sun Yat-Sen University, Guangzhou, China

Objectives: To show the clinical characteristics of atypical neuroblastoma in three Chinese pediatric patients.
Methods: Retrospective analysis was made of three cases of atypical neuroblastoma.
Results: Atypical neuoblastoma refers to the primary onset of neuroblastoma without a detectable mass in common sites, but in bone marrow or/and other metastasis parts, is an infrequent occurrence. We present three unusual cases of Chinese atypical neuroblastoma that the extramedullary substantial mass not be found. Moreover, the three cases both presented with typical neuroblastoma cells that forming Homer-Wright rosettes in bone marrow smear. The diagnosis of neuroblastoma was further established by markedly elevated of vanillylmandelic acid (VMA) in urine, serum neuron-specific enolase (NSE) and neuroblastoma MRD level in peripheral blood, amplifications of bone marrow N-myc were all absent. Noteworthy, the first case showed no other parts of the tumor infiltration in addition to bone marrow, while in the second case and third case the involvement of neurobalstoma both in bone marrow and bone. The three patients were treated with nine courses of induction chemotherapy as high-risk neuroblastoma protocol, which includes CAV (Cyclophosphamide+Pirarubicin+Vincristine), PVP (Cisplatinum+ Etoposide) and CT (Cyclophosphamide+Topotecan). Although the first patient achived complete remission, the child is not free of recurrence at a follow-up of half a year due to lack of consolidation chemotherapy. In the second case, by contrast, complete remission was not obtained, and then he abandoned further treatment for economic reason. The third case achieved partial remission after the entire induction chemotherapy, and he experiences consolidation chemotherapy at present.
Conclusions: In case of atypical neuroblastoma, chemotherapy might be the only effective firstline treatment for the absense of visible solid mass. In our limited experience, it seems that the patients of atypical neuroblastoma have unfavorable prognosis after conventional intensive chemotherapy, especially in the presence of bone involvement.

EP-358

EFFECTS OF ARSENIC TRIOXIDE AND CONVENTIONAL CHEMOTHERAPEUTIC DRUGS ON EXPRESSION OF P-GLYCOPROTEIN IN HUMAN NEUROBLASTOMA CELL LINE SK-N-SH

L. Liu[1], Y. Li[1]

[1]Pediatric Hematology/Oncology, Sun Yat-Sen Memorial Hospital Sun Yat-Sen University, Guangzhou, China

Objectives: The aim of this study was to investigate the effects of arsenic trioxide (As_2O_3) and conventional chemotherapeutic drugs on the apoptosis and P-glycoprotein (P-gp) expression of neuroblastoma SK-N-SH cells.
Methods: The change of expression level of P-gp was measured by Western blotting after SK-N-SH cells were incubated with various anti-cancer drugs including As_2O_3, cisplatin (DDP) and etoposide (Vp16). Flow cytometry with Annexin V-PI staining was used to monitor the ability of As_2O_3 to induce SK-N-SH cells apoptosis.
Results: In our previous studies, we found that As_2O_3 may be a potent anti-cancer agent in human neuroblastoma cell lines. Our results further determined findings reported previously and shown that As_2O_3 had a dose- and time-dependent toxic effect on SK-N-SH cells via induction of apoptosis. The IC50 of As_2O_3 for 72h treatment was found to be 3uM. The Western analysis showed that the expression of P-glycoprotein began to decrease with in the micromolar range As_2O_3 exposure for 48h and further decrease after 72h and 96h. With 3uM As_2O_3 exposure for 72h, the expression of P-glycoprotein reduced mostly rapidly. However, the expression of P-glycoprotein of SK-N-SH cells was increased when treating with DDP and VP16 as the drugs concentration and effective time increase.
Conclusions: We show that As_2O_3 exerted its anti-tumor effect in SK-N-SH cells via induction of apoptosis. These findings of western analysis provide experimental evidence that low dose As_2O_3 reduces the P-gp expression in human neuroblastoma cell line. To the contrary, conventional chemotherapeutic drugs increase the P-gp expression. Taken together, we propose that As_2O_3 was probably not the substrate to be extruded by P-glycoprotein in SK-N-SH cells because it reduces cellular P-glycoprotein expression.

EP-359

MULTIDISCIPLINARY TREATMENT FOR HIGH RISK NEUROBLASTOMA IN BEIJING CHILDREN'S HOSPITAL FOR 3-YEAR RESULTS

X. Ma[1], M. Jin[1], D.W. Zhang[1], M.Q. Qin[1], B. Wang[1], X. Zhou[1], H.M. Wang[2], H. Qin[2], C.J. Zhou[3], Q. Zeng[4]

[1]Hematology Oncology Center, Beijing Children's Hospital Capital Medical University, Beijing, China; [2]Oncological Surgery, Beijing Children's Hospital Capital Medical University, Beijing, China; [3]Pathology Department, Beijing Children's Hospital Capital Medical University, Beijing, China; [4]Thoracic surgery, Beijing Children's Hospital Capital Medical University, Beijing, China

Objectives: Beijing Children's Hospital (BCH) has established a multidisciplinary program for neuroblastomas (NB) since early 2007. We summarized high-risk NB (HR-NB) in BCH for 3-year results.
Methods: Retrospectively reviewed medical records of children presenting with clinically and/or histologically confirmed NB between Apr 1, 2007 to March 31,2011. HR-NB must have over 1 year of age. All stage III unresectable, IV and patients with tumour genomic N-myc copy number more than 10 (irrespective of stage or age) were eligible. Multimodality treatment for HR-NB protocol included intensive chemotherapy, surgery and radiation therapy for local control, followed by autologous haematopoietic stem cell transplantation (auto-PBSCT) for consolidation therapy and also isotretinoin for maintenance treatment. Total courses were 1.5years. All children followed up to Dec 31,2013.
Results: Total 67 HR-NB children, 43 males,24 females, median age 49 months (12∼147), 66 of INSS-IV and 1 of INSS-III, 16 of primary postmediastinal tumor, 51 of retroperitoneal and pelvic tumor. Of 52 patients with fully known biologic features, 31 cases of NB or NB chemotherapy change, 19 cases of ganglioneuroblastoma, only one for ganglioneuroma. 4 had N-myc gene amplification by FISH. 51 of HR-NB children were treated and followed-up regularly, median time 36 (6 ∼76) months for follow up, 26 occurred event, 7 were relapsed after stopped treatment for median 28 (8∼50) months, 17 for tumor progression, 2 patients were died by severe infections. Using *Kaplan-Meier* analysis showed the expected 3-year overall survival rate was 49%.
Conclusions: HR-NB prognosis is far lower than the common childhood leukemia and lymphoma. The most important role was multidisciplinary treatment in order to improve HR-NB children survival rates. Moreover, it's still the possibility for recurrence and relapse after stopping treatment 1∼5 years, the long-term follow up for HR-NB was necessary.

EP-360

COMPARATIVE STUDY BETWEEN PET AND MIBG IN DIAGNOSIS AND MANAGEMENT OF NEUROBLASTOMA

E. Moussa[1], M.F. Fawzy[2], A.H. Hamouda[2], A.Z. Zaher[3], O.H. Hassanain[4], S.A. Azmy[4]

[1]Clinical Oncology, Menoufia University, Cairo, Egypt; [2]Pediatric Oncology, National cancer Institute, Cairo, Egypt; [3]Nuclear Medicine, National cancer Institute, Cairo, Egypt; [4]Research, The Children's Cancer Hospital, Cairo, Egypt

Objectives: ^{123}I-metadiodbenzylguandine is the conventional radiopharmaceutical imaging (^{123}I-MIBG) in neuroblastoma diagnosis, with a sensitivity of about 90% and specificity of nearly 100%. Although neuroblastoma cells can concentrate ^{18}F-FDG, several conflicting results about PET scan in the evaluation of Neuroblastoma, were reported. The purpose of the study was to prospectively evaluate the diagnostic significance of PET/CT imaging and to compare its diagnostic and prognostic value to ^{123}I-MIBG scintigraphy in patients with neuroblastoma at different phases of disease.
Methods: A Total of 30 patients (14 males and 16 females), less than 18 years, all diagnosed and treated at the Children's Cancer Hospital-Egypt according to COG A3973 for high risk patients and COG A3961 for intermediate risk patients. They all did ^{123}I-MIBG and ^{18}F-FDG PET scans (within 1 month) at diagnosis and at different points during their management.
Results: Scans (MIBG and PET) were examined for 30 patients at different management stages with comparison to CT scans for primary tumor site, with bone scan for bone involvement, and with bone marrow biopsy result for bone marrow infiltration. PET scan was

positive in 60% of scans for primary site, in 23.3% for bone involvement, and in 13.3% for bone marrow infiltration, whereas MIBG scan was positive in 36.7% for primary site, in 10% for bone, and in 10% for bone marrow infiltration. PET scan was more sensitive than MIBG in detecting primary tumor (0.8 for PET versus 0.5 for MIBG), in detecting bone metastases (0.6 for PET versus 0.3 for MIBG), and for bone marrow involvement (0.28 for PET versus 0.21 for MIBG). Incorporating all modalities lead to better treatment decisions.
Conclusions: The authors recommend the use of PET/CT in evaluating primary tumor either at diagnosis or at different stages of therapy although further extended double blinded studies are needed.

EP-361

NEUROBLASTOMA IN PATIENTS UNDER 18 MONTHS: A SINGLE INSTITUTION EXPERIENCE IN ARGENTINA

A. Rossa[1], W. Cacciavillano[1], A. Rose[1], M. Cadario[2], J. Lopez Marti[3], G. Chantada[1], P. Zubizarreta[1]

[1]Hematologia y Oncologia, Hospital JP Garrahan, Ciudad Autónoma de Buenos Aire, Argentina; [2]Cirugia, Hospital JP Garrahan, Ciudad Autónoma de Buenos Aire, Argentina; [3]Patología, Hospital JP Garrahan, Ciudad Autónoma de Buenos Aire, Argentina

Objectives: To evaluate the outcome of patients under 18 months diagnosed with neuroblastoma.
Methods: Between April 2006 and October 2012, 38 consecutive patients were retrospectively reviewed.
Results: Mean age of 8.9 months (0.7-18 months). Frequently sites: adrenal gland (n = 15) paravertebral (n = 8), 2 or more sites involved (n = 7), cervical (n = 4), and mediastinal (n = 4). Histopathological diagnosis: poorly differentiated neuroblastoma (n = 24), in differentiation (n = 3), metastatic neuroblastoma (n = 2), intermixed ganglioneuroblastoma (n = 1), neuroblastoma uncharacterized (n = 7), not biopsied (n = 1). *N-myc* amplification was detected in 4 patients (7 not studied), deletion of 1p (*del1p*) in 3 patients (12 without evaluating), and 11q aberration in one patient (only 8 patients studied). According to INRG pretreatment classification schema, 19 patients belonged to the L1 category, receiving chemotherapy (n = 1), surgery (n = 15), chemotherapy+surgery (n = 3) and observation only (n = 1). Nine patients were L2 category, 3 received chemotherapy, 4 surgical treatment and 2 surgery+chemotherapy (1 *N-myc* amplified and 1 del1p). Seven patients were stage M, (1 amplification of N-myc, one *del1p*, one aberration of 11q, 2 amplification of N-myc with *del1p*) receiving treatment for intermediate-risk (n = 2) and high-risk groups (n = 5). Three patients were classified as stage Ms, one received treatment for intermediate and 2 for low-risk groups. With a median follow-up of 25 months (3-80 months), at 24 months the EFS of all patients was 85% (SE 6%) and OS of 91% (SE 5%). Significant difference was found in OS and EFS between patients with stages L1, L2 and Ms vs stage M. EFS for each stage: L1 89% (SE 7%), L2 100%, MS 100%, vs M 57% (SE 18%), p = 0,01. OS: L1 94% (SE 6%), L2 100%, MS 100%, vs M 71% (SE 19%), p = 0.03.
Conclusions: Although OS and EFS results are similar to those reported in international studies, improvements in obtaining results of biological prognostic factors will warrant an accurate staging and consequently an appropriate treatment.

EP-362

RETROSPECTIVE EVALUATION OF CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH HIGH-RISK NEUROBLASTOMA TREATED AT THE CHILDREN'S CANCER INSTITUTE IN LEBANON

F. Saad[1], R. Nader[2], S. Akel[3], M. Abboud[1], S. Muwakkit[1], H. El Solh[1], R. Saab[1]

[1]Pediatrics and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; [2]Internal Medicine, American University of Beirut, Beirut, Lebanon; [3]Surgery, American University of Beirut, Beirut, Lebanon

Objectives: To evaluate clinical characteristics and outcome of patients with high-risk neuroblastoma treated at the Children's Cancer Institute in Lebanon.
Methods: After IRB-approval, clinical data for 35 patients diagnosed between April 2002 and December 2013 at a single multidisciplinary center were retrospectively analyzed. Risk stratification was based on Children's Oncology Group (COG 9641/3961 studies).
Results: Twenty-one patients had high-risk disease. Median age at diagnosis was 3.6 years (range 0.5–13.9 years) with a male-to-female ratio of 1.3:1, and a median follow-up of 22.6 months (range 5–116 months). Based on International Neuroblastoma Staging System, all patients had stage IV disease. MYCN-gene was amplified in 6/15 tested tumors (40%). All patients were treated as per COG-A3973 protocol, and 81% (n = 17) achieved complete response (CR), while 19% (n = 4) had progressive disease on therapy (PD). Sixteen patients (76%) underwent autologous stem-cell transplantation (ASCT) as consolidation therapy; the rest did not qualify due to poor response (n = 4) or relapse before consolidation (n = 1). Thirteen patients (62%) received radiotherapy as part of local control; reasons for not receiving radiotherapy included PD (n = 5) and death of toxicity (n = 3). Currently, 48% (n = 10 patients) are alive at a median follow-up time of 2.7 years: Eight patients are in CR1 and two are in CR2. Eleven patients died, eight (38%) due to tumor progression, and 3 (14%) due to toxicity during consolidation (CNS toxoplasmosis, failure of engraftment, and sinusoidal obstruction syndrome, respectively).
Conclusions: Overall survival for high-risk neuroblastoma in Lebanon seems to be comparable to that in developed countries when multimodality therapy is given in a multidisciplinary setting. Further improvements will likely depend on the availability of novel therapies that are not yet easily accessible in developing countries.

EP-363

HOW THE EUROPEAN CLINICAL TRIAL DIRECTIVE IMPACTS TRIAL IMPLEMENTATION: LINES, ON BEHALF OF SIOPEN COOPERATIVE GROUP

V. Segura[1], A. Alpash[2], A. DiCataldo[3], G. Schleiermacher[4], J.D. Bermúdez[5], V. Mosseri[6], V. Papadakis[7], K. Wheeler[8], R. Ladenstein[2], A. Cañete[9]

[1]Paediatric Oncology, Instituto de Investigacion Sanitaria La FE, Valencia, Spain; [2]Studies & Statistics for Integrated Research and Projects, St. Anna Kinderkrebsforschung, Viena, Austria; [3]Pediatric Hematology and Oncology, University of Catania, Catania, Italy; [4]Department of Pediatric Oncology, Institut Curie, Paris, France; [5]Departamento de estadística, Universidad de Valencia, Valencia, Spain; [6]Service de Biostatistique, Institut Curie, Paris, France; [7]Department of Pediatric Hematology-Oncology, Aghia Sophia Children's Hospital, Athens, Greece; [8]Department of Paediatric Haematology and Oncology, Oxford Children's Hospital, Oxford, United Kingdom; [9]Unidad de Oncología Pediátrica, Hospital Universitario y Politécnico La Fe, Valencia, Spain

Objectives: European Low and Intermediate Risk Neuroblastoma (LINES, EudraCT: 2010-021396-81, ClinicalTrials.gov Identifier: NCT01728155) is an international SIOPEN clinical trial, in the framework WP10 (ENCCA PROJECT: European Network for Cancer research in Children and Adolescents). LINES stratifies patient's treatment according to biological and clinical markers in order to: i) minimize the treatment burden in those low-risk patients who in previous studies were shown to have an excellent long-term outcome, ii) intensify treatment in those patients with biologically unfavourable but not MYCN amplified neuroblastoma to improve outcome.
Methods: LINES includes ten separate therapeutic groups, one of them randomised. All the cases are registered at *Siopen-r-net* database with check-points to monitor the quality of prospectively entered staging data, including real time central review for biology and histology. Neonatal adrenal masses (NAM) in infants below 3 months are also registered and observed, without initial surgery.
Results: LINES trial-sponsored by IIsLaFE was first launched in Spain (28 sites) in July 2011 and it was opened in Italy (21 sites), Austria (5 sites) and Denmark (3 sites) in 2012. Then, France (29 sites), Norway (4 sites), Israel (1 site) and Belgium (2 sites) were authorized in 2013. Switzerland, Ireland, Slovenia and New Zeeland are expected to be authorized in the coming months. In summary, only 8 of 21 expected participating countries have been opened for recruitment and 142 patients have been enrolled and grouped (73 low risk, 32 intermediate risk and 37 NAM) in the last 2.5 years.
Conclusions: Since European Clinical Trial Directive 2001/20/EC implementation, it has been very difficult to launch academic pediatric cancer trials due to high cost, additional national requirements and bureaucracy, delaying clinical trial initiation. We hope the new Clinical Trial Regulation will bring a process of harmonisation and shorten timelines across Europe.
Acknowledgements: *FP7 2007-2013_project ENCCA grant agreement-no-261743.*

EP-364

GANGLIONEUROMA: SINGLE CENTER EXPERIENCE IN RUSSIA

T. Shamanskaya[1], D. Kachanov[1], G. Muftahova[1], Y. Olshanskaya[2], E. Andreev[3], V. Roschin[4], Y. Likar[5], S. Varfolomeeva[1]

[1]Clinical Oncology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [2]Laboratory of Cytogenetics, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [3]Surgery, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [4]Pathology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [5]Nuclear Medicine, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia

Objectives: Ganglioneuroma is a rare benign tumor of the sympathetic nervous system. The standards of care including indications for surgery and radiation therapy for this rare condition have to be determined. The aim of the study was to analyze the clinical features and outcomes in the cohort of patients in single center in Russia.
Methods: There were193 patients with sympathetic nervous tumors treated during the period 01.2012-03.2014. Initial work-up included CT/MRI of the primary site, tumor markers, MIBG scintigraphy and bone marrow evaluation. Pathological diagnosis was done according to the International Neuroblastoma Pathology Classification. Patients were stratified and treated according to the NB2004 protocol. Surgery was the treatment of choice in patients without image-defined risk factors.
Results: Ganglioneuroma was confirmed by histology in 6 (3.1%) cases. Primary GN was diagnosed in 5 patients, secondary in 1 patients (second-look operation after 5 cycles of chemotherapy). Male-to-female ratio was 2:1. All patients were older than 1 year. Median age was 60.3 months (range 51.0-82.1). All 5 patients with primary GN were symptomatic at the time of the diagnosis, mild pain was the most common symptom. Distribution of patients by

the primary site: 3/6 – retpoperitoneum, 2/6 – posterior mediastinum, 1/6 – presacral. 3/6 had elevated neuron-specific enolase level (< than 2 upper limits). 3/4 patients had MIBG-positive tumor. The extent of surgery was gross total resection (3/6, 50%), macroscopic residual tumor (1/6, 17%), biopsy (2/6, 33%). Surgery was limited to biopsy because major vessels involvement in 2 patients (presacral and retroperitoneum localization). Median follow-up was 8.4 months (range 0.4-22.4). All patients alive without evidence of disease progression. Two patients after biopsy showed no progression of both the tumor and symptoms.
Conclusions: Surgical treatment depends on the presence of image-defined risk factors. In cases with image-defined risk factors the benefits of the surgery should be balanced with the risk of severe morbidity.

EP-365

ANALYSIS OF SHORT TERM EFFICACY FOR 59 CASES OF CHILDREN WITH NEUROBLASTOMA

J. Shao[1]

[1]*Hemotology/Oncology, Shanghai Children's Hospital, Shanghai, China*

Objectives: A retrospective analysis of 59 cases of children with neuroblastoma (NB) correlation short term efficacy and prognostical factors.
Methods: Total 59 newly diagnosed NB patients from July 1, 2008 to June 30,2013 were divided into low risk (LR), medium risk (MR) and high risk (HR) groups depends on age and clinical stage. Chemotherapy and 13-cis-retinoid acid and/or second tumor resection were used at the end of treatment referring to different risk groups.
Results: 1. According to INSS, the number of cases in stage I, II, III, IV and IVs was 4 (6.8%), 7 (11.9%), 18 (30.5%), 22 (37.3%) and 8 (13.5%), respectively. Follow up to Dec 31, 2013, 43 cases (43/59, 72.9%) achieved complete remission (CR) or partial remission (PR). The 3-year overall survival (OS) of stage I, II, III, IV and IVs were 100%, 100%, 65.6%,34.8% and 85.7%; and the EFS were 100%, 66.7%, 65.6%,30.4% and 34.3% ($P = 0.013$, 0.004). The 3-year OS and EFS of LR, MR, HR were 100%,92.7%,28.3% and 100%,53%,25% ($P = 0.001$,0.001).2. In 59 cases, 45 of diagnosed with pathologic diagnosis whose different histopathological subtype, stroma and mitosis karyorrhexis index (MKI) were not statistically significant with survival. The 3 year OS and EFS were obviously higher from the patients with favorable histology (FH) than the one with unfavorable histology (UH) ($P = 0.046$,0.030).
3. Univariate statistical analysis showed that the factors significantly correlated with prognosis were age, stage and risk group ($P = 0.004$,0.013,0.001). Age, bone marrow metastasis at diagnosis and risk group were important for event of NB patients ($P = 0.005$,0.009,0.002).
Conclusions: 1. Stage, risk group and age are important prognostic factors for NB. In the absence of N-MYC data, 18 months is the dividing line for prognosis of patients. 2. Histologic category combined with age, MKI and pathology is in favor of prediction the prognosis of NB patients.

EP-366

DIAGNOSTIC IMPLICATIONS OF N-MYC ONCOGENE AMPLIFICATION IN UNILATERAL PEDIATRIC RENAL TUMOR: A CASE REPORT

S. Sharma[1], **R.N. Makroo**[1], **M. Chowdhry**[1], **P. Srivastava**[1], **M. Mishra**[1], **M. Singh**[1], **Y. Thakur**[1]

[1]*Molecular Biology and Transplant Immunology, Indraprastha Apollo Hospital, New Delhi, India*

Objectives: Renal tumors of childhood occasionally exhibit histopathologic and clinical features that prevent accurate diagnosis. Molecular and cell culture techniques may be helpful in better characterizing these cases
Methods: In this case report, n-myc FISH was used to examine unusual renal tumors from a 11 month old female to establish the accurate assessment of the tumor and to stratify the risk group. FISH testing was performed on formalin fixed paraffin embedded tissue of suprarenal area using commercially available probe.
Results: Histopathological evaluation of right kidney showed features of Wilm's tumor with predominant epithelial component. The resected margin of the ureter and capsule were free of tumor. She also had mass in right suprarenal area which on histopathology showed features suggestive of undifferentiated neuroblastoma. Three lymph nodes isolated from the hilar area showed deposit of Wilm's tumor. FISH analyses of the supra renal mass revealed amplification of n-myc gene thus favouring neuroblastoma.
Conclusions: Although histopathologic features could not clearly distinguish between Wilms' tumor and neuroblastoma, but n-myc gene amplification strongly suggested that this neoplasm would behave as an aggressive neuroblastoma. FISH analyses therefore contributed to a revised diagnosis of neuroblastoma and is an effective approach in case such dilemmas occur.

EP-367

TREATMENT OUTCOME OF LOW-RISK AND MEDIUM-RISK NEUROBLASTOMA TREATED ACCORDING TO GERMAN NB 2004 PROTOCOL

E. Shorikov[1], **A. Druy**[1], **S. Tuponogov**[2], **O. Lemesheva**[2], **T. Popova**[2], **A. Zaichikov**[2], **D. Chusovitin**[2], **I. Vyatkin**[2], **G. Tsaur**[2], **A. Popov**[2], **L. Saveliev**[3], **L. Fechina**[1]

[1]*Pediatric Oncology and Hematology, Regional Children's Hospital/Research Institute of Medical Cell Technologies, Yekaterinburg, Russia;* [2]*Pediatric Oncology and Hematology, Regional Children's Hospital, Yekaterinburg, Russia;* [3]*Pediatric Oncology and Hematology, Ural State Medical Academy, Yekaterinburg, Russia*

Objectives: Retrospectiveevaluation of the treatment outcome in patients from observation (OG) and medium-risk (MRG) groups of NB2004 Protocol.
Methods: Among 90 children with primary neuroblastoma treated according to NB2004 in our hospital from December 2005 till October 2013 58 (64%) patients were stratified to OG and 12 (13%) ones referred to MRG. Median age of these OG/MRG patients was 8 months (range 10 days-15 years). Patients' distribution by stage was as follow: stage I had 35 (50%) children; stages II, III, IV and IVS were diagnosed in 5 (7.1%), 17 (20.7%), 6 (8.6%) and 7 (10%) patients respectively. Median of follow up period is 43 months.
Results: In 13 (22,4%) patients from OG (10 with stage III, 3 with stage IVS) chemotherapy started immediately after diagnosis because of the huge size of primary tumor or life-threatening symptoms. All the patients from MRG were treated according to medium-risk arm. At present time 66 (94.3%) patients are alive; 63 (90%) are alive without progression. Unfavorable events were registered in 7 (10%) cases. Among them there were 2 (2.9%) relapses, 4 (5.7%) cases of progressive disease, 1 (1.4%) therapy-related death. Other 3 (4.2%) patients died from tumor progression. 7-years EFS in the whole group was $86\% \pm 4\%$ and OS was $90\% \pm 4\%$. EFS and OS in patients from OG and MRG did not differ significantly: $85\% \pm 5\%$ vs. $90\% \pm 9\%$ ($p = 0.69$) and $88\% \pm 5\%$ vs. 100% ($p = 0.30$), respectively. The worst prognosis had patients with stage IVS in comparison with other children: EFS is $35\% \pm 19\%$ vs. $91\% \pm 4\%$ ($p < 0{,}0001$) and OS is $57\% \pm 24\%$ vs. $94\% \pm 4\%$ ($p = 0.003$), correspondingly. The worst outcome had patients with stage IVS in comparison with other children. EFS $35\% \pm 19\%$ vs. $91\% \pm 4\%$ ($p < 0{,}0001$) and OS $57\% \pm 24\%$ vs. $94\% \pm 4\%$ ($p = 0.003$), correspondingly.
Conclusions: The prognosis of children with low-risk and medium-risk neuroblastoma is excellent. Existing NB2004 Protocol criteria of patients' stratification demonstrated their effectiveness and in the majority of cases allow reducing the treatment intensity.

EP-368

LOCALIZED ABDOMINAL NEUROBLASTOMA, PRESENTING WITH CHYLOTHORAX- A RARE ASSOCIATION

S. Siddaiahgari[1], **D. Makadia**[1]

[1]*Pediatric Hematology-Oncology, Rainbow Childrens Hospital, Hyderabad, India*

Objectives: to describe the rare association between localized abdominal neuroblastoma and chylothorax
Methods: 3.7 years old male presented with respiratory distress secondary chylothorax and found to have abdominal neuroblastoma
Results: A 3.7 years male presented with one month fever, abdominal pain & distention. He developed breathing difficulty 20 days prior to presentation and greenish discoloration of left upper chest a day before. He was tachycardic, tachypneic and had retractio ns along with reduced air entry on left side of chest. Abdomen distended in left upper quadrant with palpable mass. His initial hemogram showed Hb 7.4 gm%, other parameters being normal. X-ray chest showed left pleural effusion. USG abdomen showed large well defined lobulated solid mass 9 $\times$ 8 $\times$ 6 cms lesion with areas of necrosis in left suprarenal region compressing renal vessels but not encasing. Pleural fluid tapped and analyzed. It was milky white fluid with specific gravity of 1.012, leukocyte count 5000/(L with 90% lymphocyte, while the triglyceride and cholesterol content 220 and 50 mg/dl respectively. Lipoprotein electrophoresis of fluid showed chylomicron band, conclusive of chylothorax. USG guided biopsy of abdominal mass HPE and immunohistochemistry suggestive of neuroblastoma with NSE and chromogrannin being positive. After initial stabilization patient was started on chemotherapy Rapid COJEC. He was started on octreotide and continued 2 weeks to control Chylothorax as it was symptomatic and was reaccumulating rapidly post tapping. Post rapid cojec mass was resected followed by autologous stem cell therapy as it was N myc amplified.
Conclusions: Thoracic Neuroblastoma produces chylothorax due to either extrinsic compression or infiltration of the thoracic duct, which causes increase in intraductal pressure. In our case interestingly the abdominal neuroblastoma has presented with chylothorax which is not described earlier. It resolved in 3 weeks with chemotherapy and octreotide.

EP-369

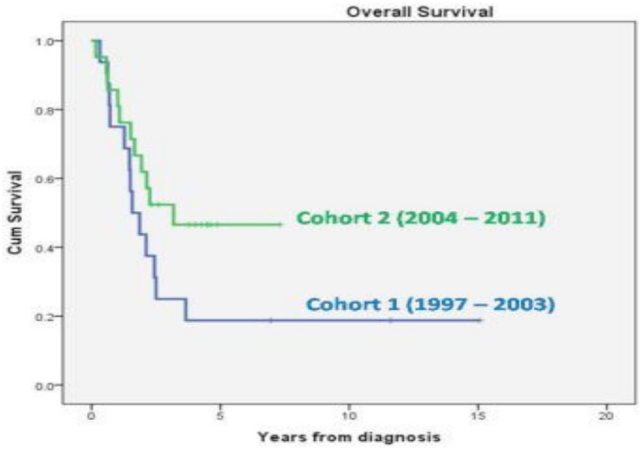
IMPROVING TREND IN SURVIVAL OUTCOME OF HIGH RISK NEUROBLASTOMA IN SINGAPORE

S.Y. Soh[1], **M.Y. Chan**[1], **A.M. Tan**[1]

[1]*Paediatric Haematology/Oncology Service, KK Women's and Children's Hospital, Singapore, Singapore*

Objectives: High-risk neuroblastoma patients in Singapore are treated with chemotherapy, surgery, myeloablative therapy (MAT), radiation and cis-retinoic acid maintenance. We

retrospectively reviewed characteristics, treatment practices and outcome of high-risk patients seen at KK Women's and Children's Hospital (KKH), the largest pediatric unit in Singapore.
Methods: The study was approved by Singhealth Centralized Institutional Review Board. We included patients who were (1) INSS stage 4 and over 12-months-old at diagnosis, or (2) stage 2/3/4S with *NMYC*-amplification, and treated at KKH from 1997 to 2011 (15 years). We excluded patients who came for second opinion or surgery only. We divided patients into earlier (1997 – 2003, cohort 1) and later cohorts (2004 – 2011, cohort 2) for comparison.
Results: There were 37 high-risk patients – 16 in cohort 1; 21 in cohort 2. The median age at diagnosis was 34.5 months (range 12.2 months to 9.9 years), and 23 (62%) were males. Majority (92%) had stage 4 disease; 3 had *NMYC*-amplified stage 3 disease. Changes in management were identified. *NMYC* status was available for 7/16 (44%) patients in cohort 1, and all in cohort 2. The chemotherapy was OPEC/OJEC before 2008, and modified N7 from 2008. MAT conditioning consisted of cisplatin, teniposide, doxorubicin and melphalan, with/without TBI (modified VAMP-TBI); TBI was omitted from 2009. 20/37 (54%) patients underwent MAT - 44% of cohort 1; 62% of cohort 2. There were 12/16 (75%) patients from cohort 1 and 10/21 (48%) from cohort 2 died of disease. Two died from sepsis. The 3-year overall survival was 18.8% (cohort 1) and 46.6% (cohort 2).



Conclusions: Although numbers were small, the trend was encouraging, and could be explained by multiple factors - regimes, surgery, supportive care, dedicated teams, uniform practices. We hope results will continue to improve with the availability in future of immunotherapy, MIBG therapy, novel agents or other modalities.

EP-370

THE ROLE OF P53/MDM2 PATHWAY ABNORMALITIES IN NEUROBLASTOMA PROGNOSIS

N. Svergun[1], G. Klymnyuk[2], N. Khranovska[1], O. Skachkova[1], M. Inomistova[1], S. Pavlyk[2], O. Shaida[2]

[1]Experimental Oncology Department, National Cancer Institute MPH of Ukraine, Kiev, Ukraine; [2]Children Oncology Department, National Cancer Institute MPH of Ukraine, Kiev, Ukraine

Objectives: Abnormalities in p53 pathway are present in 30-40% of neuroblastoma (NB) cases at diagnosis and occur predominantly by MDM2 hyperexpression and p14ARF inactivation. The aim of our study was to estimate the role of p53/MDM2 pathway abnormalities in neuroblastoma prognosis.
Methods: The case group comprised 84 patients with histologically confirmed NB (median age: 39.6 month; range: 1.5 – 204 months; I-II stages: 15; III-IV stages: 69; MYCN-amplified tumors: 27%). Patients were treated according to a risk groups under the international standard protocols. Primary tumor tissue obtained from patients at diagnosis was used for molecular-genetic analysis. TP53 deletion and MYCN gene amplification were detected by FISH method. The MDM2 gene expression level was analyzed by TaqMan real time RT-PCR.
Results: Deletion of TP53 was observed only in one case of NB (1.2%). MDM2 expression level increases proportionally to the stage of the disease ($p = 0.02$) with maximum value in stage IV. MDM2 expression level was higher in MYCN-amplified tumors than in those without MYCN amplification ($p = 0.02$). Primary resistant tumors had significantly higher levels of MDM2 gene expression compared to chemotherapy sensitive tumors ($p = 0.001$). ROC analysis revealed that MDM2 expression level is an important marker which is associated with event-free survival (EFS) of primary childhood NB patients (Se = 85.7%; Sp = 61.0%; AUC = 0.75; $p = 0.002$). Tumors were categorized into two groups (high or low MDM2 expression) based on cutoff point - optimal criterion, that was determined by ROC analysis. High MDM2 expression was associated with reduced EFS in NB patients. The 2-year EFS rate for NB patients with high MDM2 expression was 35% compared to 81% for patients with low MDM2 expression ($p = 0.001$).
Conclusions: Our results suggest the possibility that MDM2 is involved to the clinical behavior of NB. Inhibition of MDM2 can restore p53 activity and sensitize NB cells to chemotherapy-induced apoptosis.

EP-371

CLINICAL FEATURES AND TREATMENT OUTCOMES IN NEUROBLASTOMA PATIENTS: A SINGLE CENTER EXPERIENCE FROM TURKEY

F. Akici[1], D. Tugcu[1], G. Aydogan[1], Z. Salcioglu[1], A. Akcay[1], H. Sen[1], M. Gokce[1], G. Keskindemirci[1], B. Bilgic[2], S. Sander[3]

[1]Pediatric Hematology-Oncology, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey; [2]Pathology, Istanbul University Istanbul Medical School, Istanbul, Turkey; [3]Pediatric Surgery, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey

Objectives: Neuroblastoma is the most common extracranial solid tumor in childhood. Prognostic factors such as age, stage and cytogenetic profiles are used for risk stratification and treatment assignment.
Methods: In this study demographic data and clinical outcome of 129 neuroblastoma cases were evaluated and within those, therapeutic results of treated with the IPOG (before 2003) and TPOG (after 2003) protocol were compared.
Results: Median age was 24 months (1-106 months) (29.6 ± 23). Primary localization were abdomen in102 patients (most localization in surrenal 92), mediastinum in 15, cervical in 5, paraspinal in 7. According the INSS system, 13 (10%) patients were classified as stage I, 16 (12%) stage II, 29 (22.5%) stage III, 65 (50.5%) stage IV, 6 (5%) stage IVS. Most frequent sites of metastasis were bone marrow, bone and liver. Patients in advanced stage, received chemotherapy (26% patients modified 6-in-one chemotherapy, 12% patients OPEC, 50% patients Turkish Pediatric Oncology Group-TPOG Protocol, 12% patients no chemotherapy) $\pm$ radiotherapy (13%). Five and 10 year general survival were found to be 64 and 52% and disease free survival was 64 and 52% with 63 ± 73 months follow-up (1-272 months). Relapses were detected in 42 (33%) patients. The 5 year general survival was 43%, 5 yr EFS was 43% in ICOG group and 62%,62% in TPOG group. Event free survival was 67% under 18 months old and 47% upper 18 months old. There was significant diferantiation between these two groups ($p = 0.023$) Survival differed according to stage. Ten year general survival in stage I, I, III, IV was 100,100, 48, and 23% respectively. Ten year event-free survival in stage I, I, III, IV was 100, 100, 43, 23 respectively.
Conclusions: In conclusion; survival rates of neuroblastoma have improved over the last decade in our center.

EP-372

SIMULATION OF SPECT/MR ATTENUATION CORRECTION DEMONSTRATES POTENTIAL FOR UPTAKE QUANTIFICATION IN NEUROBLASTOMA

H.J. Wallace[1], M.S. Bradnam[1], A.A. Bolster[1], J. Foster[1], A. Watt[2], G.J. Irwin[2], H. Kaur[2], M. Ronghe[3], J. Sastry[3], D. Murphy[3]

[1]Department of Clinical Physics and Bioengineering, Greater Glasgow and Clyde Health Board & University of Glasgow, Glasgow, United Kingdom; [2]Radiology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [3]Oncology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom

Objectives: Neuroblastoma is an extremely heterogeneous neuro-endocrine cancer which requires a multitude of diagnostic tests, including imaging with ^{123}I-mIBG scintigraphy and MRI. An audit of RHSC mIBG clinical reports from 2013 suggested that quantification of radionuclide uptake would have been useful in 69% (18/26) of cases. One major confounder of accurate uptake quantification is photon attenuation. This can be corrected using non-uniform attenuation correction (AC) derived from SPECT/CT. However, CT introduces an additional radiation burden. An alternative approach would be to derive AC from MRI data. In PET/MR, Dixon-based sequences enable segmentation of soft tissues but lack the ability to discriminate cortical bone. The purpose of this study was to simulate and evaluate Dixon-based MRAC for SPECT, using a readily available SPECT/CT dataset; adult bone scans.
Methods: Eleven sequential bone SPECT/CT scans were selected from the GRI Nuclear Medicine database. Each CT dataset was segmented into five tissue types; air, lung, water-based soft tissue ('water'), adipose tissue and cortical bone. Adipose tissue and 'water' were assigned population averaged Hounsfield Unit values. Cortical bone was assigned the same value as 'water' to simulate a morphological filling process. Each MRAC SPECT reconstruction was then compared to the corresponding CTAC SPECT by visual assessment and voxel value analysis.
Results: Visual assessment identified no clinically significant changes in MRAC SPECT datasets. Voxel value analysis showed that SPECT uptake was reduced by 11% on average compared to CTAC.
Conclusions: MRAC produces qualitatively similar SPECT images to CTAC with an average reduction of radionuclide uptake of 11%. 10% is quoted in PET/MR literature as the threshold of clinical significance. In practice the use of more sophisticated atlas- or sequence-based approaches should enable the average voxel error to be further improved. Based on this study, MRAC is feasible for SPECT reconstruction and should provide a superior baseline SPECT scan for quantification of neuroblastoma without additional patient dose.

EP-373

LOCALLY ADVANCED CERVICAL NEUROBLASTOMA PRESENTING IN THE PRENATAL PERIOD

M. Weismiller[1], M. Cullen[2], J. Haouilou[3], A. Lorenzana[4]

[1]General Surgery, Providence Hospital and Medical Centers, Southfield, USA; [2]Pediatric Surgery, St. John Hospital and Medical Center, Detroit, USA; [3]Vascular Surgery, St. John Hospital and Medical Center, Detroit, USA; [4]Pediatric Hematology/Oncology, St. John Hospital and Medical Center, Detroit, USA

Objectives: To describe a locally advanced neonatal cervical neuroblastoma first detected on an antenatal ultrasound.
Methods: Congenital cervical neuroblastoma is extremely rare, representing less than one percent of all neonatal cases[1]. Most neonatal cases are stage 1 or stage 4S with small abdominal primaries. We describe a congenital cervical neuroblastoma identified on antenatal ultrasound at 29 weeks gestation and ultimately proven to be stage 2B.
Results: Postnatal urinary VMA (vanillylmandelic acid) was high at 117 mg/g (normal 27 mg/g) as was uHVA (homovanillic acid) at 78 mg/g (normal 42 mg/g). Postnatal ultrasound showed a 4.7 cm solid mass with calcifications. An MRI showed a mass extending from the thoracic inlet to the base of the skull. The mass compressed and involved surrounding structures including the carotid artery, trachea, thyroid and parotid gland (Figure 1). A complete resection with lymphadenectomy was performed. The tumor completely effaced and partially encased the common carotid artery (greater than 50 percent), carotid bifurcation, and internal and external jugular veins (75 percent). It displaced and compressed the trachea medially and elevated the parotid gland superiorly. The vagus nerve was encased but was preserved by capsular incision and meticulous neurolysis. Five lymph nodes were positive. The MKI (mitotic karyorrhetic index) was low, the DNA index was greater than one, and *N-myc* was non-amplified. A postoperative MIBG scan revealed asymmetric uptake in the left neck, felt to represent a salivary gland rather than metastatic disease. The tumor was classified as low risk and the infant will be followed by serial labs and examinations.
Conclusions: This represents a unique case of a locally advanced neonatal cervical neuroblastoma that was successfully treated with surgical excision without the need for chemotherapy.

EP-374

IRINOTECAN AND TEMOZOLAMIDE AS EFFECTIVE SCHEDULE IN PROGRESSIVE AND THERAPY RESISTANT NEUROBLASTOMA – EXPERIENCE OF POLISH PEDIATRIC SOLID TUMORS GROUP

A. Wieczorek[1], M. Stypinska[2], M. Hennig[3], M. Wieczorek[4], D. Januszkiewicz-Lewandowska[5], M. Zubowska[6], K. Peszynska-Bialczynska[7], G. Sobol-Milewska[8], M. Ussowicz[9], W. Balwierz[1]

[1]Pediatric Oncology/Hematology, Polish-American Institute of Pediatrics Jagiellonian University Med. Colleg, Krakow, Poland; [2]Pediatric Oncology, The Children's Memorial Health Institute, Warsaw, Poland; [3]Pediatrics Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland; [4]Pediatrics and Oncology, Chorzow Center of Pediatrics and Oncology, Chorzow, Poland; [5]Pediatric Oncology Hematology and Bone Marrow Transplantation, Medical University, Poznan, Poland; [6]Oncology Hematology and Diabetology, Medical University, Lodz, Poland; [7]Pediatrics Hematology and Oncology, Nicolaus Copernicus University in Torun Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland; [8]Pediatric Oncology Hematology and Chemotherapy, Medical University of Silesia Upper Silesia Children's Care Health Centre, Katowice, Poland; [9]Bone Marrow Transplantation Pediatric Oncology and Hematology, Medical University, Wroclaw, Poland

Objectives: Irinotecan/temozolamide (IT) chemotherapy (Kushner 2006) was evaluated as a possible therapy schedule in progressive or therapy resistant neuroblastoma (NBL) in patients treated in the centers of Polish Pediatric Solid Tumors Group.
The endpoints of the study were the best response to IT, overall and progression-free survival (OS, PFS), side effects and quality of life.
Methods: Patients treated from 2000-2012 were included (n = 697). Therapy failure was diagnosed in 194 (28%). IT was employed in 46 patients (1 stage 1, 1 stage 2, 5 stage 3, 1 stage 4s and 38 stage 4 at diagnosis), age 1-189 months at diagnosis. All patients were treated with previous chemotherapy. Seven patients had primary resistant disease, 28 the first and 11 at least second therapy failure. Four patients with additional vincristine were excluded. The objective response was observed in 38 patients (11 CR, 8 PR and 19 SD).
Results: The number of IT cycles in responding patients was 1-39 (median 6); 15 patients are alive (5 with CR, 3 with PR and 7 with SD). All received additional chemotherapy, 17 patients received HSCT (autologous in 9 and allogeneic in 8 cases, 7 of them with MIBG therapy), 10 – radiotherapy, 5 – 13-cis RA cycles and one immunotherapy. Mean OS was 44 months (12-172,7) and PFS from IT employment – 8,3 months (0,2-54 months). Adverse events were observed in 31 cases (67%). Diarrhea was present in 19 (41%) patients, cured with loperamid (only in 1 case atropine was necessary) and hematologic toxicities. Only 12 (26%) of patients required modifications in drugs dosage or frequency, all of them heavily pre-treated or with bone marrow involvement.
Conclusions: The chemotherapy was accepted by all patients and parents. Generally, patients did not require hospitalization between the cycles.
We found IT as effective therapeutic option both as intensive and palliative treatment.

EP-375

CLINICAL FEATURES AND PROGNOSTIC FACTORS IN CHINESE CHILDREN WITH NEUROBLASTOMA

X.Y. Yuan[1], X. An[1], Z. Tan[1], Q. Sheng[1], Q. Zhang[1], M.W. Jiang[2], Y.M. Wu[3]

[1]Pediatric Hematology/Oncology, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China; [2]Dept. Oncology/Radiotherapy, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China; [3]Dept. Pediatric Surgery, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China

Objectives: To explore the clinical features and prognostic factors in Chinese children with neuroblastoma (NB).
Methods: One hundred and three NB patients were registered in our hospital from Jan. 2007 to Dec. 2013. Their clinical data and prognostic factors were retrospectively analysed. Kaplan-Meier was used for survival analysis.
Results: Ninety-two newly diagnosed NB children were enrolled in this study. Their median age at onset was 32.3 months (2.0∼159.8 months), male to female ratio was 1.5. The median follow-up time was 32 months (12∼80 months). Five-year overall survival (OS) was $64.4\% \pm 5.6\%$, and event-free survival (EFS) was $53.4\% \pm 6.0\%$. Total fourteen recurrent cases were observed. The median interval from initial diagnosis to relapse was 13 months (4∼27 months) and 3y- OS after relapse was $42.9\% \pm 13.2\%$. The patients whose recurrent time was later than 18 months from diagnosis had a higher 3y-OS than those relapsed within 18 months ($83.3\% \pm 15.2\%$ vs $12.5\% \pm 11.7\%$, $P = 0.007$). Among 29 deaths, the leading cause was severe chemotherapy -related infection (17/29, 58.6%), followed by death due to tumor progression (10/29, 34.5%). Univariate analysis revealed that the INSS stage III and stage IV, high-risk and very high-risk, LDH >500 U/L, bone metastases, N-MYC amplification were negative prognostic factors. Multivariate analysis suggested that only INSS stage and N-MYC amplification were independent prognostic factors.
Conclusions: INSS stage and N-MYC amplification were independent prognostic factors for Chinese Children with NB. Death caused by severe chemotherapy-related infection should be paid more attention. The patients who relapsed within 18 months after diagnosis had inferior prognosis, but patients with stage I or II or recurrence in situ could acquire a long-term survival after being treated timely.

EP-377

REPORT ON LONG-TERM FOLLOW-UP OF STAGE 4 NEUROBLASTOMA

A. Zhang[1], J.Y. Tang[1], C. Pan[1], Q.D. Ye[1], M. Zhou[1], J. Chen[1], C.Y. Luo[1], J.M. Wang[1], Y.J. Tang[1], H.L. Xue[1], S.H. Shen[1]

[1]Hematology/Oncology, Shanghai Children's Medical Center Medical College of Shanghai Jiaotong University, Shanghai, China

Objectives: To evaluate the long-term outcomes of childhood stage 4 Neuroblastoma (NB) and its correlative prognostic factors.
Methods: Comprehensive protocols including tumor resection, intensive chemotherapy, radiotherapy, ABMT and 13-cis-retinoid were designed and put into practice. Total 112 NB stage 4 patients in Shanghai Children's Medical Center collected from June 1998 to December 2010 were treated according to comprehensive protocols. The clinical features, therapeutic effects over different periods, long-term outcomes and prognostic factors were analyzed.
Results: Among 112 patients, 12 patients didn't complete treatment because of the parents' decision although the patients turned to become better. The rest completed the protocols, in which 62 cases (62.0%) achieved verygood partial remission (VGPR), 20cases (20.0%) achieved partial remission (PR), but another 18 cases (18.0%) progressed during the treatment. The efficiency rate (including VGPR+PR) of treatment was 82.0% (82cases). The median follow-up period was 78 months (39 -153).13 cases of patients were lost after a median follow-up of 16 months. The 2-,3-,5 year event free survival (EFS) Of all patients was 56.2%,40.8%,21.1%, respectively. Age (>18 months), poor curative effect (fail to achieve VGPR at the end of treatment), high levels of LDH (> 5-times the normal value), bone marrow involvement were poor prognostic factors. (chi = *12.01,13.66,6.29,5.44, all* $P < 0.05$). As to the multivariate estimates of hazards, age, poor curative effect, high levels of LDH were associated with a worse survival (*OR = 3.44,3.32,1.76, all* $P < 0.05$). Brain metastasis predicted a worse outcome with 100% death rate. Compared to the traditional chemotherapy, Topotecan included chemotherapy could not improved the efficiency (52.6% vs 63.2%, $P = 0.416$) and long-term outcome (2 year EFS 42.1% vs 56.4%, $P = 0.487$) of stage 4 NB.
Conclusions: The prognosis for neuroblastoma of stage 4 remains poor. Age (>18 months), poor curative effect, high level of LDH (> 5-times the normal value), bone marrow infiltration were associated with worse prognosis. Brain metastasis predicted the worst with 100% death rate. Topotecan included chemotherapy could not be proved more effective in this study.

EP-378

CLINICAL EFFICACY ANALYSIS OF 16 CASES OF INFANT NEUROBLASTOMA

Y. Zhang[1], W. Zhang[1], D. Huang[1]

[1]Pediatric, Beijing Tongren Hospital Capital Medical University, Beijing, China

Objectives: The purpose of this paper is the analysis of clinical characteristics and clinical efficacy of Nb less than 1-year old.

Methods: 16 cases of infant Nb confirmed and diagnosis using pathology or / and imaging from February 2007 to August 2013. 10 cases of male and 6 cases of female. The median age was 9.5 months.1 case of 1 stage, 7 cases of 4 stage, 8 cases of special 4s stage. Combining chemotherapy and operation. Statistic Analysis of the primary site, and the first symptom characteristics, and the level of serum NSE, and the chemotherapy efficacy, and the prognosis.
Results: (1) 5 cases of less than 3 months old accounting for 31.25%; 2 cases of 3-6 month old, accounted for 12.5%; 9 cases of 6-12 months old, accounting for 56.25%. (2) In all of patients, 15 cases of middle risk group accounted for 93.75%, 1 cases of high risk group accounted for 6.25%. (3) all of 16 cases were higher than normal while diagnosis, reached 100%, and the median of the level of serum NSE was 59.95mg/dl (17.48∼264mg/dl). After the treatment, 3 cases of slightly higher than the normal accounting for 18.75%, 1 case of decreased significantly accounted for 6.25%, 12 cases of decreased to normal level accounting for 75%. (4) follow up to February 2014, except for 1 case of treating, 15 cases for followed-up. In 15 cases, 14 cases achieved complete remission (CR) and accounted for 86.67%, and 2cases achieved partial remission (PR) and accounted for 13.33%. Overall survival rate was 100% (15/15).
Conclusions: Infant Nb sensitive to chemotherapy. the disease incidence rate of stage 4S in infant Nb is high. Remisson rate and prognosis of infant Nb after comprehensive treatment was high.

EP-379

CHROMOSOME ANALYSIS OF NEUROBLASTOMA IN CHILDREN

O. Zhao[1], D. Zhang[1]

[1]hematology-oncology center, Beijing children's hospital, Beijing, China

Objectives: To study the clinical features and prognosis of 55 children with neuroblastoma acorrding to their chromosome status in our hospital, and analyze the relationship between the chromosome status and characteristics and the short-term curative effect. Improving the understanding of neuroblastoma with chromosomal abnormalities.
Methods: The clinical characteristics, treatment and survival status of 55 children with neuroblastoma were retrospectively analysed, and with review of literature.
Results: There was a total of 5 patients with chromosomal abnormalities among 55 cases which were adopted in our hospital, including 4 cases with 17q gain, 1 case with both 17q gain and 1p deletion, and no abnormalities were found in the rest. Tumor markers in 5 cases with chromosomal abnormalities were elevated in different range, Serum NSE was 280 ± 18ng/ml, which was higher than 125 ± 12ng/ml in neuroblastoma children with normal chromosome; All 5 cases with chromosomal abnormalities had MYCN gain; During treatment, 1 case was lost of follow-up, 2 cases progressed, 1 case died, the rest one with both 17q gain and 1p deletion was complete remission after regular chemotherapy, surgery and autologous peripheral blood stem cell transplantation, followed-up with 33 months in out-patient. The different EFS rate was found in patients with different chromosome status, a 2-year EFS rate was higher in normal chromosome group than abnormal group, P value <0.05.
Conclusions: Based on our cases and relevant literatures shows that: 17q gain and 1p deletion were risk factors in neuroblastoma, there was certain clinical significance in the diagnosis and evaluation of prognosis in neuroblastoma. But in our research, the positive rate of abnormal chromosome with conventional detect method is lower than previous report, it is considered to be related with methodology which needs further improvement.

EP-380

THE LEVEL AND CLINICAL SIGNIFICANCE OF TH1/TH2 CYTOKINES IN SERUM OF CHILDREN NEUROBLASTOMA

W. Zhao[1]

[1]hematology department, Beijing Children's Hospital Capital Medical University, Beijing, China

Objectives: To study the levels of Th1 and Th2 in children with neuroblastma (NB) and their relation to clinical stages, to provide the basis for immunomodutatory and supportive therapy in the NB chemotherapy.
Methods: The study enrolled children with the new NB patients treated in our hospital from November 2011 to December 2012. The level of Th1 type cytokines include interleukin-2 (IL-2), interferon-γ, (IFN-γ), tumor necrosis factor-α (TNF-α) and Th2 include interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10). Th1/Th2 cytokines in serm were detected by flow fluorenscence immunmicrobeads assay (FFIA) from 66 children of high risk and 22 children of low and medium risk with NB.
Results: The level of Th1 type cytokines such as IL-2 were significantly lower in patients of high risk than low and medium risk with NB ($P < 0.05$). IFN-(were lower in patients of high risk than low and medium risk with NB, but there was no statistically significant differences ($P = 0.076$). The level of TNF-α were significant higher than low and medium risk with NB patients ($P = 0$). The level of Th2 type cytokines such as IL-4 and IL-6 were higher in patients of high risk than low and medium risk with NB, but there was no statistically significant differences (IL-4, $P = 0.058$. IL-6, $P = 0.078$). The level of IL-10 patients were significant higher than low and medium risk with NB patients ($P < 0.05$).
Conclusions: Th1/Th2 was imbalance in children with NB. Th1 type cytokines were inhibited and Th2 type cytokines were relatively enhanced, so Th1/Th2 shift to Th2. With the increase of risk, the trend was more obvious. Serum levels of Th subsets may be related to immune functiongs of lung cancer patients and be a good sign of prognosis.

NEW DRUGS/EXPERIMENTAL THERAPEUTICS

EP-381

EFFECTS OF ZEBULARINE ALONE OR IN COMBINATION WITH THE HISTONE DEACETYLASE INHIBITOR SAHA ON MEDULLOBLASTOMA CELLS

A.F. Andrade[1], K.S. Borges[1], V.K. Suazo[2], A.M. Castro-Gamero[2], C.A. Scrideli[2], L.G. Tone[1]

[1]Genetics, Ribeirão Preto Medical School - USP, Ribeirão Preto, Brazil; [2]Pediatrics, Ribeirão Preto Medical School - USP, Ribeirão Preto, Brazil

Objectives: Medulloblastoma (MB) is an aggressively growing tumor, arising in the cerebellum, and is the most common malignant one in children. Current treatment cures reaches about 50-80% of patients however approximately 40% of children experience tumor recurrence, and 30% will die from their disease. Thus new approaches are urgently needed. Drug combination using inhibitors of DNA methyltransferases (iDNMTs) and histone deacetylase (iHDAC) have shown antineoplastic effects in different tumors. Zebularine (ZB) blocks DNA methylation by inhibiting DNA methyltransferases activity and exhibits minimal cytotoxicity both *in vitro* and *in vivo*. However, its effects on MB have not been previously reported. This study aimed to investigate the anti-cancer efficacy of ZB alone or in combination with SAHA *in vitro* using MB cell lines.
Methods: The effects of ZB alone or in combination were evaluated by cell viability, clonogenic and apoptosis assays on MB cells UW402 e UW473. Combined-effects analyses were conducted according to the median-effect principle established by Chou and Talalay. Drug combination analyzes using two different schedules of administration (simultaneous and sequential) were performed. Statistical analysis was performed by one- and two-way ANOVA and Bonferoni post-hoc.
Results: ZB decreased cell proliferation and clonogenic capacity in all cell lines in a time- and dose-dependent manner, respectively ($P < 0.05$). The drug increased apoptosis rate. The combination index values of the ZB and SAHA treatments were all greater than 1, indicating that the two agents induced antagonistic effects on the MB cells, independently of the schedule used.
Conclusions: Administered alone, both ZB and SAHA exert anti-tumoral activity on *in vitro* MB cells. The ZB and SAHA combination treatment produces antagonistic, rather than synergistic, effects. Further studies are being conducted with different drug combination schedules, aiming to better characterize the effects of this combination.
Financial Support: FAPESP (process 2011/22440-7)

EP-382

SIROLIMUS FOR THE TREATMENT OF VASCULAR ANOMALIES

C. Akyuz[1], H. Susam Sen[1], B. Aydin[1], B. Oguz[2], T. Kutluk[1], B. Yalcin[1], A. Varan[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey; [2]Radiology, Hacettepe University- Faculty of Medicine, Ankara, Turkey

Objectives: Vascular anomalies (VA) are heterogeneous group of benign disease which require multidisciplinary treatment approach. "Mammalian target of rapamycin" (mTOR) inhibitor Sirolimus has been recently used in the treatment of VA and successful results have been reported. In this study, clinical characteristics and outcome of patients with VA treated with Sirolimus were evaluated.
Methods: Files of 21 patients with VA who was treated with Sirolimus were analyzed retrospectively for clinical features and treatment results. The patients were diagnosed either radiologically or histologically after biopsy.
Results: The median age of 14 males and 7 females at diagnosis was 5 years (ranged 3 days - 13 years). Patients were given Sirolimus at a median age of 8 (ranged 2 months - 13 years). The sub-types were venolymphatic malformation in 7, lymphangioma in 6, vascular malformation in 3, venous malformation in 2, Gorham Stout syndrome in 2 and Blue rubber bleb nevus syndrome in 1 patient. Most of the patients (18/21) received at least one previous treatment. Sirolimus were given for 1 to 24 months (median 6 months). The most frequent clinical responses were improvement in pain, feeding and exercise capacity, reduction in hospitalizations, tracheostomy closure and extubation. Clinical and radiological response was between 50-90% in 7 patients and less than 50% in 8 patients. There was no response in 6 patients radiologically. Five patients had oral aphthous lesions and 4 patients had hyperlipidemia during treatment. Both side effects were mild and reversible.
Conclusions: Sirolimus can be used effectively and reliably in patients with VA who were refractory to previous therapies with acceptable toxicity.

EP-383

PROMISING USE OF SIROLIMUS IN PROLIFERATIVE DISORDERS

M.Y. Chan[1], S.Y. Soh[1], K. Chang[2], A.M. Tan[1]

[1]Paediatric Subspecialties, KK Women's and Children's Hospital, Singapore, Singapore; [2]Pathology, KK Women's and Children's Hospital, Singapore, Singapore

Objectives: Mammalian target of rapamycin (mTOR) signaling stimulates cell growth and is inhibited by rapamycin, a naturally occurring antifungal compound first discovered on Easter Island. Rapamycin (or Sirolimus) has been used as an immunosuppressant in kidney transplants but is also known recently to reduce proliferative tumours on harmartoma syndromes and refractory vascular anomalies, with few serious adverse side effects. We describe our experience in the use of Sirolimus in a variety of proliferative disorders.
Methods: Five patients were put on Sirolimus according to an institutional protocol from June 2012. The latest patient was recruited in January 2014. The diagnoses were Gorham's disease (2), metastatic haemangioendothelioma, lymphangiomatosis and extensive inflammatory myofibroblastic tumour (IMT). All patients had failed a variety of therapies before they were offered Sirolimus. Monthly Sirolimus blood levels were kept between 5 to 15 ng/ml. Monthly full blood counts, renal panel, liver function, fasting lipids and urinary total protein were monitored. Prophylactic cotrimoxazole was given.
Results: Out of the 5 patients, 1 (metastatic haemangioendothelioma) showed near complete response, 1 (Gorham's) showed good response, 1 (Gorham's) showed stable disease, 1 (extensive IMT) showed possible partial response while the latest patient recruited cannot be assessed as yet. Their ages range from 1.2 to 16.8 years at the time of treatment. Interestingly the patient with IMT also had chronic ITP which responded to Sirolimus with platelets normalising after 3 months. Two patients had transient hypercholesterolaemia and 1 had transient proteinuria. One patient had mucositis which, together with cost issues, caused her to stop treatment after 9 months. Treatment was otherwise well tolerated. As of 28th February 2014, the duration of treatment ranged from 2 to 20 months.
Conclusions: Sirolimus shows promising results in the treatment of proliferative disorders refractory to other therapies. It is well tolerated, however long term effects on young children have not been determined.

EP-384

ANTITUMOR ACTIVITY OF A NOVEL S1P2 ANTAGONIST AB1

M.H. Li[1], R. Swenson[2], T. Hla[3], L. Shapiro[1], F. Ferrer[4]

[1]Center for Vascular Biology, University of Connecticut Health Center, Farmington, USA; [2]Drug Discovery, Arroyo Biosciences LLC, Princeton, USA; [3]Department of Pathology and Laboratory Medicine, Weill Medical College of Cornell University, New York, USA; [4]Department of Surgery/Center for Vascular Biology, Connecticut Children's Medical Center/University of Connecticut Health Center, Hartford/Farmington, USA

Objectives: The bioactive lipid sphingosine-1-phosphate (S1P) and its receptors ($S1P_{1-5}$) play critical roles in many pathological processes including cancer. The S1P axis is becoming a potential therapeutic target. JTE-013 is a literature standard $S1P_2$ antagonist with potential instability *in vivo*. Through its structure modification, we try to develop more specific and more stable JTE-013 analogs.
Methods: FLIPR assay was conducted to assess the agonism/antagonism of JTE-013 analogs against $S1P_{1-5}$. Pharmacokinetic analysis was performed to detect their blood concentrations in mice over different time. Migration assay in glioblastoma (GB) and neuroblastoma (NB) xenograft model were utilized to compare the biological efficacy between JTE-013 and its analogs. Western blot and real-time PCR were performed to compare their efficacy on modulating the expression of $S1P_2$ downstream molecules such as p-Akt, p-ERK, VEGF and CTGF.
Results: One of the JTE-013 analogs, AB1, exhibited better $S1P_2$ antagonism effect compared to JTE-013, with an IC50 of 3.5 nM versus 11 nM of JTE-013. Intravenous pharmacokinetics showed that the blood concentration of AB1 in mice remained higher than that of JTE-013 over 12 hours, indicating better stability or slower clearance of AB1 *in vivo*. Migration assay in GB showed that AB1 was more potent than JTE-013 to either reverse S1P-mediated cell migration inhibition in $S1P_2$-predominant U118 cells or further enhance S1P-stimulated cell migration in $S1P_1$-predominant U87 cells. In a NB cell line SK-N-AS, AB1 displayed at least the same potency as JTE-013, in reversing S1P-mediated p-Akt inhibition and inhibiting S1P-mediated p-ERK activation, and in inhibiting S1P-induced VEGF and CTGF expression. Further, in SK-N-AS cell-based xenograft tumor model, AB1 displayed stronger tumor inhibition effect compared to that of JTE-013.
Conclusions: AB1 has improved potency and intravenous pharmacokinetics, better cellular activity, and displays stronger anti-tumor activity compared to JTE-013 in NB, and may have enhanced clinical applicability.

EP-385

DATABASE OVERVIEW FOR INFORMATION RETRIEVAL OF EXPRESSION LEVELS FOR THE BRIC 7 GENE IN TUMORS :NEUROBLASTOMA, MEDULLOBLASTOMA, RHABDOMYOSARCOMA, EWING-SARCOMA AND LEUKEMIA

J. Kapelushnik[1], A. Manor[2], I. Plaschkes[3], V. Caspi[3]

[1]pediatrics hemato oncology, Ben Gurion University of The Negev, Beer-Sheva, Israel; [2]genetics, Ben Gurion University of The Negev and Sorka medical center, Beer-Sheva, Israel; [3]genetics, Ben Gurion University of The Negev and Bioinformatics Core Fcility, Beer-Sheva, Israel

Objectives: Newcastle disease virus (NDV) is an avian paramyxovirus that has a potential selective oncolytic effect on human tumors. It is shown that Newcastle virus (NDV-HUJ, a one-cycle replicating virus), overcomes the resistance to apoptosis of melanoma primary cultures that over express the Livin protein. In contrast, melanoma tumor cells that do not express Livin are relatively resistant to NDV-HUJ treatment. NDV-HUJ is a potent inducer of apoptosis that can overcome the antiapoptotic effect of Livin and allow cleavage of Livin into the proapoptotic tLivin. The over expression of Living protein in tumor can predict the oncolysis effects of Newcastle virus protein.
Methods: We have searched Gene Expression Database GEO for microarray experiments which description contains the name of one of the requested cancer types: Neuroblastoma, medulloblastoma, Rhabdomyosarcoma and EWING-sarcoma.
The retrieved experiments were searched for the BIRC7 gene, and the gene expression profile was either taken from the pre-calculated "GEO profiles" (if available), or calculated and visualized using the GEO2R tool.
Results: Medulloblastomas (from children ages 3 to 16 years): 24 of 72 expressions of the gene were above the background and only 3 of 72 have very high expression. In Neuroblastoma cell line: One of 4 cell lines has expression of brich 7 gene. In Glioblastoma (GBM) :10 of 27 with expression of the gene. Rhabdomyosarcoma in (mice): Only 1 of 4 has expression of the gene. Ewing sarcoma family: 10 of 44 with expression of the gene. Leukemia in children: More than 600 patients were checked for the gene. Most children with good risk leukemia (etv6-runx1) with higher expression of the gene
Conclusions: Higher expressions of Bric 7 gene in brain tumors frequently in GBM than other tumors. All higher expressions resulted in good prognosis in leukemia. We are currently investigating the gene expression in children who contracted the Newcastle virus.

EP-386

THE VECTORIZED ANTI-CANCER DRUG F14512 DEMONSTRATES A HIGHER PRECLINICAL ACTIVITY IN NEUROBLASTOMA THAN IN PEDIATRIC GLIOMA CELL LINES: FIRST DATA IN PEDIATRIC ONCOLOGY

P. Leblond[1], E. Boulet[2], C. Bal-Mahieu[2], A. Pillon[3], A. Kruczynski[3], N. Guilbaud[3], C. Bailly[3], E. Lartigau[4], A. Lansiaux[2], S. Meignan[2]

[1]Pediatric oncology, Centre Oscar Lambret and INSERM U837, Lille, France; [2]Antitumoral Pharmacology Laboratory, Centre Oscar Lambret INSERM U837 and IRCL, Lille, France; [3]Research and Development Center, Pierre Fabre, Toulouse, France; [4]Radiotherapy, Centre Oscar Lambret, Lille, France

Objectives: The prognosis of children with high grade glioma (HGG) and high risk neuroblastoma remains poor despite aggressive multidisciplinary therapeutic approaches. F14512 combines an epipodophyllotoxin core-targeting topoisomerase II with a spermine moiety introduced as a cell delivery vector. This spermine moiety facilitates selective uptake by tumor cells *via* the Polyamine Transport System (PTS) and reinforces topoisomerase II poisoning.
Methods: F14512 was evaluated in three pediatric HGG and four neuroblastoma cell lines. PTS activity and specificity were evaluated by confocal microscopy and flow cytometry using the fluorescent probe F17073 which contains the same spermine moiety as F14512. Cytotoxicity of F14512, alone or in association with cisplatin, carboplatin, melphalan, and radio-sensitizing effects were investigated *in vitro*. The antitumor activity of F14512 was assessed *in vivo* using a bioluminescent liver-metastatic neuroblastoma model.
Results: An active PTS was evidenced in all tested pediatric cell lines, providing a specific and rapid transfer of spermine-coupled compounds into cell nuclei as assessed in three neuroblastoma cell lines. Competition experiments with spermine confirmed the essential role of the PTS in the cell uptake and cytotoxicity of F14512. This cytotoxicity appeared greater in neuroblastoma compared to HGG cells but seemed independent from the PTS activity levels. Interestingly, F14512 presented a significant higher cytotoxic effect than etoposide (lacking the spermine chain). *In vivo* evaluation confirmed an important and prolonged antitumoral effect in neuroblastoma. The combinations of F14512 with cisplatin and carboplatin were found to be often synergistic, and combinations with melphalan appeared various. Finally, we demonstrated the significant radio-sensitizing potential of F14512 in the MYCN-amplified Kelly cell line.
Conclusions: F14512 appears more effective than etoposide in pediatric tumor cell lines, with a higher efficacy in neuroblastoma cells. The synergistic effects observed with platinum compounds and its radiosensitizing effect could lead to a great potential development in pediatric oncology.

EP-387

RESVERATROL INDUCES APOPTOSIS OF MEDULLOBLASTOMA CELLS WITHOUT AFFECTING ASTROCYTES AND NEURONS

X.H. Shu[1], X.X. Sun[1], H. Li[1], X. Song[1], L.L. Wang[1], S. Shi[1], J. Liu[1]

[1]Liaoning Laboratory of Cancer Genetics and Epigenetics and Department of Cell Biology, Dalian Medical University, Dalian, China

Objectives: Medulloblastoma is a lethal pediatric brain malignancy due to aggressive growth and frequent recurrence. Adjuvant therapies are employed to prevent cancer relapse but cause long term side effects. Resveratrol in 100mM and 150mM induces differentiation and leads medulloblastoma cells to growth arrest and apoptosis. This study aims to further prove the practical values of resveratrol by evaluating the effects of resveratrol on normal brain cells.
Methods: The glial cells and neurons were isolated from the fetal rat brains after getting the permission of Experimental Animal Warfare Committee of Dalian Medical University. They were separately cultured under optimal conditions for 7 days and then treated by 100mM or 150mM resveratrol for 96 hours. The morphology of the treated cells was checked in 12 hour intervals and the cell bearing coverslips were collected at each of observation points for immunocytochemical, MTT and TUNEL analyses. Resveratrol-treated UW228-3 medulloblastoma cells were cited as control.
Results: Unlike UW228-3 cells, rat glial cells and neurons have little response to resveratrol treatment because the proliferation rates and/or morphology of resveratrol-treated cells are similar with that of their normally cultured counterparts. STAT3 is expressed in both glial cells and neurons but lack of nuclear translocation and its level is not altered by resveratrol. Nuclear labeling of STAT3 is evidenced in UW228-3 cells and becomes diminished upon resveratrol treatment accompanies with extensive apoptosis.
Conclusions: The safety of the effective anti-medulloblastoma doses of resveratrol for rat glial cells and neurons is confirmed, presumably due to the inactivated status of resveratrol targeted STAT3 signaling in those cells. Therefore, this non-toxic compound would be useful in the clinical treatment of medulloblastomas.
A*cknowlegement
This work is supported by the grants of Natural Science Foundation of China (Nos. 81272786 and 30971038) and Research Fund for PhD supervisors from Education Department of China (20122105110005).

EP-388

DHMEQ IN PEDIATRIC MEDULLOBLASTOMA CELL LINES

P.M.M. Ramos[1], J.A. Pezuk[1], A.M. Castro-Gamero[1], C.A. Scrideli[2], K. Umezawa[3], L.G. Tone[2]

[1]Genetics, Ribeirão Preto Medical School - USP, Ribeirão Preto, Brazil; [2]Pediatrics, Ribeirão Preto Medical School - USP, Ribeirão Preto, Brazil; [3]Molecular Target Medicine Screening, Aichi Medical University, Aichi, Japan

Objectives: Medulloblastoma is a pediatric cancer of the central nervous system, highly invasive, of embryonic origin, located in the cerebellum. The most common treatments are surgery and chemotherapy, and radiotherapy is only tochildren older than 3 years old due to its side effects. NF-κB is a key transcription factor in the regulation of immune response and inflammation process, and it is involved in the transcriptional regulation of a large number of genes related to the tumorigenesis process, and constitutively active in many types of cancer, being an important potential therapeutic target. DHMEQ (Dehidroximetilepoxiquinomicina) is a drug that inhibits the translocation of NF-(B from the cytoplasm to the nucleus, thus inhibiting its activity as a transcriptional activator. Several studies have shown the antineoplastic effects of DHMEQ in numerous tumor types, however, there is no surveys that have tested their effects in medulloblastoma.
Methods: The present study evaluated the effects of DHMEQ in UW402, UW473 and ONS-76 pediatric medulloblastoma cell lines through proliferation, clonogenic capacity, apoptosis, invasion and migration assays, besides drug combination and radio sensitization assays.
Results: The proliferation test results demonstrated a significant decrease in the cell growth, strongly inhibition of the clonogenic capacity and the migration and cell invasion in the three medulloblastoma cell lines. Additionally, increased the level of apoptosis, it was synergistic in combination with other chemotherapeutic agents in most combination points, and radiosensitization strongly the three cell lines.
Conclusions: The results are congruent with the potential antitumor effect of DHMEQ and pointed clearly the possible use of it as new therapeutic agent to medulloblastoma treatment.

EP-389

ROLE OF WNT/ß-CATENIN PATHWAY IN THERAPY RELATED MYELOID NEOPLASMS (T-MDS/T-AML) WITH 5Q DELETION: A NEW THERAPEUTIC TARGET

N. Mittal[1], A. Seba[2], Z. Qian[3]

[1]Pediatric Hematology Oncology, University of Illinois, Chicago, US; [2]Medicine Division Hematology/Oncology, University of Illinois, Chicago, US; [3]Medicine, University of Illinois, Chicago, US

Objectives: Successful therapy for pediatric malignancies has led to rise in incidence of t-MDS/t- AML. Del (5q) is a recurring cytogenetic abnormality in approximately 25% of pediatric t-MDS/t-AML. With current therapies 5 yr survival is only 25%. Del (5q) is associated with haplo-insufficiency of APC gene in hematopoietic stem cells (HSCs) which leads to MDS-like disease in mice. APC regulates the function of HSCs through (-catenin dependent mechanisms. Our objective is to show effects of Wnt/(-catenin pathway blockade on del (5q) leukemia.
Methods: The expression of β-catenin is higher in UoCM1 [human myeloid leukemia cell line with del (5q)] versus REH [lymphoid line without del (5q)]. We treated UoCM1 and REH cells with 100uM Indomethacin. Lentiviral particles expressing a control empty backbone or (-catenin targeting inhibitory shRNA were transduced into UoCM1 and REH and β-catenin knockdown achieved. The cells were analyzed for effects on growth, cell cycle and apoptosis. In vitro colony forming assay was performed.
Results: UoCM1 cells showed significant more growth inhibition compared to REH with Indomethacin ($p < 0.05$). β-catenin inhibition with treatment was confirmed. UoCM1 cells transduced with β-catenin shRNA showed 60% growth inhibition compared to control vector. In contrast, REH demonstrated comparable growth in control and β-catenin shRNA transduced cells. There was a decrease in the S and G2/M fractions and increase in apoptosis ($p < 0.05$) in UoCM1 cells with β-catenin inhibition compared to control. REH showed no difference in distribution in cell-cycle and similar frequency of apoptosis in inhibited and control cells. Decrease in colony formation was observed in UoCM1 cells with β-catenin inhibition.
Conclusions: Chromosome 5q del leads to up-regulation of β-catenin. Blockade of Wnt/β-catenin pathway suppresses cell growth and induces apoptosis in a myeloid leukemia cell line with del (5q). This discovery paves the way for new therapeutic strategies targeting β-catenin and improving survival in del (5q) t-AML/MDS.

EP-390

DECITABINE ENHANCES CYTOTOXIC EFFECT OF OTHER ANTI-LEUKEMIC AGENTS SYNERGISTICALLY IN ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINE

K. Sakaguchi[1], H. Takahashi[1]

[1]Department of Pediatrics, Hamamatsu University School of Medicine, Hamamatsu, Japan

Objectives: We examine the combined effects of decitabine (DAC) and anti-leukemic agents such as clofarabine (CLO) and etoposide (ETO) on the Acute Lymphoblastic Leukemia (ALL) cell line CCRF-CEM.
Methods: We measured *in vitro* drug sensitivity of DAC, CLO, ETO, DAC+CLO and DAC+ETO on CCRF-CEM, using MTT assay. The combination Index (CI) was produced with Calcusyn® software. We also assayed with caspase-3/7 to detect apoptosis. Using RQ-PCR in CCRF-CEM cells, we examined mRNA expression levels for the pro-apoptotic genes *BAK*, *BID*, *BAX*, *BAD*, *BIM*, *PUMA*, *ATM*, *TP53*, and *NOXA*, as well as those for the anti-apoptotic genes *BCL2*, *BCL2L1*, and *XIAP*. The expression level of each target gene was calculated by normalizing it to *GAPDH*. We then analyzed the methylation status of these genes after 48 hours incubation with or without DAC.
Results: IC50 for ETO, ETO+DAC, CLO, and CLO+DAC was 3.36, 0.625, 4.96, and 1.92, respectively. The CI was 0.026 for ETO+DAC and 0.431 for CLO+DAC. We observed greater caspase-3/7 activity with DAC + CLO and DAC + ETO than with CLO and ETO. We observed DAC increased mRNA expression levels of *BAX* and *NOXA*, but decreased those for *BAK*, *BID*, *PUMA*, *BCL2L1*, *ATM*, *TP53*, and *XIAP*. Methylation status of *BAK*, *NOXA*, *BCL2L1* and *XIAP* incubation with DAC was 1.3%, 3.3%, 2.5% and 72.9%, respectively and incubation without DAC was 1.9%, 3.6%, 0.7% and 92.3%, respectively.
Conclusions: Our results showed that DAC synergistically enhances CLO and ETO cytotoxicity, and this cytotoxic effect depends on caspase-3/7 activity. We found that DAC decreased some pro-apoptotic genes, such as *BAK*, *BID*, *PUMA*, *ATM*, and *TP53*. Our results show that DAC did not demethylate the CpG of *BAK*, *NOXA*, *BCL2L1*, or *XIAP*. Thus, DAC must demethylate the CpG of other genes. Nevertheless, many genes are involved in apoptosis, and it remains unclear which genes are demethylated by DAC.

EP-391

ANTITUMOR ACTIVITY OF INDISULAM ON PEDIATRIC AND ADULT GLIOBLASTOMA CELL LINES AND XENOGRAFT TUMORS

C.A. Scrideli[1], S.A. Teixeira[1], J.A. Pezuk[2], A.F. Andrade[2], M.S. Brassesco[2], V.K. Suazo[1], C.A. Carlotti Jr[3], E.M. Rego[4], C.L.A. Silva[4], R.P.Q. Gomes[1], L.G. Tone[1], C.A. Scrideli[1]

[1]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [2]Genetics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [3]Surgery, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [4]Internal Medicine, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil

Objectives: Glioblastoma (GBM) is the most aggressive form of brain cancer, with a dismal prognosis in children and adults. Carbonic anhydrases isoforms 9 and 12 (CA9/12) are highly overexpressed in many types of cancer including GBM. The aim this study was to evaluate the effects of inhibition of the CAs 9/12 by Indisulam (a novel anticancer drug with potent inhibition of CAs) *in vitro* and *in vivo* models.
Methods: In this study, we investigated the effects of the inhibition of CA9/12 by Indisulam on cell survival in 9 pediatric and adult GBM cell lines. The cell lines were cultured in conditions of hypoxia (1%) and proliferation, cell cycle, apoptosis were evaluated. The *in vivo* antitumor and chemo-sensitizing effects of Indisulam were assessed in Swiss nude mice ($n = 6$ by group) inoculated with the GBM cell line U-87. Indisulam was administered by different treatment approaches. Tumor growth and potential treatment toxicity were monitored.

Results: CA 9/12 inhibition *in vitro* significantly reduced proliferation in dose-time dependent ($p < 0.05$) with G2/M arrest when compared with control and increased apoptosis upon hypoxia exposure. Moreover, concurrent combination with temozolamide (TMZ) inhibited cell growth in all cell lines, as determined by proliferation. Results of animal tests using human tumor xenograft indicated that Indisulam significantly reduced the growth of tumors (66-84%, $P < 0.05$). Pretreatment with Indisulam equally sensitized cells to chemotherapy with TMZ and leads to 96-98% reduction in xenograft tumor volume ($P < 0.05$). No differences were observed with TMZ alone when compared with controls.
Conclusions: This study provides evidence of the therapeutic potential of Indisulam as a chemo-sensitizing agent in drug-resistant tumor cells and might, therefore, be an attractive treatment strategy in GBM.

EP-392

SUCCESSFUL MANAGEMENT OF LYMPHATIC MALFORMATION OF THE TONGUE USING SIROLIMUS

S. Yesil[1], C. Bozkurt[1], G. Tanyildiz[1], M.O. Candir[1], S. Tekgündüz[1], S. Toprak[1], G. Sahin[1]

[1]Pediatric Oncology, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey

Objectives: Lymphatic malformation is a congenital malformation and can lead to significant disfigurement from soft tissue hypertrophy and skeletal overgrowth, bony abnormalities, and/or infection. Treatments for removal include surgical resection and a variety of sclerosing agents. In this report, we present a novel approach to treatment of lymphatic malformation of the tongue using sirolimus.
Methods: One year old female admitted with the complaint of macroglossia. She was born at term to a 23 years old woman by vaginal delivery with a birth weight 3000 gram. She had macroglossia. She hadn't any further significant antenatal, maternal medical or family history. On physical examination she had scabbed ridges on the tongue and the dimensions of the tongue were diffuse elevated. She couldn't chew so she had been fed only with liquid nutrients. MR imaging revealed a heterogeneous hypervascular solid/cystic mass with unclear borders that mainly localized at anterior 2/3 of the tongue. Chest x-ray and abdomen USG were normal. Laboratory examinations including chromosomal microarray testing and testing for metabolic disorders were also normal.
Results: The patient began treatment with sirolimus which is a mammalian target of the rapamycin inhibitor. Initial dosing was 0.04/mg/kg/day, administered oral, twice daily. Subsequent dosing adjustments were made in order to maintain a goal drug trough level of 10-15 ng/ml. She continued on a therapeutic dose of sirolimus for nine months without any adverse effects. She was able to close her mouth and eat everything.
Conclusions: Sirolimus therapy offers a promising treatment option for lymphatic malformation in children.

EP-393

PYRROLE-IMIDAZOLE POLYAMIDES TARGETING KCNQ1OT1 INDUCE APOPTOSIS IN WILM'S TUMOR CELL LINE (G401)

S. Yoshizawa[1], K. Sugito[1], Y. Ishizuka[1], R. Hoshi[1], Y. Watanabe[1], S. Uekusa[1], H. Kawashima[1], T. Koshinaga[1], K. Fujiwara[2], H. Nagase[3]

[1]Pediatric Surgery, Nihon University School of Medicine, Tokyo, Japan; [2]General Medicine, Nihon University School of Medicine, Tokyo, Japan; [3]Division of Cancer Genetics, Chiba Cancer Center Research Institute, Chiba, Japan

Objectives: KvDMR is one of imprinting control regions assigned to chromosome 11p15.5 in human. Since KvDMR is located on the promoter of *KCNQ1OT1*, genomic alteration of this region, such as deletion, paternal UPD, and de-methylation in maternal allele lead to over-expression of *KCNQ1OT1*. The non-coding RNA *KCNQ1OT1* is known to suppress circumjacent genes, including tumor suppressor gene *KIP2*, and over-expression of *KCNQ1OT1* accompanied with down-regulation of *KIP2* has been reported in several tumors. De-methylation of KvDMR is frequently observed in Beckwith-Wiedemann syndrome (BWS), and around 10% of BWS patients develop embryonal tumor (Wilm's tumor, Hepatoblastoma). Based on these facts, we hypothesize that suppression of *KCNQ1OT1* could show anti-tumor effect.
Methods: Pyrrole-Imidazole polyamides (PIPs) are small synthetic chemicals composed of the aromatic amino acids and recognize a specific DNA sequence. PIPs designed against transcription factor binding site can suppress the expression of downstream genes. We generated PIPs targeting *KCNQ1OT1* promoter and investigated their anti-tumor effect on human BWS fibroblast (BWS6, 9) and G401.
Results: It was clearly shown by real-time PCR that the expression level of *KCNQ1OT1* was significantly reduced in BWS6, 9, G401 treated with PIPs compared to the control cells. Induction of KIP2protein in G401 cells after treatment withPIPs was detected by Western Blotting. WST8 assay revealed that G401 cells treated with PIPs showed significantly lower viability than that of the control cells. And we found the higher number of cells undergoing apoptosis in the PIPs treated group than in the control group by FACS analysis.
Conclusions: Our current data strongly suggested that PIPs induce apoptosis in G401 by suppressing *KCNQ1OT1* expression, followed by the up-regulation of KIP2 protein. We believe that the PIPs targeting *KCNQ1OT1* have possibility to be new therapeutic agents for tumors harboring de-methylatedCpG island on *KCNQ1OT1* promoter.

NURSING

EP-394

SUPPORT FOR WOMEN SURVIVORS OF CHILDHOOD CANCER: A LITERATURE REVIEW

A. Tomioka[1], M. Maru[1]

[1]Health care Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Objectives: As the cure rates of childhood cancers continue to improve, more long-term survivors are living with the late effects of treatment. Support for women survivors of childhood cancer has not been sufficiently studied thus far, particularly in regard to women of childbearing age. We therefore conducted a literature review to clarify the current status of women survivors of childhood cancerand the support they receive.
Methods: MEDLINE and CINAHL were searched for articles published from 2004 to 2013 on adult childhood cancer survivors. Included studies focused on issues specific to women survivors of childhood cancer or compared these women with their male counterparts.
Results: Women survivors of childhood cancer had lower quality of life than their male counterparts and a higher risk of posttraumatic stress disorder. The women were concerned about their reproductive health and felt uncertainty about the future.
Conclusions: The results indicate that further support is needed for childhood cancer survivors, particularly women.

OTHERS

EP-395

ROLE OF INTERLEUKINS IL10, IL12 AND IL23 IN PREDICTING TUMOR AGGRESSIVENESS AND RESPONSE TO THERAPY IN PEDIATRIC MALIGNANCIES

A. Abd Elmoneim[1], Z. Alhawsawy[2], M. Zolaly[3], E. Abd Elmoneim[3]

[1]Pediatric Department, Sohag University, Sohag, Egypt; [2]Pediatric Department, Maternity and Children Hospital, Almadinah Almounourah, Saudi Arabia; [3]Pediatric Department, Taibah University, Almadinah Almounourah, Saudi Arabia

Objectives: Upon contact with tumor cells when co-cultured *in vitro*, human monocytes become unresponsive to re-stimulation and demonstrate decreased production of IL-12 and enhanced IL-10 secretion. Clinically, deregulated serum level of IL10 and IL12 and their reciprocal balance have been stated in many cancers. On the other hand, IL-23 dampens directly tumor growth *in vitro* and *in vivo* through the inhibition of tumor cell proliferation and induction of apoptosis. We aimed in our study to detect the pretreatment serum level of IL10, IL12, their ratio and IL23 in pediatric hematological malignancies as well as solid tumors, and correlate them with the chemotherapy response.
Methods: Pre treatment serum level of IL10, IL12 and IL23 are detected in blood samples of 20 children diagnosed with different types of malignancies and 20 healthy peers using ELISA. A correlation between serum level of these Interleukins and disease severity and patients' response to chemotherapy is conducted.
Results: Median IL-10 and IL-12 levels were significantly higher in cancer diseased children than in healthy controls, while median IL23 level was significantly decreased. Elevated IL-10 and IL-10/IL-12 ratios and decreased IL-12 and IL23 correlated with poor-risk histology, poor response to therapy, relapse and death from cancer.
Conclusions: Pre-treatment serum levels of IL-10, IL-12, IL-10/IL-12 balance and IL23 in children with cancers may be of value as additional prognostic tools to predict the response to therapy. Our analysis potentiate the theory of the anti tumor effect of IL23 and the possibilities of its use as a candidate novel drug in resistant malignancies.

EP-396

ASSESSMENT OF MYOCARDIAL FUNCTION IN CHILDREN BEFORE AND AFTER AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

Y. Al-Tonbary[1], H.A.L.A. Al-Marsafawy[1], M. Mattar[1], R. El-Ashry[1], M. Sarhan[1]

[1]Pediatrics, Mansoura University Children Hospital, Mansoura, Egypt

Objectives: More interest is focused on the long-term adverse effects of bone marrow transplantation. Subclinical cardiac involvement appears to be common in adults, but only a few reports concern pediatric patients.
Methods: A Prospective case-control study performed on 19 children with normal cardiac function undergoing autologous hematopoietic stem cell transplantation (HSCT). Tissue Doppler imaging (TDI) and echocardiographic measurements were obtained according to guidelines of the American Society of Echocardiography.

Results: Lateralmitralannulus before HSCT showed significant reduced mitral systolic annular velocity ($p < 0.0001$), early diastolic annular velocity ($p < 0.0001$), late diastolic annular velocity (p0.02) and prolonged is volumetric relaxation time ($p < 0.0001$) in comparison to control. Significant reduced mitral systolic annular velocity ($p < 0.0001$), early diastolic annular velocity (p0.0005) and Em/Am ratio (p0.004), with higher late diastolic annular velocity (p0.02) and prolonged ICT (P0.003) and IRT (P0.002) after HSCT were observed. Study of lateral tricuspid annulus showed nearly similar results as the lateralmitralannulus. LV and RV Tei indices were found to be higher before HSCT in comparison to control and remain higher after HSCT.
Conclusions: TDI could detect the subtle abnormalities in the systolic and diastolic functions before and after HSCT which can imply that conditioning regimen may affect cardiac function.

EP-397

ACTIVE DRUG CONCENTRATION OF GENERIC VINCRISTINE FORMULATIONS IN SOUTHEAST ASIA

A.P. Alcasabas[1], Y.M. Khoo[2], A.E. Yeoh[3], H.S. Lee[2], T.C. Quah[3]

[1]Paediatrics, Philippine General Hospital, Manila, Philippines; [2]Pharmacology, National University Singapore, Singapore, Singapore; [3]Paediatrics, Khoo Teck Puat-National University Children's Medical Institute, Singapore, Singapore

Objectives: Availability of generic drugs aid the rising cost of healthcare especially in developing countries. These are more affordable than the innovator product however there is public perception they may be of inferior in quality. There are established guidelines ensuring pharmaceutical quality, but many countries do not have resources to implement them. In Asia, there are numerous cases of fake and substandard generic medicines such as anti-malarials and anti-microbials. Few studies have evaluated generic chemotherapy formulations; and low active drug levels, contamination and increased toxicity have been reported. For old agents such as Vincristine, only generic brands are available in Asia. The purpose of this study is to determine the active drug concentration of Vincristine among different brands available in Southeast Asia.
Methods: Generic vincristine formulations were obtained from Southeast Asian countries, including India, and transported in cold storage to National University Singapore. Vincristine levels were measured using high performance liquid chromatography and compared to Vincristine lab standard (Sigma), as modified from US Pharmacopeia methodology.
Results: Ten generic Vincristine formulations were obtained from Malaysia, Sri Lanka, Vietnam, Indonesia, India, Philippines and Singapore. Two brands had 4 samples each; 5 brands had 2 samples each; and 3 brands had a sample each. These were manufactured in India, South Korea, Netherlands and Hungary; and were within prescribed shelf life. The mean Vincristine levels obtained per brand all fell between 90-110% of the control; values ranged from 92.07% to 109.6%.
Conclusions: Selected generic vincristine formulations from Southeast Asia and India have acceptable active drug levels between 90-110% of the lab standard. The presence and quantity of impurities which may be clinically significant were not tested in this study.

EP-398

CHILD TUMORS IN THE AFRICAN ENVIRONMENT: DIFFICULTIES IN MANAGEMENT AND ADVOCACY FOR HEALTH SCREENING AND CARE

D. Alumeti[1], N. Luhiriri[1], B. Cikwanine[1], K. Nfundiko[1], F. Iteke[1], M. Birindwa[1], C. Guhanika[1], M. Bahala[1], L. Ahuka Ona[1]

[1]Department of Surgery and Specialties, General Reference Panzi Hospital, Bukavu, Democratic Republic of Congo

Introduction: Childhood cancer is a complex. The aim of this study was to discuss the difficulties of managing children with cancer in eastern DR Congo, to bring awareness of the problem and advocate for policy change.
Patients and methods: The study was conducted in the city of Bukavu, eastern DR Congo. A questionnaire was administered to caregivers working in various health care facilities.
Results: The Wilms tumor was the most common followed by leukemia, retinoblastoma and malignant lymphomas. The clinical diagnosis was supported by ultrasound and histopathology. Treatment however was limited, by the high cost (the middle cost is 600$ USA) and lack of inventory. Cyclophosphamide, Methotrexate and Prednisolone are the available drugs most used in the two general reference hospitals in Bukavu meeting the criteria for the management of childhood cancers, meaning the presence of qualified staff (Pediatrician, Surgeon, and Pathologist), a laboratory capable of determining tumor markers and a pharmacy capable of providing the anticancer drugs.
Conclusion: Childhood Cancer is a serious problem in eastern DR Congo. With the current challenges in diagnosis and treatment, a unit capable of caring for childhood cancer is essential. It will also begin addressing the popular misconception that "childhood cancer always ends in the cemetery."

EP-399

ABDOMINAL TUMORS IN CONGOLESE CHILDREN: DIFFICULTIES IN THE MANAGEMENT OF 16 CASES

D. Alumeti[1], N. Luhiriri[1], K. Nfundiko[1], B. Cikwanine[1], M. Bahala[1], L. Malekera[1], M. Lotin[1], A. Muka[1], B. Kampimba[1], J. Kitumaini[1], L. Ahuka Ona[1]

[1]Department of Surgery and Specialties, General Reference Panzi Hospital, Bukavu, Democratic Republic of Congo

Introduction: /p>Abdominal tumors in children are many diagnostic and therapeutic challenges, especially in developing countries such as DR Congo. The aim of this study is to determine the frequency of abdominal tumors in children and to describe the therapeutic modalities in a country with limited resources.
Patients and methods: It's a retrospective study for five years (2008-2012) in our department of Pediatric Surgery. All children 0 to 15 years old presenting to Hospital with an abdominal mass were followed. Epidemiological, clinical and therapeutic parameters were documented and analyzed.
Results: Females made up a higher percentage of children presenting with an abdominal mass (56.2%), the average age was 7.5 years. The age group of 5 to 10 was most affected (37.5%). The clinical diagnosis was supported by ultrasound in 98%. Wilms Tumor was the most common tumor (50%), followed by genital tumors (25%), neuroblastoma (18.7%) and pancreatic tumors (6.25%). 98% of cases underwent surgery. The postoperative course was uneventful (81.1%). There were no deaths; however, 3 children were released under palliative care.
Conclusion: Abdominal tumors in children represent 50% of childhood tumors. Diagnosis is primarily clinical, howver, ultrasound is an important tool. Surgical treatment but must be complimented by chemotherapy, however, it is not always available in our community.

EP-400

THE ROLE OF A PARENT GROUP IN AWARENESS CREATION OF CHILDHOOD CANCERS

F. Aveh[1], J. Ahenkorah[2], M. Opoku[3], L. Renner[2]

[1]Accounting, University of Professional Studies, Accra, Ghana; [2]Medical School, University of Ghana, Accra, Ghana; [3]Parent Group, Ghana Parents Association for Childhood Cancers, Accra, Ghana

Objectives: To raise awareness of childhood cancers in Ghana
Methods: A high profile launching of the Ghana Parents' Association for Childhood Cancers (GHAPACC) in 2009 with publicity about challenges faced by children affected by cancer and their families. Awareness creation, fundraising walk organised during the International Childhood Cancer day in 2010. Coverage was by national TV. Needs of children affected by cancer and their parents made public through articles in the national daily papers. Members of the parents' group have participated in radio and television talk shows. Family funfair organised during Easter 2011 was used as an avenue for awareness creation. In September 2011 a media meeting was organised by GHAPACC. 35 media houses were involved to disseminate the early warning signs on television, radio and the print media.
Results: Nationwide publicity about childhood cancers ongoing. Over 5000 posters distributed by GHAPACC including schools and churches. Several organisations made substantial contributions directly towards childhood cancer treatment and many NGOs have sprung up as result. We are currently about to launch a project to construct a 30 bed hostel for families of children on admission at the hospital.
Conclusions: Level of awareness of childhood cancers in Ghana has improved but more needs to be done. Superstitious beliefs and stigmatization by society are some of the hindrances to early reporting of cases to health facilities. More education through the media would be an effective way for continued awareness, help get better access to care and improve outcomes for childhood cancer.

EP-401

IMPROVING THE STAGING OF INFECTION RISK IN CHILDREN WITH FEBRILE NEUTROPENIA BY MULTIPLEX VIRAL PCR AND CYTOKINE DETERMINATION

B. Santiago[1], C. Mata[2], B. Hernández-Rupérez[3], R. Herráiz[2], C. Garrido[2], L. Díaz[4], M.M. Santos[5], C. Beléndez[2], E. Cela[2], J. Huerta[2], I. Casas[6], M.A. Muñoz Fernández[4], J. Saavedra-Lozano[5], M. Navarro[5], S. Begoña[5]

[1]Molecular Immunobiology Department. Pedaitric Infectious Diseases Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Pediatric Oncohematology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [3]Infectious Diseases Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [4]Molecular Immunobiology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [5]Pediatric Infectious Diseases Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [6]Influenza and Respiratory Virus Laboratory., Instituto de Salud Carlos III, Madrid, Spain

Objectives: Respiratory viral infections (RVI) are a common cause of febrile neutropenia (FN) episodes in children with cancer. We present a cohort of children with FN evaluated for RVI by multiple-PCR in conjunction with cytokine profile in order to describe the incidence, clinical outcome, and potential early biomarkers of RVI.

Methods: Children with FN admitted to the hospital between Oct'10 and Dec'13 were prospectively enrolled. On admission, children were evaluated for 16 RV in nasopharyngeal wash by multiple-PCR, and cytokine profile was determined in blood by flow citometry. Children with RVI were compared to children with bacterial infection (BI) by analyzing risk staging on admission, clinical outcome, laboratory parameters and cytokine profile.
Results: A total of 130 episodes of FN in 45 children were enrolled (56.2% female, median age 5.6 years [3.1-13.8]). On admission, 16.9% were classified as low risk of BI (LRBI) according to our own protocol. Overall, microbiologic confirmation was obtained in 49.2%. RV were identified in 28.3% episodes, being 4.6% mixed RV-BI. BI were detected in 24.6%. Rhinovirus was the most common virus (n = 21), followed by parainfluenza (n = 4), RSV (n = 2), coronavirus (n = 2), influenza B (n = 2) and adenovirus (n = 1). RV were more common in children with LRBI compared to high risk (40.9% vs. 25.7%, p = 0.1). On admission, children with RVI presented lower median PCT (0.2[0.1-0.5] vs. 0.7[0.3-5.1]; p = 0.01), IL12 (1.8[0-50.6 vs. 188.2[5.4-1117.8];p = 0.04) and TNFa (0 vs. 94.8 (0-1,593); p = 0.06) compared to children with BI. The outcome of children whose only isolation was a RV was favorable regardless of the risk established on admission.
Conclusions: In our cohort of children with FN, RV were the infectious agents most frequently isolated. Early detection of RV by multiple-PCR in conjunction with low PCT, TNFa and IL12 levels on admission may enhance the identification of these patients, improving the risk staging of children with FN.

EP-402

CLOSTRIDIUM DIFFICILE-ASSOCIATED DIARRHEA IN CHILDREN WITH HEMATOLOGICAL MALIGNANCY

F. Begum[1], A. Islam[1], R. Haque[2], Y. Chowdhury[3], A. Mia[4], F. Yasmin[1], M. Begum[1], L.R. Molla[1], Z. Ara[1], M. Doherty[5]

[1]Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [2]Parasitology Laboratory, Icddrb, Dhaka, Bangladesh; [3]Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [4]Medical Education, Centre for Medical Education, Dhaka, Bangladesh; [5]Pediatric Palliative Care, Children's Hospital of Eastern Ontario, Ottawa, Canada

Objectives: Clostridium difficile associated diarrhea (CDAD) is now considered to be one of the commonest causes of nosocomial diarrhea worldwide. Gastro-intestinal infection in the form of diarrhea and dysenteric illness are the leading causes of infection in pediatric oncology patients in BSMMU, Dhaka, Bangladesh. The study was conducted to see the frequency of Clostridium difficile infection by EIA among diarrheal children with hematological malignancy in BSMMU.
Methods: This prospective observational study was conducted from april 2012 to march 2013 to see the rate of Clostridium difficile infection in children with hematological malignancy. A total of 58 diarrheal episodes experienced by 51 children with different hematological malignancies were consecutively included if developed diarrhea at any point of hospitalization. Fecal samples were sent to ICDDRB laboratory EIA for C. difficile, aerobic culture for common bacteria and PCR for common parasitic infection.
Results: Among the total 58 diarrheal episodes 22.4% samples were positive and 77.6% samples were negative for GDH antigen by EIA test. But None of the fecal samples were positive for toxin A and/or B by EIA. Potential pathogenic bacteria were isolated from 5.2% sample by aerobic stool culture. Different parasites were identified from **70.4**% samples by PCR and most frequently identified protozoa was Giardia lamblia (**68.5**%)**.** During episode 81% children were neutropenic and severe neutropenia had significant corerelation with GDH positivity. Usage of Imipenem, high dose cytosar and omeprazole had significant correlation with GDH positive diarrheal episodes.
Conclusions: The study found colonization rate of Clostridium dificile 22.4% but none was toxigenic among diarrheal children with hematological malignancy. Parasitic infections were seen more frequently in children with malignancy.

EP-403

MALIGNANCIES IN INFANTS IMPLEMENTS METASTATIC POTENTIAL AS TUMORS REACH THE PEAK OF ITS GROWTH RATE

I. Begun[1], O. Krasko[2], O. Aleinikova[3]

[1]Functional diagnostics, Belarusian Research Center for Pediatric Oncology Hematology and Immunolog, Minsk region, Belarus; [2]Bioinformatics, United Institute of Informatics Problems, Minsk, Belarus; [3]Management, Belarusian Research Center for Pediatric Oncology Hematology and Immunolog, Minsk region, Belarus

Objectives: To rate kinetic characteristics of growth embryonic tumor in relation with the terms of implementation metastatic potential of the primary tumor.
Methods: A retrospective analysis of the primary malignancies by ultrasound diagnosis in 109 children aged 1-366 days both sexes (with nephroblastoma - 31, 58 - with retroperitoneal neuroblastoma neuroblastoma and adrenal gland, 20 - with hepatoblastoma) was made. The point of maximum velocity (inflection point) for the Gompertz model was calculated based on the vanishing of the second derivative of the Gompertz. ROC-analysis was used to determine the threshold age at which the disease goes to prognostically unfavorable stage.
Results: Median of actual volume of abdominal tumor at the primary imaging was 176 (40-355) cm^3. Was obtained Spearman rank correlation ($\rho = 0.53$; $p < 0.0001$) between the tumor volume at the time of initial diagnosis and age. Based on the evaluation of the Gompertz model parameters was calculated the point of maximum rate of tumor growth - Tmax. Its value corresponded to 124 days since birth and was indicating at critical change in the growth rate of malignancies in the first four months of life. According to the results of ROC-analysis was found threshold of exceeding of age at which the chances of malignancies diagnosis at an advanced stage in sick infants are increased 4.35 fold (95% CI 1.7-11.5). This threshold was 129.5 days (51% specificity (95% CI 39-63), the sensitivity of 81% (95% CI 69-91), AUC = 0.61 (95% CI 0.49-0.71).
Conclusions: Thus, on the clinical data of the cohort of infants was modeled a situation where in the first 4 months life occurs the greatest intensification the process of malignancies growth realizing metastatic potentials when reach the peak of its growth rate.

EP-404

INVESTIGATING HEPATITIS B IMMUNITY IN CHILDREN PRESENTING TO A PAEDIATRIC HAEMATOLOGY AND ONCOLOGY UNIT IN SOUTH AFRICA

A. Buchner[1], F.E. Omar[1], J. Vermeulen[1], D.T. Reynders[1]

[1]Paediatric Oncology Unit, University of Pretoria, Pretoria, South Africa

Objectives: Hepatitis B is an important public health issue in South Africa. The hepatitis B vaccine was introduced into the South African Expanded Programme of Immunisation (EPI) in 1995, without any catch-up programme. The duration of protection after hepatitis B vaccination is unknown, and waning of vaccine-induced immunity leaves children at risk of hepatitis B infection in a setting where the prevalence is high and horizontal transmission is likely. The aim of this study is to assess the immunity to hepatitis B in patients at first presentation to a paediatric oncology unit.
Methods: A retrospective audit was done of all new patients seen in the unit from January 2012 to December 2013. None of these patients had received previous immunosuppressive therapy. A total of 210 patients' results were available for review. Patients were classified as immune (anti HBs >100mIU/mL), low immune (anti HBs 10-100mIU/mL) and not immune (anti HBs <10mIU/mL).
Results: Of the 210 patients included (median age 6.5 years), 84 (40%) had no immunity to hepatitis B despite presumed vaccination as part of the EPI schedule. Six patients tested positive for hepatitis B core antigen (anti-HBc) consistent with previous infection. No patients had active hepatitis B infection (hepatitis B surface antigen positive). Most of the patients with HIV infection were not immune (80%).
Conclusions: A significant number of children are not immune to hepatitis B despite vaccination being part of the South African EPI. Revaccination should be considered for all oncology and haematology patients where the opportunity exists for exposure to hepatitis B virus. Consideration should also be given to offering booster vaccination to the population as a whole.

EP-405

WATER QUALITY CHARACTERIZATION IN 4 CHILDREN'S HOSPITALS IN SANTIAGO, CHILE

M. Zubieta[1], J. Bustos[1], E. Vogel[1], R. Rabagliati[2], M.T. Ulloa[3], M. Díaz[3], P. Catalán[4]

[1]Research Department, Fundación Nuestros Hijos, Santiago, Chile; [2]Infectious Disease Specialists at Medical Center, Medicine Faculty Catholic University of Chile, Santiago, Chile; [3]Microbiology and Mycology Program, Faculty of Medicine of the University of Chile, Santiago, Chile; [4]Transplant Unit, Luis Calvo Mackena Hospital, Santiago, Chile

Objectives: Good water quality in a hospital is critical for mitigating risks in immune-compromised children. In order to understand the reality in the Santiago, Chile metropolitan area, we conducted an investigation of our local hospitals' water supplies at PINDA (National Antineoplastic Drugs Children's Program) Centers. The samples were taken in the Santiago, Chile metropolitan area during the months of April, July, November 2013, and January 2014.
Methods: The Microbiology and Mycology Program of the Faculty of Medicine of the University of Chile conducted analyses of bacteriological, fungal, and parasitological presence were conducted. The statistical analyses employed a non-parametric test, where the response variable was the microbiological load of each hospital.
Results: We identified the presence of at least one microorganism at 90.32% of the locations tested. *Microsporidia spp.* was the most prevalent, with a 37% presence in the samples. In decreasing order, we identified the following organisms: *Pseudomonas fluoresence, Enterobacter cloacae, Pseudomonas aeruginosa, Pseudomonas oleovorans, Pseudomonas putida, Stenotrophomonas maltophilia, Pseudomonas stutzeri, Alcaligenes faecalis faecalis*, and also a unidentified bacterium (a gram negative non fermentative bacilli), and fungus. Although quantitative analyses showed there was a presence of microorganisms, there was not a consistent enough presence in the samples to detect statistical differences (P>0.05) among the 4 hospitals tested.
Conclusions: We have discovered generalized water quality deficiency in the tested hospitals. Thus, as these hospitals treat immunocompromised patients, the present data suggests it necessary to take specific measures to ensure the health of each child treated at hospitals in the Santiago, Chile metropolitan area.

EP-406

ROLE OF THE PEDIATRIC SURGEON ONCOLOGIST WITH ACUTE PANCREATITIS IN CHILDREN WITH LEUKEMIA TREATED WITH ACUTE LYMPHOBLASTIC L - ASPARAGINASE. EXPERIENCE IN THE NATIONAL INSTITUTE OF PEDIATRICS

V. Carrasquel Valecillos[1], J. Palacios Acosta[1], A. Leon Hernandez[1], D. Hernandez Arrazola[1]

[1]*Pediatric Surgical Oncology, Instituto Nacional de Pediatría, Mexico City, Mexico*

Objectives: Pancreatitis is an inflammatory disease of the exocrine pancreas, self-digestion of the tissue by its own enzymes. The aim of this paper is to evaluate the role of de oncology pediatric surgeon in management of acute pancreatitis
Methods: This is a retrospective study analyzing cases of patients with ALL who had acute pancreatitis induced by L -asparaginase treated at the National Institute of Pediatrics (INP) in the Department of Surgical Oncology for a period of 11 years. In order to establish the role of the pediatric surgeon oncologist in the management of patients with acute pancreatitis by L - Asp. The clinical records of 120 patients admitted to the surgical oncology with acute pancreatitis during the period 2002 to 2013, of which 30 patients had acute pancreatitis induced by L - Asp were reviewed. Clinical and biochemical data, ultrasound, computed tomography, treatment, complications and intensive care stay were analyzed.
Results: Patients who had acute pancreatitis by L - Asp, the mean age was 12 years, gender was found with a ratio of 12 male patients (40%) and 18 female (60%). All patients had abdominal pain, nausea, vomiting and elevated pancreatic enzymes lipase and amylase. CT pancreatic necrosis was found in 3 patients (13%), 2 patients underwent peritoneal drainage catheter and patient Tenchkoff I performed necrosectomy. 8 died (26%) patients, only one due to toxicity of the pancreas.
Conclusions: L - Asp is an effective drug for the treatment of ALL, but because of its toxicity requires close monitoring due to the main complication is pancreatitis in order to start treatment as soon as possible. Surgery in acute pancreatitis is limited to removal of infected necrotic pancreatic tissue, so that the role of the surgeon is of paramount importance to determine the window of opportunity and timely management.

EP-407

POEM (PEDIATRIC ONCOLOGY EXERCISE MANUAL): A KNOWLEDGE SYNTHESIS TO IMPROVE AWARENESS ABOUT PHYSICAL ACTIVITY BENEFITS DURING AND AFTER CHILDHOOD CANCER

C. Chamorro Vina[1], M. Keats[2], A. Wurz[1], N. Culos-Reed[1,3,4]

[1]*Health and Wellness Lab, Faculty of Kinesiology, University of Calgary, Canada;* [2]*School of Health and Human Performance, Division of Kinesiology, Dalhousie University, Canada;* [3]*Department of Psychosocial Resources, Tom Baker Cancer Centre, Alberta Health Services, Calgary, Canada;* [4]*Department of Oncology, Faculty of Medicine, University of Calgary, Canada*

Purpose: To promote physical activity (PA) in children with cancer, thereby improving their overall quality of life (QOL). The Pediatric Oncology Exercise Manual (POEM) and its website will be distributed among clinicians, fitness professionals and educators (CFEs) and well as to families. Specifically, this project seeks to increase the awareness of the benefits of PA during cancer treatment by equipping CFEs and families with tools, resources and evidence-based information.
Methods: We convened an internationally (Spain, Germany, The Netherlands, USA, and Canada) acclaimed panel of experts in pediatric oncology to develop the first worldwide evidenced-informed PA manual for children with cancer. The manual has been developed in both professional and lay versions. Highlighted topics include general evidence on the benefits of PA and cancer, recommendations, and precautions in survivors experiencing late-effects. The POEM will be distributed along with educational sessions. An online platform is being created to: (a) evaluate quality of POEM; (b) provide ongoing resources; (c) foster ongoing international collaborations; (d) further develop an online training to create global capacity in this area.
Results: The dissemination of the POEM across Alberta will begin in Spring 2014, with planned expansion nationally, throughout Canada and then internationally, to contributors' countries. Finally, a plan to disseminate POEM to low-income countries is being developed. Dissemination of the manual will be tracked, along with use of website resources. Survey results will be analyzed and incorporated into yearly quality improvement cycles, ensuring the best evidence-to-practice translation occurs.
Conclusion: The creation of the POEM along, with the online support, will enhance awareness about the role of PA in pediatric oncology in an economically sustainable manner. Increased PA levels results in enhanced QOL for pediatric cancer survivors and diminished risk of developing comorbid conditions in survivorship.
Acknowledgements: Canadian Institute of Health Research, Alberta Children's Hospital and the POEM Contributors.

EP-408

DEVELOPMENTAL DELAY IN A CHILD WITH AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME

Y.R. Chopra[1], M. Ramzan[1], R. Sharma[1], S. Katewa[1], S. Yadav[1]

[1]*Pediatric Hematology Oncology and Bone Marrow Transplant Unit, Fortis Memorial Research Institute, Gurgaon, India*

Objectives: Autoimmune lymphoproliferative syndrome (ALPS) is an inherited lymphoid disorder, attributed to a defect in apoptosis, characterized by non-malignant lymphoproliferation, autoimmunity and cytopenias with raised circulating double negative T cells (DNT). Developmental Delay (DD) has not been reported with this condition. Here we describe a female with ALPS who had developmental delay.
Methods: A detailed analysis of the child's history, examination, laboratory investigations along with review of literature of the two conditions has been done.
Results: A 9-year-old female presented with intermittent fever and repeated hospitalization for the same for last 3-4 years. On physical examination she had splenohepatomegaly and developmental delay. She was evaluated for infections (malaria, kala-azar), leukaemia, lymphoma, inborn error of metabolism (glycogen storage disorders) and connective tissue disorders. Investigations revealed neutropenia, hypergammaglobulinemia. Chest X ray was normal and Mantoux was negative. Almost all infectious causes were ruled out by serological tests. ANA was negative. Bone marrow examination was normal. In view of persistent neutropenia (> 6 months) which was non -infectious non -malignant with splenohepatomegaly possibility of ALPS was thought and flow cytometry done which revealed 4.18% double negative T cells (CD3+ CD4-CD8-) confirming ALPS. She had resolution of neutropenia after starting of prednisolone. She was also started on sirolimus so as to decrease the organomegaly. Though no improvement occurred in her developmental milestones
Conclusions: ALPS should be suspected in a child with isolated persistent neutropenia and organomegaly for which common causes like infection, malignancy and autoimmunity have been ruled out. To our best knowledge, developmental delay has not been reported with ALPS. We report this to make paediatric oncologists aware of this rare association.

EP-409

DEFICITS IN CLINICAL TRIAL ENROLLMENT AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER TREATED AT AN ACADEMIC MEDICAL CENTER

C. Collins[1], D.R. Freyer[1]

[1]*Pediatric Hematology/Oncology, Children's Hospital Los Angeles, Los Angeles, USA*

Objectives: Improvement in survival for adolescents and young adults (AYAs, age 15-39) with cancer is worse compared to children and older adults. This trend may be partly due to poor accrual to clinical trials. We determined clinical trial enrollment at an academic medical center and compared the proportion of AYAs enrolled with children (age$\leq$14) and older adults (age$\geq$40) and between institutions within the center.
Methods: The California Cancer Registry provided data on patients diagnosed with cancer 1/2008-12/2012 and treated at a University of Southern California (USC) Cancer Center institution. At USC, oncology care is delivered in 3 settings: a children's hospital, an adult cancer hospital and a county-run facility, which provides care to children and adults. Patients identified by the registry were matched to institutional databases that track trial enrollments. Differences in enrollment were determined by the chi-square test.
Results: Overall, 174 of 793 children (22%) were enrolled on therapeutic clinical trials compared to 104 of 1699 AYAs (6%) and 518 of 9311 of adults (6%) ($p < 0.01$). Enrollments among AYAs were higher at the children's hospital (29/191, 15%) compared to either the adult cancer hospital (10/320, 3%, $p < 0.01$) or county facility (65/1188, 5%, $p < 0.01$). However, within the children's hospital, the proportion of AYAs enrolled on therapeutic trials (29/191, 15%) was significantly lower compared to children (174/761, 23%, $p < 0.01$). Of the 10 most frequent AYA diagnoses, 7 had clinical trials available, compared to 10 of 10 in children and 9 of 10 in adults.
Conclusions: The proportion of AYAs and adults enrolled on therapeutic trials is low, suggesting administrative barriers to enrollment. Within a children's hospital, lower enrollment among AYAs suggests other age-related barriers. Trial availability may also contribute. However, reasons for non-enrollment are not routinely captured, which prevents further analysis of the causes of low enrollment, and should be documented prospectively across treatment settings.

EP-410

CYSTEINE CATHEPSINS, CYSTATIN C AND VEGF IN TUMOR VASCULOGENESIS

N. Dementieva[1]

[1]*Surgery and Oncology, Regional Children Hospital of Dnipropetrovsk, Dnipropetrovsk, Ukraine*

Objectives: Studying activity of cysteine proteases - cathepsins B, L, H, and their endogenous inhibitor cystatin C, vascular endothelial growth factor (VEGF) in the blood serum of children with infantile hemangiomas before and after propranolol-therapy compared with the control.
Methods: Studying the activity of cathepsins B, L, H and the concentration of cystatin C and VEGF in blood serum from 24 healthy children and 80 children with infantile hemangiomas

treated with propranolol: 64 (group 1) with good response and 16 (group 2) with relapse after discontinuation of propranolol by using standard methods.
Results: Serum level activity of VEGF and cathepsins B, L and H in patients with hemangiomas significantly higher than that in the serum of healthy children. VEGF serum concentration is higher in the group 1 comparing to the control ($p = 0.008$) and have gradually normalizing during the course of treatment. VEGF concentration was not different from control in the group 2. There was the activity of cathepsins B, L and H in the group 2 before treatment more comparing to the control (p-levels: 0.001, 0.000 and 0.003) and to the Group 1 (p-levels: 0.000, 0.000, and 0.003); have not reached the level of healthy children with the severe propranolol-induced involution of hemangiomas. There was not pattern of level cystatin Cconcentration.
Conclusions: Unfavorable and aggressive course of hemangiomas associates with the elevated concentrations of VEGF and the activity of cathepsins B, L and H in the blood serum. Understanding the role of cysteine proteases - cathepsins B, L, H, and their endogenous inhibitor cystatin C, vascular endothelial growth factor (VEGF) in tumor vasculogenesis could lead to the development of more efficacious therapies.

EP-411

UNTANGLING THE CORD: A POLICY ANALYSIS OF NATIONAL PUBLIC UMBILICAL CORD BLOOD BANKING IN CANADA

A. Denburg[1], J. Abelson[2]

[1]Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Centre for Health Economics and Policy Analysis, McMaster University, Toronto, Canada

Objectives: Recognition of the value of cord blood has prompted widespread efforts at its collection and banking, both privately and publicly. Until recently, Canada was the only Group of 8 country without a national public cord blood bank. The explanation for Canada's relative delay in developing a national cord blood banking (CBB) program is unclear, and has received almost no scholarly attention.
Methods: Data for this analysis derive from searches of the published and grey literature on CBB. Sources of data include academic articles, governmental and non-governmental documents, media sources, organizational and industry websites, and online media. To map the determinants of CBB policy in Canada, we employ an analytic framework developed by Jonathan Lomas that considers the manner in which information, values and institutions configure the context for policy decision-making.
Results: Our analysis highlights the predominance of institutional structure as a determinant of policy stasis on CBB. Structures of blood system governance conditioned the use of values and information to influence problem definition, agenda-setting, and decision-making on CBB in Canada. Diffusion of agenda-setting roles hampered early and sustained stewardship of CBB policy. Disjuncture between the political responsibility for, and ambit of, national CBB policy slowed the development of a national cord blood bank.
Conclusions: Our analysis suggests that locating greater responsibility for agenda-setting and funding at the federal level would facilitate coordinated national responses to the policy challenges that emerge as stem cell science evolves. Explicit frameworks for policymaking on cord blood and other rapidly evolving areas of blood system policy would provide transparent blueprints for decision-making. Formal efforts at public consultation, through deliberative processes or otherwise, could help plait public perceptions with evolving scientific evidence, and align broadly held moral intuitions with the ethical principles justifying policy choices.

EP-412

OUTCOME OF ACUTE GUT GVHD POST STEM CELL TRANSPLANT IN CHILDREN – IMPORTANCE OF NUTRITIONAL STATUS

M. Dhamija[1], V. Khandelwal[1], D. Choudhary[1], S. Sharma[1], N. Gupta[1]

[1]Hemato Oncology and BMT, BLK Super Speciality Hospital, New Delhi, India

Objectives: Acute Graft-versus-host disease (aGvHD) after allogeneic hematopoietic cell transplantation is associated with considerable morbidity and mortality. Gut aGvHD remains the most difficult to manage and the morbidity and mortality increases with malnutrition. This study was undertaken to report outcome of gut aGvHD in children at a tertiary care center in India and the effect of malnutrition on morbidity and mortality.
Methods: It was a retrospective, observational study reporting the outcome of 15 patients (age 4 – 18 years) with gut aGvHD out of which 8 were grade IV and 6 were steroid refractory. Nine children (60%) were malnourished at the time of starting conditioning regimen (weight for age less than 25th centile of CDC standards).
Results: Nine children had matched sibling donor; 4, 1 and 1 had matched unrelated, haploidentical related and one antigen mismatched related donors respectively. Source of stem cells was peripheral blood in 10 patients and bone marrow in five. Mean CD34+ cell dose was 6.62×10^6/Kg/L. Mean time of appearance of symptoms was 20.9 days. The mortality was 46.66% in our cohort and most common immediate cause of death was gram negative sepsis secondary to immunosuppression. Four patients (66.66%) with steroid refractory gut GvHD did not survive ($P < 0.05$). Five out 7 malnourished children succumbed ($P < 0.01$).
Conclusions: Out come of children with malnutrition and gut aGvHD is worse and steroid refractory gut aGvHD holds to have a very poor outcome.

EP-413

BREAST DISEASES IN CHILDREN AND ADOLESCENTS: RISK FACTORS FOR BREAST CANCER

M. Dragomir[1], C. Comsa[1], M. Badoi[1], E. Gruber[1], S. Voinea[2], A. Blidaru[2], C. Radu[3]

[1]Pediatric oncology, Institute of Oncology, Bucharest, Romania; [2]Surgery department, Institute of Oncology, Bucharest, Romania; [3]Endocrinology, Institute of Oncology, Bucharest, Romania

Objectives: To analyze the breast diseases in children and adolescents and to estimate the risk factors for breast cancer.
Methods: There were 317 patients included from 0-19 years of age, with breast diseases and treated (surgery and non-surgery treatment) between 1990 and 2013 in the Institute of Oncology Bucharest. We were looking for the risk factors for breast cancer, family history of breast, ovarian malignanacies, diet and the outcome of disease. Surgical treatment (164 pts): lumpectomy, tumorectomy. 82 pts. received drug therapy. In 71 cases of small tumors (<2 cm) the choice was expectancy.
Results: There were 8 cases of male patients. The highest incidence was between 15 - 21 year old (55%). Types of breast tumors: fibro-adenomas 68%, Phyllodes tumor, ductal papilloma. 23% of the mammary disordes were fibrocystic changes. Signs and symptoms: physiologic swelling and tenderness (212 pts.), nodularity (82 pts.), breast pain (289 pts.), palpable breast lumps (244 pts.). Family history events were found in 76% of patients: mothers or relatives with benign mammary lesions, breast and/or ovarian cancer (15%). 64% pts. have had symptomatic high serum estrogen levels (menstruation disorders, ovarian cysts, early menarche). Excessive carbohydrates diet, overweightness and obesity were presented in 58% of cases. 5- 10 years follow up for 65. with small tumors (<2 cm) has revealed that 30% of them became smaller, 18% kept the same size and 52% became larger.
Conclusions: A significant number of children and adolescents with breast benign tumors and fibrocystic changs have risk factors for breast cancer. Effective and accurate counseling for adolescents and their parents regarding breast cancer prevention should be a routine component of preventive health.

EP-414

WORKING TOGETHER ON ETHICS: ETHICAL DELIBERATIONS INVOLVING PROFESSIONALS AS WELL AS PATIENTS' AND PARENTS' REPRESENTATIVES. LESSONS AND RESULTS FROM THE EU-FP7 ENCCA PROJECT

J.C.K. Dupont[1], S. Karner[2], F. Doz[1], A. Kienesberger[2], K. Pritchard-Jones[3]
[1]Paediatric Oncology Department, Institut Curie, Paris, France; [2]Österreichische Kinder-Krebs-Hilfe, Österreichische Kinder-Krebs-Hilfe, Vienna, Austria; [3]Institute of Child Health, University College London, London, United Kingdom

Objectives: In the ethics work-package (WP18) of the European Network for Cancer research in Children and Adolescents (ENCCA), the use of validated methodologies for ethical evaluation and deliberation aimed at making a state of the art review of relevant ethical issues in paediatric oncology research and at balancing the perspectives of professionals and of patients' and parents' representatives.
Methods: European representatives from the International Confederation of Childhood Cancer Parent Organizations (ICCCPO) and professionals involved in ENCCA where invited to participate in ethical deliberations on clinical trials and on bio-banks. These deliberations were conceived as a means to get the stakeholders' expert conclusions on ethical issues by making them participate in "a game of giving and asking for reasons" in which they had to justify their stances by sound arguments. By their ability to (dis) agree, stakeholders became the very "scorekeepers" in this game. Ethical deliberation is fully inclusive of all views.
Results: Fromthe scope and nature of (dis) agreements, three kinds of results could be distilled, namely 'like-mindedness' (e.g. the value of research participation), 'rallying' (e.g. "community equipoise" in clinical trials), and 'discrepancies' (e.g. re-consent after 18 in bio-banks). Voluntary participation and exclusive membership ('ENCCA partners') found these deliberations a meaningful scoping exercise that have allowed design of ethics interventions and identification of empirical and normative research avenues relevant for the paediatric oncology community as a whole (professionals and lay people).
Conclusions: Ethical deliberation is not a consensus-forming process and does not preclude disagreements. Therefore, why is it important to develop "a more exhaustive balancing of perspectives"? Two answers are to be made to this question. One relates to the value of pluralism for biomedical research and for ethical knowledge. Another consists of feed-back presented by a patients' representative on the value of ENCCA's experience in ethics.

EP-415

JENEECE PLACE: A HOME AWAY FROM HOME WHERE FAMILIES CAN STAY WHILE UNDERGOING MEDICAL TREATMENT

J. Edroff[1]

[1]Board of Directors, Jeneece Edroff Society, Victoria, Canada

Objectives: The purpose was to build a home for families who needed a place to stay in Victoria while undergoing medical treatment. The home would provide a warm, safe, and inviting environment for pediatric families and hopefully eliminating stresses during their stay. To also raise approximately 10 years of operational costs, eliminated the need for fundraising in the early years of operation.
Methods: Using my personal story of overcoming medical challenges and my past history of raising over a million dollars in pennies for Variety, The Children's Charity, secured me the recognition, and support of notable partners, such as TELUS, The Children's Health Foundation and Norgaard Foundation. These corporate sponsors donated very large amounts of money and the rest was donated by the island communities. Securing donations in kind from the contractors and securing 6 figure donations from various local corporate sponsors, to name a room helped us achieve our goal in a very short period of time. Media coverage was paramount.
Results: From the first shovel in the ground to finish, Jeneece Place was built in 9 months, a 10,000 square foot home, to accommodate 10 families. We raised more than projected goals and built Jeneece Place significantly under budget due to in kind donations from the contractors. A first time accomplishment for this 20 year old young lady.
Conclusions: Jeneece Place has been open for 2 years now and has served over 700 families. Over 96% of the families that visit Jeneece place come from Vancouver Island and the Golf Island but few have come from as far away as France, there by serving its purpose of helping BC families.

EP-416

PROTOCOL FOR THE ABDOMINAL COMPUTED TOMOGRAPHY FOR REDUCTION OF IONIZING RADIATION IN PEDIATRIC ONCOLOGY PATIENTS.

C.E. Cavalcante[1], R. Rossini[1], M. Lederman[2], M. Carvalho[1], L. Lopes[3]

[1]Diagnostic Imaging and Radiology, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Diagnostic Imaging and Radiology, UNIFESP - Universidade Federal de São Paulo, São Paulo, Brazil; [3]Medical Director, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: Dose reduction of ionizing radiation in pediatric oncology patients, changing the protocol of computed tomography scanning to stage only with intravenous contrast, "early portal phase" described.
Methods: 30 patients were selected who underwent computed tomography (CT) examination of the upper abdomen, lower abdomen, for the total period of November 12, 2012 until August 23, 2013, was describeb "Old Protocol Group" and 30 patients who underwent CT during the period of September 23, 2013 until January 31, 2014, was describe "New Protocol Group". From the total dose, average total dose equivalent was done for each group.
Results: Based on the average equivalent dose of CTs there was a reduction of more than 50% of the radiation dose for all patients of the "New Protocol Group" compared to the "Old Protocol Group". Moreover, the protocol change did not cause damage to diagnostic imaging.
Conclusions: The principal objective of this work was to verify the results of the reduction of the total equivalent dose in CT examination, within the possible limits is based on the principle of ALARA (Radiation Safety Manual University of Washigton's Radiation Safety).

EP-417

MISDIAGNOSIS AND REFERRAL OF PATIENTS WITH NON-MALIGNANT DISORDERS TO PEDIATRIC ONCOLOGY UNITS

A. Farrag[1], M. Ghazaly[2]

[1]Pediatric Oncology Department, South Egypt Cancer Institute Assiut University, Assiut, Egypt; [2]Department of Pediatrics, Faculty of Medicine Assiut University, Assiut, Egypt

Objectives: To evaluate patients who were wrongly misdiagnosed and referred to a Pediatric oncology unit with initial suspicion of cancer to evaluate the size of this problem in one large Cancer institute in a developing country.
Methods: A retrospective analysis was performed on all patients referred to the pediatric oncology department, South Egypt Cancer Institute (SECI) between 2006 and 2010.
Results: For all available data of the 712 patients who were admitted in SECI 570 (80.1%) were suffering from malignant tumors, 19 (2.7%) referred/escaped/lost before full diagnosis, 21 (2.9%) died early after admission before reaching a final diagnosis and 102 (14.3%) proved to have a non-malignant disease, of them 25 (24.51%) were benign tumors, 24 (23.53%) were benign hematological diseases, 24 (23.53%) were infections, 22 (21.57%) were inflammatory cases, 2 (1.96%) were metabolic diseases, and 5 (4.90%) have other different diagnoses.
Conclusions: Misdiagnosis of cancer in children is a problem that should be excluded before starting of therapy in pediatric oncology units, especially in developing countries were diagnostic facilities are restricted.

EP-418

STRATEGIES TO PREVENT TREATMENT ABANDONMENT IN CHILDHOOD CANCER IN RIO DE JANEIRO, BRAZIL

S. Ferman[1], F. Lima[1], A. Suzuki[1], C. Lage[1], L. Portela[1], B. De Camargo[2], R. Ribeiro[3]

[1]Pediatric Oncology Department, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [2]Pediatric Hematology and Oncology Program, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [3]Pediatric Oncology Department, St Jude Children's Research Hospital, Memphis, USA

Objectives: Abandonment of treatment in childhood cancer has been considered one of the major limitations to achieving high cure rates in developing countries. The aim of the study is to describe the impact of a simple strategy to prevent treatment abandonment.
Methods: The study period was 08/01/2012 to 02/28/2014. Patients younger than 18 years, diagnosed and treated with solid tumors at the Instituto Nacional de Câncer- Rio de Janeiro-Brazil were prospectively monitored for adherence to appointments. Daily, one health care professional registered all patients that missed the scheduled oncology consultation. Family members were contacted within 24 hours of the missed appointments by phone call and/or telegram. The primary physician was informed as well as the multidisciplinary team. Interventions addressing lack of resources as travel expenses, lodging, transportation, food basket, were provided to all families. Abandonment was defined as 4 weeks of missing appointments during active treatment.
Results: During the study period 2056 patients had 8570 scheduled oncology consultations and 201 (9.8%) patients missed at least one. All families were contacted by the data manager. The number of absences on diagnostic investigation or 'on treatment' was: 109/201 (54.2%) and the number of absences by pt was: n = 1 in 85 (78.0%); n = 2 in 16 (14.6%); n = 3 in 3 (2.8%); n = 4 in 3 (2.8%); n = 5 in 1 (0.9%) and n = 6 in 1 (0.9%) pt. One hundred and five (96.3%) pts returned to treatment, but 4 pts abandoned treatment despite all efforts. In 92/201 (45.8%) the absences occurred in pts 'off treatment'.
Conclusions: Monitoring missing appointments, early intervention to address the issues associated with them and providing resources to help families during treatment is associated with very low abandonment rates.

EP-419

EARLY DIAGNOSIS OF CHILDHOOD CANCER IS CHALLENGE IN DEVELOPING COUNTRIES

C.M.C.M. Fiori[1], Rosa A.C.[1], C.G. Santos[1], S.C. Buettner[1], M.I.A.A. Melo[1], R.Y. Sakurada[1]

[1]Hospital of Cancer, UOPECCAN Cascavel, State University of West Paraná, UNIOESTE, Cascavel, Paraná- Brazil

Introduction: In developed countries the cure rate of cancer children exceeds 75%, this reality is far from being achieved in Brazil and the main reason is the difficulty that health professionals have to diagnose the disease early. The Cancer Hospital of Cascavel - UOPECCAN in partnership with the Ronald McDonald Institute through the early diagnosis of cancer children and adolescents program, train professionals of health and pediatrics of the municipalities of Parana-Brasil.
Objective: Train professionals of health and pediatricians to contribute to the early identification of cancer in children and adolescents, reducing the time between the onset of signs and symptoms and diagnosis in a specialized center providing an increase of the probability of cure.
Methodology: Health professionals from 16 cities were trained from April / 2008 to Dec/ 2013, received basic information about children cancer and adolescents (Epidemiology; signs and symptoms of suspicion; care needed for the attention to children and adolescents with cancer). The groups were formed with 40 professionals, 20 hours / course.
Results: 1007 professionals, 63 doctors, 117 nurses, 162 technicians / nursing assistants, 475 community health agents, 81 upper level and 88 medium-level professionals or auxiliary.
Comments: Among the diagnosed cases of cancer in children in Brasil, many are referred to treatment centers with the disease at an advanced stage. One goal of the campaign is to encourage educational and preventive actions, becoming known to more people about symptoms and signs of disease. This program was performed in 86 Brazilian cities, showed a reduction in the time course in weeks (13 to 5) for the arrival of children at a referral center in the regions trained. Shortening the time between the suspicion of cancer and early diagnosis and treatment, will certainly contribute to the increasing expectations of cure in developing countries.

EP-420

DILUTION OF VINCA-ALKALOIDS IN PEDIATRIC ONCOLOGY: FROM GUIDELINES TO PRACTICAL APPLICATION

L. Fruit[1], P. Leblond[2], I. Sakji[1], H. Sudour[2], G. Marliot[1], C. Lervat[2], S. Mercier[2], S. Delbey[1], A.S. Defachelles[2]

[1]Clinical Pharmacy Departement, Oscar Lambret Center, Lille, France; [2]Pediatric Oncology Unit, Oscar Lambret Center, Lille, France

Objectives: Since 1968, cases of accidental intrathecal injections of vinca-alkaloids have been reported worldwide and are responsible for severe and irreversible neurological disorders. In order to avoid those adverse events, several Health Authorities have published

recommendations. Among them is the dilution of vinca-alkaloids. In 2013, 4,370 chemotherapies were produced for our pediatric unit, among which 792 preparations of vinca-alkaloids. Our purpose was to study the feasibility of implementation of these guidelines.
Methods: We analyzed 11 international recommendations (France / WHO / USA / Canada / England / Ireland / Spain / Australia / Hong Kong). The use of mini-bags is mainly recommended (n = 7) in adults and pediatrics. Four guidelines recommend the use of syringes only in pediatrics. In our pediatric oncology unit, 3 vinca-alkaloids are prescribed: vinblastine, vincristine and vinorelbine. We worked together with pediatricians to dilute these chemotherapies in mini-bags.
Results: We managed to dilute vinorelbine in minibags. The main issue was the total administered volume (dilution and flush of the infusor), sometimes too large for smaller children. As a consequence, we couldn't do the same for vincristine and vinblastine (shorter administration time) for which a dilution in large syringe (60mL) was implemented. The aim of this kind of preparation is to reduce the probability of accidental intrathecal administration. Larger volumes on a short period could lead to cardiovascular adverse effects.
Conclusions: In pediatric oncology, recommendations made to secure the use of the vinca-alkaloids are difficult to apply. We still have to use luer syringes for some preparations. The only way to efficiently secure the use of the vinca-alkaloids would be the use of non-luer devices for intrathecal injections (not yet available in France). The spread of these devices would be a major step.

EP-421

IDENTIFICATION OF INSTRUMENTS USED TO EVALUATE SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH CANCER - SYSTEMATIC REVIEW

D. Geronutti[1], M. Murra[1], L.F. Lopes[2], B.S. Paiva[3]

[1]Pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Hospital Director, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Researcher, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: A systematic literature review to identify instruments used to assess the symptoms of children and adolescents with cancer.
Methods: Review carried out in PUBMED database using the keywords: *(' Questionnaires ' [Mesh] OR scale OR OR instrument OR questionnaire inventory) AND (' Symptom Assessment ' [Mesh] OR pain OR 'pain ' [MESH] OR ' fatigue ' [MESH] OR fatigue OR weakness OR lack of energy tiredness OR OR ' depression ' [MESH] OR depression sadness OR sleepiness ' Sleep Stages/complications ' [Mesh] OR' dyspnea' [MESH] OR dyspnoea dyspnea OR lack of air nausea OR* vomit ' anxiety' [MESH] OR anxiety OR constipation OR ' constipation' [MESH] OR drowsiness) AND (' neoplasms' [MESH] OR cancer OR tumor OR tumor OR neoplasm) AND * pediatric*. Inclusion criteria were: titles and abstracts in English, Portuguese and Spanish, without restriction period that addressed single or multiple symptoms scales, questionnaires or pediatric instruments.
Results: There were 481 articles initially identified. Of these, 343 were excluded after review of these, 49 addressed instruments of quality of life and symptoms after completion of treatment, 10 scales of mucositis and the other 284 dealt with other themes and population. Thus, 138 articles, of which, 62 were excluded were analyzed, all deleted, 1 occurred in adults, 3 in follow up, 3 were related to the critical instruments, one on communication, 2 on systematic review, 4 on other pathologies, 1 side Effects, 15 addressed interventions to improve quality of life, 7 reported experiences of patients undergoing cancer treatment, 8 discussing pharmacological interventions on pain and 16 the perception of parents or staff about treatment. Thus, 76 studies were analyzed.
Conclusions: It was possible to identify that there is shortage of instruments to assess symptoms in pediatric patients. Likewise, it happens for pediatric oncology. Therefore, it's necessary to the development and validation of instruments to assess symptoms of children with cancer.

EP-422

USE OF INTERACTIVE PLAY WITH CHILDREN IN A 3RD WORLD COUNTRY, WHERE ACCESS TO SCHOOLING HAS BEEN DISRUPTED THROUGH DIAGNOSIS AND SUBSEQUENT TREATMENT

A. Govender[1], D. Kleinenberg[1]

[1]NGO, CHOC - Childhood Cancer Foundation SA, Durban, South Africa

Objectives: Based on this premise of UBUNTU we provide basic interactive play for the hospitalised young person allowing them the opportunity to interact with each other, as well as adults, learn new skills and ultimately reintegrate into society. With limited to no schooling owing to their age or circumstance, CHOC fills the gap with interactive play whilst on treatment.
Methods: Power Point Presentation with a discussion. Interactive packs prepared for each delegate in order to achieve 2/4 activities
Results: To create a personal experience that can be duplicated in any country with diminished resources.
Conclusions: We do not advocate Interactive Play as a replacement for schooling. Interactive play fulfils a social, emotional, cognitive and interactive function. Our role is to close the gap so that a child with cancer can reintegrate into society painlessly having learnt skills that they can incorporate into their schooling. We want to impart tried and tested skills.

EP-423

MICROBIOLOGICAL PROFILE OF INFECTIONS IN CHILDREN WITH SOLID TUMORS RECEIVING ANTICANCER TREATMENT IN ONE CENTER

O. Gryniewicz-Kwiatkowska[1], A. Kolodziejczyk-Gietka[1], K. Semczuk[2], B. Dembowska-Baginska[1], K. Dzierzanowska-Fangrat[2], J. Styczynski[3]

[1]Pediatric Oncology, The Children's Memorial Helath Institute, Warsaw, Poland; [2]Department of Clinical Microbiology and Immunology, The Children's Memorial Helath Institute, Warsaw, Poland; [3]Department of Pediatric Hematology and Oncology, Collegium Medicum Nicolaus Copernicus University, Bydgoszcz, Poland

Objectives: One of the most common complications of anticancer treatment are infections. Neutropenia, mucositis, prolonged hospitalization, central venous catheters are the main risk factors. Changing pattern of microbiological agents responsible for serious infections and growing antibiotic resistance warrant continuous epidemiological and microbiological monitoring. The aim of the study was to assess the type and frequency of etiological agents of infectious complications in children with solid tumors treated at a single institution.
Methods: During 2 years (2012-2013) 5849 chemotherapy related hospitalizations (treatment and complications) were registered in our Department. Each year about 400 children aged 0 to 18 years of age are treated. Blood, urine, stool and other specimens were collected and cultured in all cases of neutropenic fever and in all non neutropenic patients from sites corresponding to symptoms of infection. Analysis of type of microbiological agents and its resistance to antibiotics was performed.
Results: Out of 5,694 microbiological studies performed, 889 (15.6%) were microbiologically positive, of which 232 (26%) correlated with clinical symptoms of infection. Gastrointestinal infections were the most common: in 61 (26%) episodes Clostridium difficile was identified, in 53 (23%) - rotaviral infection. Bacterial central venous catheter-related infections were confirmed in 55 episodes, 33 with Gram positive agent, 19 with Gram negative. The most common Gram positive bacteria were Staphylococcus spp - 94%. There were 3 episodes of candidaemia (CVC) and 3 episodes of Candida spp cultured in urine specimens
Conclusions: In our material etiological agent was identified in 15% of specimens only. Clostridium difficile was most frequently identified which can be attributed to broad spectrum antibiotics administered in children undergoing anticancer treatment. In case of fever targeted treatment is often not possible, as the cultures are usually negative. Gram positive agents remain the most frequent etiology of CVC-related infections.

EP-424

RESULTS OF PARENT SUPPORT GROUP AND HEALTH PROFESSIONAL SURVEYS ON KNOWLEDGE ABOUT AND ACCESS TO ESSENTIAL MEDICINES IN LOW/MIDDLE INCOME COUNTRIES (LMICS)

E. Grynszpancholc[1], J. Wernikowski[2], R. Barr[3]

[1]Presidency, Fundación Natalí Dafne Flexer, Ciudad Autónoma de Buenos Aire, Argentina; [2]Clinical Pharmacist Paediatrics, Paediatric Haematology/Oncology McMaster Children's Hospita, Hamilton, Canada; [3]Departments of Pediatrics Pathology and Medicine, McMaster University and McMaster Children's Hospital, Hamilton, Canada

Objectives: To gauge knowledge about and identify barriers to access of drugs on the WHO Essential Medicines List from health professionals and parents
Methods: Two surveys were delivered last year, one to SIOP Members, the other to The International Confederation of Childhood Cancer Parents' Organizations (ICCCPO) Members
Results: From SIOP, 82% of respondents (n = 65) were from low and low middle income countries. 74% of respondents knew about the WHO Essential Medicines list (EML) but only 28% were certain that their Government used the EML to guide purchasing of drugs. In 82% of respondent said that drugs were sourced from a combination of Government and NGO's. In the past year, 2/3 of respondents had to delay or cancel treatment due to drug unavailability with 39% experiencing this on a weekly or monthly basis. Forty-five percent felt that drug cost was always a barrier, and 42% felt was sometimes a barrier to access. Fifty-nine percent felt that the price charged to families for drugs was a significant barrier. From ICCCPO, 69% of respondents (n: 48) were from low and low middle income countries. There were 67.5% of respondents who believed there are problems with shortages and delays in their country. Shortage problems are most pronounced in Low- to Middle-Income countries. Delays in medications are due largely to too much bureaucracy. In Low- to Middle-Income Countries, the main reasons for patients/doctors requesting medications is that health insurance companies and government do not supply medications 77% of respondents from L/LMIC budgeted for the purchase of medicines/drugs and 50% of respondents from HIC provide medication.
Conclusions: Access to medicines remains a significant concern in LMICs with Cost/Price, unavailability and beaurocracy being major barriers in delivering treatment.

EP-425

A SUPPORT SYSTEM FOR CHILDHOOD CANCER SURVIVORS WITH JOB-HUNTING DIFFICULTY

M. Hayashi[1], I. Fumiko[2], Y. Ishida[3]

[1]Management, NPO Heart-Link-Working Project, Niigata city, Japan; [2]Management, NPO Hear-Link-Working-Project, Chiba city, Japan; [3]Pediatric Medical Center, Ehime Prefectural Central Hospital, Matsuyama city, Japan

Objectives: There are many childhood cancer survivors (CCSs) launching themselves in various fields because of increasing cure rate. Some CCSs, however, have to struggle with hardship to work. Although the government delivers disability certificates as a social welfare service for handicapped people, there are quite a few CCSs with some problems who are not covered by it. Even in the case of brain tumor CCSs with higher brain dysfunction, only 10% of them can be covered. The handicapped person's employment law gives an opportunity for disable people to find employment. But, again, it is not applied to almost all CCSs who may face with the job-hunting difficulty. We started a project to improve this circumstance.
Methods: We sent out questionnaires to 672 CCSs to grasp their employment situation and 240 answered. We found out some CCSs, even in their late twenties to forties, financially depend on their family.
Results: Last April, we opened a tearoom and hired 5 CCSs. The aim is job-training and the ultimate goal is getting them hired by business society in future. They learn how to communicate people working at the tearoom as waiters/waitress and simple paper working on the computer, as well. They also have opportunities to learn something they want, like getting certified for some special skills. We also assign them to keep daily work description to find what they are not good at and how they overcome it by themselves.
Conclusions: Now it has passed a year since opening the tearoom. The hired CCSs are confident in themselves and positive as a member of society who pays tax. One of them has got married and expects a baby soon. Other one has got hired by a company and started a new life.

EP-426

CLOFARABINE IN CHILDREN WITH RELAPSED ACUTE LEUKEMIA: ISTANBUL EXPERIENCE

Z. Karakas[1], B. Sirin Koc[1], S. Karaman[1], S. Anak[1], A. Unuvar[1], E. Uysalol[1], L. Agaoglu[1], G. Ozturk[1], O. Devecioglu[1]

[1]Pediatric Hematology/Oncology, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey

Objectives: Although Clofarabine is known as an effective novel agent in relapsed acute leukemia, optimum combination and time to use remain a challenge. Aim of this study is to evaluate a clofarabine based protocol in children with multi-relapsed acute leukemia.
Methods: We retrospectively analyzed data of twelve children treated with CLOVE protocol for third or greater bone marrow relapsed acute leukemia between 2009 and 2013. Seven of 12 patients were ALL,5 of them were AML. Patients with relapsed ALL were treated with one or two cure of FLAG after performing BFM-95 REZ protocol and relapsed AML were treated with two cure FLAG after MRC protocol. The cases with no response to at least two relapsed protocol were received CLOVE protocol in one or two cure.
Results: Clofarabine was effective to induce remission in six patients and half of them had hematopoietic stem cell transplantation (HSCT) (Table 1). All of them relapsed after the HSCT, one of them also relapsed after the second HSCT. Although clofarabine was effective to induce remission, overall survive was poor in our study. The 3-month and 12-month overall survival rates from start of CLOVE protocol were 45.5% and 9%, respectively (Figure1). The most common adverse event was prolonged neutropenia, although only one patient died from severe infection, all of the patients had severe bacterial and invasive fungal infections. Also, we observed elevated liver enzymes in 92% of the patients. One patient with refractory AML needed pediatric intensive care due to severe hepatotoxicity and VOD after clofarabine therapy.
Conclusions: All of the patients except one died from relapsed/refractory leukemia even though four of them had HSCT. Although we have provided longer lifetime using the CLOVE for multiple relapsed acute leukemia, subsequently the patients died from uncontrolled leukemia. Therefore, we suggest that clofarabine can be used at the first relapse in leukemia with MRD determination to obtain better results. The main question remains if better outcomes could be obtained with earlier Clofarabine based chemotherapy.

EP-427

INFECTIONS WITH RESPIRATORY VIRUSES IN CHILDREN WITH CANCER IN ISTANBUL

R. Kebudi[1], S. Bay Kapu[2], B. Oflaz Sozmen[3], M. Ciblak[4], O. Gorgun[1], B. Zulfikar[1], S. Badur[4]

[1]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute, Istanbul, Turkey; [2]Pediatric Hematology - Oncology, Istanbul University Oncology Institute, Istanbul, Turkey; [3]Pediatric Hematology - Oncology, Koc University and American Hospital, Istanbul, Turkey; [4]Microbiology, Istanbul University Medical Faculty, Istanbul, Turkey

Objectives: Respiratory virus (RV) infection can cause significant morbidity and mortality in pediatric cancer patients. The aim of this study is to identify the RV infections in children with cancer presenting with signs and symptoms of respiratory tract infection.
Methods: During January1-March 15 2014, all children with cancer presenting with signs and symptoms of respiratory tract infection were assessed for RV with algorithms and molecular techniques (rRT-PCR) suggested by CDC and WHO in the reference Virology laboratory, of Istanbul University.
Results: Samples in 34 episodes of 31 children with cancer were evaluated. The following 20 RV were identified in 17 episodes: influenza A (H3N2) 5, Influenza B 1, Respiratory Syncytial Virus 4, Rhinovirus 4, Coronavirus 3, Metapneumovirus 2, Bocavirus 1. Five patients had lower respiratory tract infection (Influenza A 2, RSV 1, a patient with Coronavirus had also pleural effusion). Fever, cough, nasal discharge and sore throat were the most common symptoms. Systemic antibiotics were also given in febrile neutropenic episodes. Patients with influenza were treated with oseltamivir. All except 2 (1 Rhinovirus, 1 Metapneumoniae + parainfluenza), required hospitalization. All recovered with specific and/or supportive treatment. Chemotherapy had to be delayed for 3-7 days in most episodes.
Conclusions: It should be kept in mind that viruses are a major cause of respiratory tract infections in children with cancer. Oseltamivir is effective in treatment of influenza in children with cancer. Since there are no effective antiviral agents for some respiratory viruses, precautionary infection control and early diagnosis is important to prevent the infection spread. In most cases, hospitalization and supportive care is needed to reduce morbidity and avoid mortality.

EP-428

IMPROVED OUTCOME OF INVASIVE FUNGAL DISEASE IN PEDIATRIC CANCER PATIENTS: LOCAL INSTITUTIONAL EXPERIENCE OVER 21 YEAR

T. Khattab[1], W. Jastaniah[1], K. Abdullah[1], K. Hanif[1], A. Mufti[1], M. Asseri[1], M. Abrar[1]

[1]Princes Noorah Oncology Center, King Abdulaziz Medical CityNational Guard Hospital, Jeddah 21423, Saudi Arabia

Background
Increased incidence of invasive fungal disease (IFD) due to increasing intensity of various chemotherapy. IFD are a common cause of morbidity and mortality in immunocompromised patients. Available many antifungal agents have an impact on outcome.
Objectives: To find type of cancer infected with IFD, types of IFD and study outcome of pediatric cancer patients with IFD and impact on survival.
Methods: Retrospective review of pediatric cancer and hematological malignancies who developed during their illness proven or probable IFD from 1993-2013. We reported at ASCO 2008 abstract No.10046 overall survival 33/61 = 54%, mortality due to cancer 18/61 = 30% and due to IFD 10/61 = 16%. We will report types of cancers, type of fungal disease, overall survival and mortality whether due to primary disease or IFD.
Results: Over this period 180 patients registered, 108 with ALL = 60% (21/108 = 20% relapsed ALL), 28 AML 16%, 13 NHL, 8 NBL, 4 RMS, 4 WT, 2 for each OS, LCH, HD, Chediak Higashi synd., MBL and aplastic anemia; 1 for each ES, CML, HLH. 49 pts. proven aspergillosis 24/49 = 49% Survived and 25 died (19 from primary disease, 6 from IFD. 49 pts. with candidiasis 28/49 = 57% survived and 21 died (14 from primary dis., 4 fungal and 2 sepsis). 76 pts. considered probable IFD 68/76 = 89%survived, 8 died of primary disease. 6 mucormycosis, 2/6 = 33% survived (2 died of primary disease after cure of cutaneous and pulmonary mucormycosis, while 2 died of mucormycosis). Overall survival 122/180 = 68%, mortality primary disease 43/180 = 24% and mortality IFD 14/180 = 8%
Conclusions: Comparing with our previous abstract showed local improved outcome of IFD due to proper timing of starting empirical antifungal, C T fungal diagnostic approach. Surgical debridement of cutaneous lesion, sinuses and lung lesion once indicated, choosing appropriate antifungal agent according to each patient clinical and functional status.

EP-429

PATIENT-REPORTED MEASUREMENTS OF ORAL MUCOSITIS IN CHILDREN WITH CANCER

I.J. Márton[1], A. Jenei[1], T. Ungvári[2], K. Gyurina[3], J. Sándor[2], C. Kiss[3]

[1]Department of Restorative Dentistry, University of Debrecen, Debrecen, Hungary; [2]Department of Biostatistics and Epdemiology, University of Debrecen, Debrecen, Hungary; [3]Department of Pediatric Hematology-Oncology, University of Debrecen, Debrecen, Hungary

Objectives: Aim of this study was to evaluate the administration of the Patient-Reported Oral Mucositis Symptom (PROMS) scale among pediatric cancer patients, to compare PROMS-derived data with dental surgeon assessed oral health measures and to establish the adverse impact of OM on quality of life (QoL).
Methods: Seventy-five children with cancer (19 males, 46 females; age 12.0 ± 4.3 yrs) were investigated between January, 2011 and December, 2012. Hungarian version of PROMS self-administered scale was used. Participants filled in the questionnaire according to the severity

of symptomes ("items") on a visual analogue scale on admission and weekly (Days 7, 14, 21, 28 and 35). The sum of item scores gave the total PROMS score. OM was diagnozed by a dental surgeon using the WHO score. Cariological and periodontal conditions, WBC, anticancer drugs and antiinfective supportive therapy were registered.
Results: OM was observed in 53/75 (71%) patients. Total PROMS score increased gradually by Day 21 followed by a transient decrease on Day 28 and a 2nd peak on Day 35. In contrast, patients with ALL, the largest homogenous subgroup of patients (No. 44) exhibited a monotonously decreasing tendency of the total PROMS score from Day 21, i.e. by concluding induction therapy. We found significant associations ($p < 0.05$) between PROMS item scores and WHO OM score and its components. Significant correlations ($p < 0.05$) were observed between item and total PROMS scores and WBC. There were no significant associations between cariological and periodontal indices and the total PROMS score and item scores.
Conclusions: PROMS questionnaire is an easy-to-use and suitable measure of OM in pediatric patients. Characterizing the incidence and severity of OM by PROMS may allow to develop a comprehensive program to reduce this highly distressing side-effect of cancer treatment in children. The study was **supported** by the TÁMOP 4.2.1./B-09/1/KONV-2010-0007, TÁMOP-4.2.2.A-11/1/KONV-2012-0025, OTKA K108885 projects.

EP-430

RELATIONSHIP OF CYP3A5 EXPRESSION AND VINCRISTINE NEUROTOXICITY IN TURKISH CHILDREN WITH MALIGNANCY

U. Kocak[1], H. Kayilioglu[1], D.K. Karaer[2], E.P. Percin[2], A. Okur[3], C. Karadeniz[3]

[1]Pediatric Hematology, Gazi University School of Medicine, Ankara, Turkey; [2]Genetics, Gazi University School of Medicine, Ankara, Turkey; [3]Pediatric Oncology, Gazi University School of Medicine, Ankara, Turkey

Objectives: Vincristine is a widely used chemotherapeutic agent in the treatment of childhood malignancies. Neuropathy which can be a combined onset of peripheral, progressive, motor, sensorial and autonomic components is not only the most common adverse effect of vincristine treatment, but also is the leading cause of dose modifications. However vincristine dose that will cause neuropathy in a particular patient can not be decisively anticipated. CYP3A4 and CYP3A5 enzymes of cytochrome p450 enzyme system are responsible in vincristine metabolism. CYP3A5*3, which is the most common allele encodes for an abnormally spliced mRNA with a premature stop codon, resulting in decreased expression of CYP3A5. CYP3A5*1, which is the most common allele in African-American people, can provide high expression rates of CYP3A5 and fast metabolism of vincristine which leads to lesser neurotoxicity. In this study, distribution of CYP3A5 alleles among Turkish children with malignancies, relation between CYP3A5 genotype and neurotoxicity rates, and severity, duration of neuropathy and total vincristine doses were investigated.
Methods: Files of 115 patients (age 1 - 17 years) who were treated with vincristine consisting chemotherapy protocols were retrospectively reviewed for neurotoxicity and CYP3A5 genotypes were analyzed. Neurotoxicity was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events Scale.
Results: Neurotoxicity occurred in 20.8% of patients. Combined sensorial and motor neuropathy was the most common form. Although it was found to occur more frequently after the 4th dose of vincristine and rates were higher in the low dose vincristine group suggesting other contributing factors. While neurotoxicity rate in the CYP3A5*1/*3 genotype was 17.6%, it was 21.6% in the CYP3A5*3/*3 genotype and the difference was not statistically significant ($p < 0.05$).
Conclusions: In conclusion, this study suggested that vincristine related neurotoxicity is dose-independent and genotype is not the only causative factor in the occurrence of neurotoxicity in these patients.

EP-431

OUT-OF-POCKET COSTS CAN LEAD TO FINANCIAL CRISIS IN FAMILIES OF CHILDREN WITH CANCER THAT COULD BE AVOIDED WITH THE PROVISION OF BASIC FINANCIAL SUPPORT

J. Lamont[1]

[1]Candlelighters Childhood Cancer Support Programs, Ottawa, Ontario, Canada

Families of children with cancer experience numerous out-of-pocket expenses that create additional emotional stress and financial challenges that can seem insurmountable. The provision of basic financial assistance lessens the financial burden on families and helps reduce the number of those who face financial crisis and other longer-term economic implications.
Input, feedback and ongoing dialogue with families and healthcare providers consistently identified areas of need (parking fees, gas costs, meal expenses incurred for parents at hospital, childcare), which were addressed by Candlelighters through the provision of programs that have genuine impact in a family's financial situation. An on-line survey was conducted in February 2014 to evaluate the significance of these programs in the childhood cancer journey. Eighty-two percent of those surveyed reported having experienced financial hardship as a result of having a child with cancer. Of the 95% of responding families who have benefitted from Candlelighters' initiatives, 74% of them reported that their family would have experienced a financial crisis without Candlelighters assistance. (Financial crisis* defined as the need to request additional financial assistance beyond what is provided to all families by Candlelighters); 91% of the survey respondents reported that they believe every family who has a child diagnosed with cancer, regardless of race, religion, culture or socioeconomic status should be eligible for this basic funding, with the knowledge that additional funding could be accessed based on additional need. Sixty-one percent feel that there is enough financial assistance available for families, in large part due to the services provided by Candlelighters. There is no avoiding the inevitable out-of-pocket costs that result when a child is diagnosed with cancer. Providing much needed financial support for "everyday" expenses results in a more stable financial situation and has a positive effect in a family's overall financial position when coping with childhood cancer.

EP-432

RESULTS OF TRACKING WILMS TUMOR PATIENTS IN KENYA

J. Libes[1], F. Njuguna[2], J. Musimbi[2], K. Patel[3], H. Lovvorn[4]

[1]Pediatric Hematology-Oncology, Vanderbilt University, Nashville, USA; [2]Pediatric Hematology-Oncology, Moi Teaching and Referral Hospital, Eldoret, Kenya; [3]Immunology, Moi Teaching and Referral Hospital, Eldoret, Kenya; [4]Pediatric Surgery, Vanderbilt University Children's Hospital, Nashville, USA

Objectives: Review of the Kenyan Wilms Tumor (WT) Registry and tracing calls revealed an estimated 2 year overall survival (OS) of 36 percent for patients diagnosed between 2008 and 2011 due to in-therapy mortality and treatment abandonment. We report preliminary results of tracking efforts for WT patients at Moi Teaching and Referral Hospital.
Methods: In January 2013, a trained research nurse called parents who had abandoned treatment or off therapy follow up for their children between 2008 and 2012 to determine vital status and encourage return to therapy. In 2013, she tracked all patients previously and newly diagnosed after each missed visit.
Results: Patients diagnosed with WT between 2008 and 2012 ($n = 56$) had a 28.6 percent in-therapy mortality rate and a 17.9 percent mortality rate from treatment abandonment. The abandonment rate was 39.3 percent, of which 27.3 percent were alive (one patient returned to therapy), 27.3 percent were not contactable and 45.5 percent died. Nine percent of patients were lost to follow up after termination of treatment, of which one patient returned after the tracing call. OS was estimated at 41 percent. While patients diagnosed in 2013 ($n = 26$) are still in therapy, there is preliminarily a 27 percent in-therapy mortality rate. One patient abandoned treatment and returned after the tracing call.
Conclusions: Results are preliminary due to documentation lag time and time short of 2 years. In-therapy mortality remains high. Tracking after missed visits results in potentially less treatment abandonment, but false beliefs and financial constraints still exist. Standardized treatment protocols, supportive care, education and financial support will be crucial to improve survival from WT in Kenya.

EP-433

SHUT IN, SHUT OUT, SHUT UP: CAREGIVERS OF LONG-TERM PAEDIATRIC BRAIN TUMOR SURVIVORS

S. Lymbery[1]

[1]Doctoral Student Educational Leadership & Policy, University of British Columbia, Vancouver, Canada

Objectives: What can a weblog for caregivers of paediatric brain tumor (PBT) survivors contribute to the current state of knowledge about their caregiving work? How might an online blog address the silencing isolation these caregivers experience? What can be learned about their needs and lifestyles? In what ways does their informal, unpaid work constrain their quality of life? How has the health of caregivers been impacted given decades of unpaid work for their child/youth/adult?
Material: More and more PBT survivors are living into adulthood, but most are unable to gain self-sustaining employment or maintain friendships, and given their health and social vulnerabilities, they require the daily supports provided by parents, particularly mothers. For the past 31 years, I have been the caregiver for my son, who had a malignant, inoperable PNET brain tumor diagnosed at age 6. Radiotherapy calcified his invasive tumor, but long-term effects continue to disable him progressively, with declines typical of the demographic: hearing and sight losses, impaired speech, endocrine issues, mobility factors, cognitive speed, and strokes. I am both a researcher *and* a research subject in a new weblog project to create knowledge and interconnect 4,000 Canadian caregivers for PBT survivors.
Methods: Using anonymous weblog data, I hope to assess the current state of caregiving knowledge for PBT survivors, including unmet needs. Qualitative narrative inquiry and post-modern standpoint theories will help assess issues of social isolation, invisibility and silencing, and economic loss. Research project and ethical approvals are now in process.
Results: Your venue will help inform caregivers about this new Canadian project, by a PBT survivor's caregiver and doctoral student.
Conclusions: It is hoped this research will identify personal, social and economic barriers faced by caregivers of PBT survivors. It is also hoped that themes for future advocacy work will also be identified.

EP-434

CHEMOTHERAPY MEDICATION ERRORS ON THE PEDIATRIC ONCOLOGY CLINIC AT THE NATIONAL CANCER INSTITUTE OF COLOMBIA

N.M. Mesa-Rincon[1], A. Carreno[2], A. Ahumada[3], C. Casas[4], J. Lagos[4], D. Ozaeta[4]

[1]Pediatric Oncology, National Cancer Institute, Bogota Dc, Colombia; [2]Clinical Investigation Group, National Cancer Institute, Bogota Dc, Colombia; [3]Pharmacy, National Cancer Institute, Bogota DC, Colombia; [4]Pediatric Oncology, National Cancer Institute, Bogota DC, Colombia

Objectives: To establish and classified the chemotherapy medical error at our Outpatient Clinic. There is worldwide a potential increase in the number of errors related to prescriptions due to the increase of new drugs on the market and the clinical practice. As well know the medication errors in oncology services is about 9% and many of them causing all kind of lesions over the patients like a disability lesions, even the death. In many of cases this errors go in unobserved and start from the prescription, preparation until administration over the patient.
Methods: It was a cross sectional study and we established a sample size for analyzing the chemotherapy prescriptions in the oncology pediatrics service care. There was a review of chemotherapy orders at the National Cancer Institute-Colombia Pediatric Oncology Outpatient Clinic during the period six months between july 2012 to december 2012. Errors types were classified using the **National Coordinating Council for Medical Error Reporting and Prevention Index for Categorizing Medication errors**
Results: In a six months period there were about 1100 chemotherapy prescriptions for oncology, hematology and pediatric oncology. The pediatric oncology sample size was 85 and we found 19 medication errors (22.4%). The most frequent errors were mainly related with the dosage and with the omission of some medications. There weren't any death or disability secondary by medication error
Conclusions: In the analysis period none of these errors led disabilities or deaths over any patient, therefore doesn't know in the future. We don't know how many errors were potentials and how many errors not were related with the prescription and how many were corrected at the administration time. With the introduction of new medications to the clinical practice it's necessary to develop a program to avoid errors related with the prescription, dosage and identification of the patients.

EP-435

ADOLESCENTS AND YOUNG ADULTS (AYA) PROGRAM IN BARRETOS, BRAZIL

S.M. Volc[1], L.F. Lopes[2], C.A. Dantas Pereira[3], S.V. Serrano[3], F.M. Carcano[3]

[1]Clinical/Pediatric oncology, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Pediatric Oncology, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Clinical Oncology, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: Adolescent and Young adult oncology is an ongoing science. As NCI recognizes, this population ranges from 15 to 39 years old, and has its own characteristics and demands. This age group has been underrepresented in clinical trials and it could be the reason for the lack of improvement in survival rates over the last 30 years. Different organization models drive pediatric oncology and medical oncology. Adult cancers are resistant to chemotherapies, exactly the opposite is seen in pediatric oncology. They should receive a different model of care. Current opinion says that training pediatric and medical oncologists in all the skills needed to manage a multidisciplinary AYA treatment strategy is the best way.
Methods: Several attempts at AYA comprehensive programs are in development all over the world. One of them is taking place in Barretos' Cancer Hospital, in Brazil. In order to improve the communication and cooperation between pediatric oncologists and medical oncologists, we designed an integrated model of care. A pediatric oncologist composes the adult sarcoma/melanoma team and a patient-focused approach has taken place. Patients under the forties enter in the pediatric clinics, where a team of pediatric and clinical oncologists is trained to recognize their specific demands.
Results: The AYA program in Barretos, Brazil, has iniciated recently with a very good acceptance.
Conclusions: Pediatric and adult oncology groups come from different backgrounds and have different priorities even when they deal with similar diseases, different practices tend to be homogenized in this model of care and it improves the institutional treatment. In 2011 and 2012, a total of 2,148 patients between 15 and 39 years old were treated in our institution. It represents almost 10% of the total patient population. The numbers are expressive and, in 2013, a differentiated model of care came to answer the specific questions and demands of the AYA patients.

EP-437

PEDIATRICS ONCOLOGY NETWORK DATABASE (POND): A USEFUL ADJUNCT IN SETTING UP OF A NEW PEDIATRICS HEMATO-ONCOLOGY UNIT AND CANCER REGISTRY IN THE DEVELOPING WORLD

R. Mohammed[1], C. Yogiraj[1], S. Rajat[1], K. Satyendra[1], Y. Satya Prakash[1]

[1]Pediatrics Hematology Oncolgy and BMT Unit, Fortis Memorial Research Institute, Gurgaon, India

Objectives: A nationwide registry is lacking for paediatric cancer patients in India. Pediatric Oncology Network Database (POND) is a useful adjunct to create or supplement cancer registry. It is a free online database provided by St. Judes Children's Hospital, USA to pediatric oncologists in the developing countries. Here we describe the usefullnessof POND in registering data of all newpatients in first one year after setting up of a newpediatrics hematology-oncology (PHO) and bone marrow transplant (BMT) unit.
Methods: All new patients registered in PHO unit in the first one year were included. Their data regarding diagnosis, treatment and outcome was prospectively entered by an experienced data base manager in POND.
Results: We had 293 new patients registered in our unit with blood and cancer disorders and their data was entered in POND. Malignant hemato-oncology- 75 patients (Acute lymphoblastic leukemia- 48, Acute myeloid leukemia-7, Chronic myeloid leukemia-5, Hodgkin lymphoma-7, Non-hodgkin lymphoma-8). Solid tumor- 28 patients (Brain tumor-7, Wilms tumor- 8, Neuroblastoma-5, Adrenocortical carcinoma-1, Rhabdoid tumor-1, Teratoma-2, Ewing sarcoma-3, Retinoblastoma-1. Benign hematology –190 patients (Immune thrombocytopenic purpura-24, Aplastic anemia-15, Thalassemia-40, Sickle cell anemia-10, LCH-7, Hemolytic anemia-8, Megaloblastic anemia-2, Pure red cell aplasia-4, Hemophilia-4, Hemophagocytic lymoho histiocytosis-2, Primary immunodeficiency- 12, Congenital dyserythropeitic anemia-1, Sideroblastic anemia-1, Congenital neutropenia-1, Protein C deficiency-1, others diseases-58. Hematopoetic stem cell transplant (HSCT) was performed in 17patients. Autologous were 5 (NHL-1, Medulloblastoma-3, AML-1) and 12 were allogeneic (Aplastic anemia-2, Thalasemia major-4, Sickle cell anemia-3, Primary Immunodeficiency-2, Myelodysplatic Syndrome-1).
Conclusions: POND is a useful adjunct in maintaining hematology-oncology patients' database. We recommend this in each PHO unit in India to create a registry.

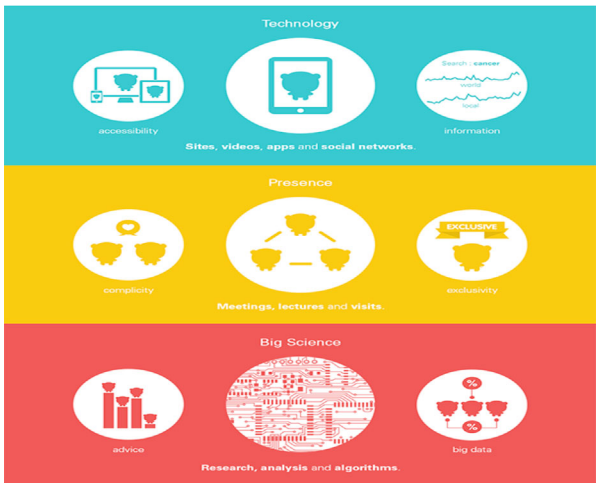
EP-438

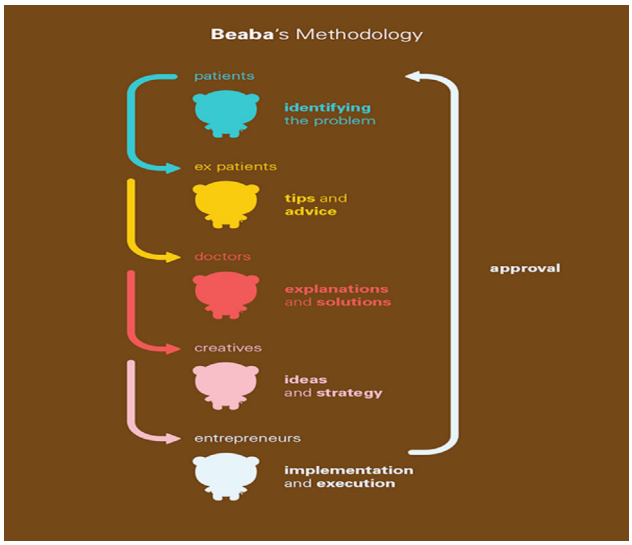
BEABA: FROM PATIENT TO TRANSFORMING AGENT - INFORMATION AS MEDICATION TO DESMYSTIFY CANCER

S. Mozzilli[1], R. Leão[1], J. Boechat[1], E. Sassi[1]

[1]Director/Creative, Instituto Beaba, Sao Paulo, Brazil

Objectives: The oncologic world is a particular universe. Each child and their family who debuts in this environment are impacted by new experiences, complex terms and meanings that are frightening. Our mission is to demystify this environment, presenting information about cancer and its treatments in a way that is clear, objective and optimistic.
Methods: Beaba is a nonprofit organization composed of young patients, ex-patients, doctors, creatives and entrepreneurs. Our difference is in the design methodology where the young patients are the ones responsible for creating the briefings. They pinpoint everything that bothers, frightens or is unknown to them. After the data is collected, they then proceed to discussions with former patients, who also give their suggestions and opinions. Then come the doctors, who are responsible for the knowledge that assesses and validates everything. With all the information at hand, the creative team figures out the best strategy to meet the little patients' needs and, after their approval, the entrepreneurs execute the idea. The material that is produced ranges from a wide variety of products, such as 'The Etiquette Manual' for society learn how to treat cancer patients and 'Personal Workshops', where small patients and ex-patients will teach the newcomers.





Results: The result was an increase in self-esteem of these young patients who, in addition to feeling the importance of being responsible for the entity's activities, realize that they actually became role models for other children. The little patient turned from a passive individual to an active one, coordinating the learning process of innumerous children and thus, promoting the exponential growth of Beaba.
Conclusions: Information still is the best way to save lives. Whether it is used for early diagnosis, to relieve symptoms or ease fears, it relaxes and invigorates the little cancer patients.

EP-439

SYMPTOMATIC THROMBOSIS IN LEBANESE CHILDREN WITH CANCER TREATED AT A TERTIARY CARE CENTER

S. Muwakkit[1], N. Hashwe[1], K. Charafeddine[2], E. AbdelRahman[1], A. Chan[3], R. Saab[1], H. Tamim[4], M. Abboud[1], H. El-Solh[1], A. El Traboulsi[5]

[1]Department of Pediatric and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; [2]Department of Pathology and Laboratory Medicine, American University of Beirut, Beirut, Lebanon; [3]Department of Pediatrics, McMaster University, Hamilton, Canada; [4]Department of Internal Medicine, American University of Beirut, Beirut, Lebanon; [5]Pediatric Hematology-Oncology Fellow, Children's Cancer Center of Lebanon, American University of Beirut Medical Center, Beirut, Lebanon

Objectives: To study the prevalence and potential risk factors for thromboembolism (TE) in children with cancer.
Methods: A retrospective chart review of children (<21 years) between 2002 and 2013 who developed symptomatic TE.
Results: 914 patients were treated at CCCL over a period of 11 years; all had central venous lines (CVL). 49 (5.4%) patients developed symptomatic TE, mean age was 10.3 years (Range, 2 months-20 years). 30 were males. 19 (39%) patients had evidence of CVL dysfunction. 15 patients (30.6%) either died or are alive with recurrent end-stage disease, while 34 remain alive and disease free (ADF). Of 213 ALL patients, 18 (8.4%) developed TE. All CNS TE occurred while receiving steroids and L-asparaginase concomitantly. 17 remain alive. All received anticoagulation. Nine patients with sarcoma had TE. All had tumors >5 cm. Six had metastatic lung disease. Seven developed disease recurrence; 2 are ADF. Eleven lymphoma patients (8.3%) developed TE; 7 had bulky mediastinal disease. Three died, 8 are ADF. 4 (2.5%) patients with brain tumors developed symptomatic TE; 3 died. 3 (6.4%) AML patients had TE; 2 are ADF. The 2 patients with neuroblastoma were infants <6 months old; both are ADF. Children with solid tumors and thrombosis had worse outcome than those without thrombosis. 31 patients were tested for inherited thrombophilia: 3 (9.7%) had heterozygous Factor II mutation and 8 (25.8%) had heterozygous Factor V Leiden.
Conclusions: Prevalence of symptomatic TE was 8.4%, 8.3% and 5.1% for patients with ALL, lymphomas and sarcomas, respectively. Patients with TE were older compared to children with the same cancer diagnosis. More than 30% had CVL dysfunction. One third of patients with TE died or reached end stage recurrent disease. Factor V Leiden was prevalent. Duration of anticoagulation was variable (mean, 10 months/patient). Brain tumor patients had low incidence of thrombosis. Solid tumor patients with thrombosis had worse outcome.

EP-440

CORRELATION OF PET-CT AND IMAGE GUIDED BIOPSY RESULTS IN CHILDREN

S. Nihayah[1], A. Shammas[1], R. Vali[1], B. Connolly[1]

[1]Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, Canada

Objectives: To evaluate our early experience in the correlation of PET-CT with image guided biopsy (IGBx) results in a pediatric population, to better understand the role PET-CT may play.
Methods: This is a single centre retrospective case series. Patients who underwent IGBx and PET CT scan between January 2007 and December 2012 were analyzed. Inclusion criteria were those whose IGBx occurred within 6 weeks of their PET-CT scan (prior to or post biopsy). Clinical, demographic, imaging and pathology reports were collected using RedCap and correlated. Descriptive statistics were employed.
Results: Forty-five patients (23 male and 22 female) were included, aged 4-17 years (median 10.5 years). Twenty-patients had known malignancy. Coaxial technique was used in 36/47, with ultrasound guidance in 40, CT in 6, and fluoroscopy in 1. Biopsies involved soft tissues (43) and bone (4). There were 3 minor and 1 major complication (bleed requiring transfusion). 39/47 PET scans were positive and 8/47 PET scans were negative. Of the 39 positive scans, biopsy in 19 showed a malignant diagnosis, 13 a benign diagnosis (nfection/inflammation), 1 normal tissue and 6 were inadequate. Of the 8 negative PET scans a benign diagnosis was found in 5 and malignant in 3 (interval chemotherapy had been given). Concordant results between biopsy and PET was obtained in 32/47 and discordant results were obtained in 15/47. Sensitivity of PET was 80% and PPV 82%.
Conclusions: PET-CT can play a valuable role in directing image guided biopsies in children.

EP-441

CHEMOTHERAPY ADMINISTRATION IN PEDIATRIC ONCOLOGY: DILUTION IS NOT THE SOLUTION

F. Normand[1], P. Leblond[2], I. Sakji[1], H. Sudour[2], G. Marliot[1], C. Lervat[2], S. Mercier[2], S. Delbey[1], A.S. Defachelles[2]

[1]Clinical Pharmacy Department, Oscar Lambret Center, Lille, France; [2]Pediatric Oncology Unit, Oscar Lambret Center, Lille, France

Objectives: Due to the young age of some of our pediatric patients (4,370 chemotherapies in 2013), administration of high volumes during a short time could be responsible for adverse effects (mainly cardiovascular). Dilution volume associated with chemotherapy rinsing volume was designated as problematic by pediatric oncologists. So our aim was to reduce these volumes to optimize medicinal treatments.
Methods: By consulting protocols used in our hospital, we have identified different doses prescribed for each anticancer drug. In cooperation with pediatric oncologists, we took care about factors affecting terms of dilution (weight, dose, route of administration: peripheral or central line infusion, risk of extravasations, physicochemical stability of molecules linked to final concentrations and infusion rates). We have based our research on our anticancer drugs thesaurus (n = 24).
Results: An adaptation of anticancer drugs dilution volumes was done for the 24 pediatric anticancer drugs prescribed. In most protocols drug doses were determined according to patient's weight, or according to body surface area. We decided to define three subgroups of patients (less than 10kg, 10 to 30 kg and over 30kg). A summary table was made and approved by pediatric oncologists, summing up dilution volumes for each subgroup of patients. Most anticancer drugs are diluted in mini-bags (78%). In 86% of cases, volume is less or equal to 100 mL. For patients less than 10kg, infused volumes are less than 50mL in 66% of cases.
Conclusions: This multidisciplinary approach has succeeded to reduce volumes infused to children and adapt our practices to pediatric specificities. Through this improvement, we have

optimized care for our patients. Due to the overfilling of industrial mini-bags, the use of empty bags should be promoted in most cases.

EP-442

CONDOM-USE PERCEPTION BY ELDERLY PEOPLE: A BIG CHALLENGE TO HIV/AIDS MITIGATION IN HIGH RISK URBAN SLUMS IN AFRICA

K. Odor[1], R. Opara[2]

[1]Health Promotion, University of Ibadan Nigeria, Ibadan, Nigeria; [2]Aged Care, Gertrude Nursing Home, Sydney, Australia

Objectives: As HIV/AIDS continues to pose a public health challenge in Africa, the pandemic cut-across borders. It affects every age group including old persons, despite engagement in risky sexual activities which increases HIV/AIDS infection. However, limited attention is paid to this sub-group in mitigating the pandemic. This study therefore examined condom-use and perceived HIV/AIDS infection among old people in Africa.
Methods: The study was cross-sectional in design. A multi-stage sampling procedure was used to select 400-geriatrics. Pre-tested questionnaire developed, using information obtained from 10 Focus Group Discussion (FGD), was used to collect information. FGD data were analyzed thematically, while questionnaire data were analyzed using descriptive and statistically.
Results: Twenty-five percent of the participants had extra-marital sex since they attained elderly age. However, among this subgroup that had extra-marital sex, few (6.8%) used a condom. More males (5.3%) than females (1.5%) used condom during the last extramarital sex. Low level of condom-use was attributed to condom not worthwhile (34.5%) and opinion (50.0%) condom not made for the elderly. Moreover, FGD participants viewed sex could not lead to pregnancy and majority (60.3%) posited patronizing traditional healers and few (10.3%) use of herbs/concussion could prevent HIV/AIDS. Similarly, non-condom use was due to confidence in traditional herbs, perceived to protect against STIs including HIV/AIDS.
Conclusions: Engagement in risky activities among elderly is a growing HIV/AIDS challenge. Condom-use is misconstrued probably due to knowledge gap. Without urgent measures to enable them protect themselves, development efforts will be in jeopardy. Investing in geriatric SRH is cost-effective intervention in mitigating HIV/AIDS pandemic.

EP-443

MALIGNANCIES IN PRIMARY IMMUNEDEFICIENCIES: SINGLE CENTER EXPERIENCE

T. Patiroglu[1], H.H. Akar[2], M. Ozdemir[1], E. Unal[1], M. Karakukcu[1], T. Patiroglu[3]

[1]Department of Pediatric Hematology and Oncology, Erciyes University Faculty of Medicine, Kayseri, Turkey; [2]Department of Pediatric Immmunolgy, Erciyes University Faculty of Medicine, Kayseri, Turkey; [3]Department of Pathology, Erciyes University Faculty of Medicine, Kayseri, Turkey

Objectives: The overall risk for developing malignancy in children with primary immunodeficiency (PID) is estimated at 4-25%. Non-Hodgkin's lymphomas predominate, accounting for 60% of cases. The PIDs known to be associated with increased incidence of malignancy are: common variable immunodeficiency (CVID), IgA deficiency, and DNA repair disorders. During recent years other types have also been included, such as severe combined immunodeficiency (SCID) and Wiskott Aldrich syndrome (WAS). Here, we aimed to study the histopathological characteristics of malignancies in PIDs and to report results from a single reference center at middle Anatolia in Turkey.
Methods: We presented eight patients (1 male, 7 females) with PIDs which were evaluated at the Pediatric Hematology-Oncology Department of Medical Faculty, Erciyes University between 1996 and 2013. The age at diagnosis of PIDs, age at diagnosis of malignancies, histopathological characteristics of malignancies, and clinical courses of patients were analyzed.
Results: In a 17-year study period, there were 8 patients with malignancies associated with PIDs. The patients ranged from 5.5-20 years of age with the mean age of 11,75 years (SD $\pm$ 5,55 years) at the diagnosis of malignancies. Histopathologically, five patients were with diffuse large B cell lymphomas, 3 of those with idiopathic CD4 deficiency, and 2 of those with DNA repair immunodeficiencies (Ataxia-telangiectasia, Nijmegen Breakage Syndrome). The remaining 3 patients had Hodgkin's Lymphoma with ataxia-telangiectasia, Osteosarcoma with Bloom's syndrome, and Gastric Signet Ring Carcinoma with ataxia-telangiectasia, respectively.
Conclusions: Here, we want to underline again that PIDs are genetic disorders which predispose patients to malignancies as well as to severe infections and autoimmunity.

EP-444

MEETING THE NEEDS OF AT-HOME SIBLINGS OF PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) PATIENTS

R. Pentz[1], T. White[2], K. Hendershot[1], M. Aldefer[3], M. Dixon[1], W. Pelletier[4], K. Stegenga[5], P. Hinds[6]

[1]School of Medicine, Emory University, Atlanta, USA; [2]School of Medicine, Emory University Winship Cancer Institute, Atlanta, USA; [3]Center for Healthcare Delivery Science, Nemours/Alfred I. duPont Hospital for Children, Wilmington, USA; [4]Hematology/Oncology/Transplant Program, Alberta Children's Hospital, Calgary, Canada; [5]Nursing Research, Children's Mercy Hospitals and Clinics, Kansas City, USA; [6]Division of Nursing, Children's National Medical Center, Washington, USA

Objectives: At-home siblings of pediatric cancer HSCT patients report lack of information, lack of inclusion, family separation, and additional responsibilities during the family's transplant experience (1). Although resources currently exist to help these siblings, these children may benefit from personal attention and information. The purpose of this study is to identify strategies for helping at-home siblings. We propose a novel cyber-intervention implemented by Certified Child Life Specialists.
Methods: We conducted a secondary semantic analysis of qualitative interviews completed with family members of pediatric HSCT patients, coding the data for strategies the family used during the cancer experience. We also interviewed HSCT healthcare team members regarding current resources for at-home siblings and suggested additional interventions.
Results: 42 family interviews were coded and 15 healthcare workers were interviewed, including Certified Child Life Specialists (CCLS), inpatient nurses, midlevel providers, psychologist, social worker, and physician. The most frequently used strategies were meetings with a member of the healthcare team, sharing all information with the child, using phone calls or Skype to communicate more often, having parents split time between hospital and home, attending sibling support groups or workshops, giving the sibling a special role, having the sibling visit the hospital, and having a special day or event for the sibling. Twelve (80%) healthcare workers expressed concern about at-home sibling distress not addressed by current support which requires travel, 11 about lack of sibling inclusion, and 5 about lack of information. All 15 nominated CCLS to intervene with these siblings via Skype to address the needs felt by at-home siblings.
Conclusions: Existing resources are inadequate to meet the needs of at-home siblings of children undergoing HSCT. These children may benefit from personal information and support delivered through a variety of strategies by both family members and healthcare workers. A novel CCLS virtual intervention may help alleviate siblings'unmet needs.

EP-446

USE OF RASBURICASE IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES: EXPERIENCE FROM A PEDIATRIC HEMATO ONCOLOGY CENTRE IN SOUTHERN INDIA

K. Rathnam[1], J. Somasundaram[1], V. Kasi[1], R. Priya[1], S.R. Vinesh[1], D. Rajeswari[1]

[1]Dept of Pediatric Hematology Oncology, Meenakshi Mission Hospital@Research Centre, Madurai, India

Objectives: Rasburicase rapidly reduces plasma uric acid (PUA) and thus markedly decreases the risk of renal failure in tumor lysis syndrome (TLS). However, there is very limited data on its use in India because of limited use due to high-cost. This study analyses use of rasburicase in a resource limited setting.
Methods: This retrospective study looks at the efficacy and safety of rasburicase in 41 children with hematologic malignancies treated over a period of 42 months. Male:Female was 32:9. Thirty-four had laboratory TLS and 7 were at risk for TLS. Diagnoses: T-cell ALL, 19; Pre-B ALL, 18; T-NHL, 2; B- NHL in 2 cases. Rasburicase was given at doses of 0.08 - 0.24 mg / kg. No one was screened for G6PD deficiency.
Results: Initial PUA: median, 8.5 mg/dl (range, 4.3 to 45.5). Six had creatinine levels of >2 mg/dl; and 10 had peak phosphate levels of >10 mg/dl. Only one patient required dialysis. Dose of rasburicase used: median, 0.12mg/kg (range, 0.08 – 0.24). Median reduction in PUA at 6 hours: 80% (range 40% to 98%). Twenty-seven needed only one dose; 12 needed 2 or 3 doses; and two needed 5 doses each. None died of TLS. None developed anaphylaxis or significant hemolysis.
Conclusions: Rasburicase is safe and effective even in lower doses ranging from 0.1 to 0.2 mg/kg, and it markedly reduces the risk of renal failure from TLS in Indian children with hematological malignancies.

EP-447

ETOPOSIDE INFUSION-RELATED REACTIONS IN PEDIATRIC ONCOLOGY PATIENTS

M. Rayar[1], L. Dupuis[1], A. Atkinson[2], F. Shaikh[1], T. Taylor[1], S. Ross[1], S. Alexander[1]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Allergy/Immunology, The Hospital for Sick Children, Toronto, Canada

Objectives: Etoposide is a common chemotherapy agent used to treat childhood cancer. Over the past year, the rate of etoposide associated reactions was perceived to be higher than expected at our institution, prompting a review of the nature of these reactions.
Methods: A retrospective chart review was conducted at a single institution. Patients aged 0-18 years who received IV etoposide from October 2012 to June 2013 were eligible for this study.

Results: 114 patients received etoposide during the study period. Ninety-seven patients met inclusion criteria. Thirty-nine patients (40%) had a reaction to etoposide. The average rate of infusion of etoposide did not differ between patients who had experienced a reaction and those who did not. Reactions occurred shortly after the start of etoposide infusions, with a mean time to adverse event of 13.3 minutes (range 2-95 minutes). Most reactions occurred during the patient's second dose of etoposide (range 1 to 6). These reactions were associated with a variety of symptoms including mucocutaneous (n = 37; 38%), respiratory (n = 25; 26%), gastrointestinal (n = 11; 11%), and hypotension (n = 6; 6%). Of the patients who displayed reactions, 20 (78%) tolerated subsequent etoposide doses given with premedication (antihistamine or/and steroid) and/or infused at a slower rate. The remaining 19 patients completed therapy with etoposide-phosphate. Two of these patients experienced a subsequent reaction; the first patient developed lip swelling and the second experienced persistent vomiting. Both patients were able to tolerate further doses with premedication.
Conclusions: An infusion-related reaction rate to etoposide of 40% was observed. Although the exact mechanism of these events is unclear, the natural history is consistent with a type I hypersensitivity reaction. Patients who developed reactions can be safely rechallenged with etoposide if given premedication. Further investigations into possible etiologies of these reactions, including examination of infusion devices, are ongoing.

EP-449

USING A CHANGE IN METHODOLOGY TO IMPROVE PATIENT FLOW AND BED USAGE: EFFECT OF ALTERING THE METHOTREXATE ASSAY SERVICE

L. Roe[1], A. Norton[2], J. Patel[3], M. Barker[1], M. Moore[1], S. Heap[4], M.W. English[1]

[1]Oncology, Birmingham Childrens Hospital, Birmingham, United Kingdom; [2]Haematology, Birmingham Childrens Hospital, Birmingham, United Kingdom; [3]Pharmacy, Birmingham Childrens Hospital, Birmingham, United Kingdom; [4]Clinical chemistry, Birmingham Childrens Hospital, Birmingham, United Kingdom

Objectives: Delayed discharge outside working hours frustrates children and families, means less safe and effective use of beds and can delay treatment.
We identified delay in receiving methotrexate assays from another hospital as contributing to this problem.
Methods: Plan: An in house assay for serum methotrexate levels was set up. Flexibility was agreed to produce the results in a timely manner without overburdening the lab service. Do: Regular meetings of pharmacists, doctors, nurses and laboratory scientists addressed any issues that developed. Several steps from the old system were eliminated (batching of specimens, transfer by courier, processing in a different hospital, telephoning of results after office hours)
Results: Check: Complaints about missing results disappeared. Patients receiving High Dose Methotrexate (HDM) who are discharged when safe levels are reached include those with acute lymphoblastic leukaemia (ALL) and patients with osteosarcoma. We compared length of stay (LOS) before and after the change in assay for 15 and 14 ALL and 14 and 15 osteosarcoma admissions. A reduction in length of stay after HDM for those patients who are discharged on the 3rd day for ALL ($p = 0.02$) and 4th day for osteosarcoma ($p = 0.05$) was noted. No difference was found in patients with prolonged excretion of methotrexate in either group, as would be expected. Importantly more than half patients were now discharged during office hours after the introduction of the local assay.
Conclusions: Act: The expense of setting up a new assay service has been offset by improvements in discharge. We plan to undertake value stream mapping to identify further aspects of admission which prolong stays occur and use PDCA cycles do help eliminate delays. We are also going to use patient level costing to measure the economic benefits realised by this and future changes.

EP-451

ON THE SELECTION OF VENOUS ACCESS SYSTEMS AND PROFESSIONALS INVOLVED IN THEIR INSTALLATION

M. Rykov[1], V. Polyakov[1]

[1]General Oncology, Institute of Pediatric Oncology and Hematology N. N. Blokhin, Moscow, Russia

Objectives: Treatment of cancer is impossible without venous access. But who must be responsible for its choice, and who – for direct provision? There should be an integrated approach involving oncologists, surgeons and anesthetists.
Methods: In 2010 - 2013 years we conducted a training on "Selection and installation of venous access for 150 doctors of various specialties: 71 oncologists (47.4%), 67 anesthesiologists (44.7%) and 12 interventional radiologists (7.9%). The training included practicing in operating theatres with demonstration of subclavian venous catheters and venous ports installation technique together with the theoretical course or some theoretical exercises only. In addition, we analyzed experience of 7 oncology clinics in Russia in approaches to provide venous access.
Results: Only 11 physicians (7.4%) have fully mastered the technique, the majority - interventional radiologists (7 physicians), 3 and 1 anesthetist surgeon. In all seven clinics the problem of choice of venous access was not considered. In 4 clinics peripheral veins were used for chemotherapy provision. Only after serious complications they began to apply subclavian catheters. In 3 clinics subclavian catheters were used from the beginning of treatment. All clinics insertion of subclavian catheters involved anesthesiologists. While in 50% of cases due to the complications caused by incorrect installation and operation of subclavian catheters a cancer treatment program was interrupted.
Conclusions: A comprehensive and targeted training of doctors directly in the field of venous access is necessary as doctors of any of the existing specializations do not have all the necessary skills for this procedure. Anesthesiologists have difficulty in section and suturing tissue, surgeons and interventional radiologists - when puncturing blood vessels. The optimal training of such specialists is among interventional radiologist, as most of them are not only proficient in general surgical skills, but also able to use intraoperative fluoroscopy effectively.

EP-452

MODERN RUSSIA – A HERITOR OF ANCIENT TRADITION OF BABYLON: THE TRAGIC STORY OF CENTRAL VENOUS CATHETERIZATION

M. Rykov[1]

[1]General Oncology, Institute of Pediatric Oncology and Hematology N. N. Blokhin, Moscow, Russia

Objectives: A lot of health problems in Russia are not given attention. Only a few clinics in the country with a population of 140 million people are paying attention to vascular access.
Methods: In Russia 2,995,566 cancer pts are recorded, there are 6539 oncologists (458.1 pt to the doctor) and 125 cancer clinics. Among them, only 7 clinics (5.6%) practice implantable venous port system for the treatment of not more than 10% of their pts. In the remaining pt clinics each pt undergoes central vein catheterization at least 5 times over the period of treatment. More commonly peripheral veins are used. Thrombophlebitis and pneumothorax are routine complication. From 6539 oncologists not more than 150 people (2.3%) are aware of the existence of venous ports and not more than 30 (0.45%) know a method of implantation. In all Russian clinics (including non-cancer ones) there are only 147 X-ray surgical operation theatres, that's the reason of the impossibility of the widespread introduction of port systems.
Results: From 1991 tens of thousands of pts' lives were ruined by the actions of illiterate health workers. The reason for its the totalitarian regime, lack of education, lack of adequate health care financing and pervasive corruption that penetrates into all spheres of daily life. Many of the complications being a consequence of negligence, however, are taken as inevitable. The exact number of complications associated with errors in the provision of vascular access and catheter associated bloodstream infections have not taken into account. According to the conservative estimates at least 40% of central venous catheterization is accompanied by the development of severe complications. Level of catheter associated bloodstream infections is not less than 35%.
Conclusions: In ancient Babylon authorities executed patients. Medical Service of the Russian Federation often does the same.

EP-453

RISK FACTORS OF LONG-TERM CENTRAL VENOUS CATHETERS (CVCS) COMPLICATION IN CHILDREN WITH HEMATO-ONCOLOGICAL DISORDERS

A. Sakoda[1], T. Kawano[1], Y. Hosoya[2], H. Yoshiwara[2], S. Hirabayashi[2], D. Hasegawa[2], M. Ozawa[2], H. Matsufuji[1], A. Manabe[2], O. Takahashi[3]

[1]Pediatric Surgery, St. Luke's International Hospital, Tokyo, Japan; [2]Pediatrics, St. Luke's International Hospital, Tokyo, Japan; [3]Center for clinical epidemiology, St. Luke's Life Science Institute, Tokyo, Japan

Objectives: To identify risk factors for long-term CVCs complications for understanding the optimal CVC managements.
Methods: Complications were analyzed retrospectively for 275 catheters which were implanted in 208 patients between June 2003 and February 2014 at St. Luke's International Hospital. Complications included centralline associated blood stream infection (CLABSI), obstruction, dislocation andrupture. Multivariate logistic regression was conducted to adjust for several potential confounders.
Results: The total number of CVC days was 64,427. The overall rate of complications was 1.4/1000 CVC days. Age at CVC insertion $< = 3$, double lumen catheter, and betadineskin preparation (vs chlorhexidine) were significant predictor of CVC complications ($p = 0.01$).
Conclusions: CVC complication rate was decreased dramatically with the use of chlorhexidine instead of betadine. Proper aseptic techniques by well-trained stuff are recommended for the further progress not only for young patients but also for those who require double lumen catheters.

EP-454

INCIDENCE OF FEBRILE NEUTROPENIA IN ACUTE LEUKEMIA CHILDREN IN INDIA USING UK PROTOCOL

S. Siddaiahgari[1], A. Manikyam[1], T. Hambir[1], B. Jillella[1]

[1]Pediatric Hematology-Oncology, Rainbow Childrens Hospital, Hyderabad, India

Objectives: Assesing febrile neutropenia episodes and mortality related to it, in Acute Leukemia children in India using UKALL 2003 and AML 15 protocols.
Methods: A prospective study performed in a tertiary care children hospital from March 2012 to May 2014, in children between 6 months to 15 years
Results: Total 72 children analysed,51/72 are males (71.83%), remaining females. Out of 72, 59 are (81.9%) Acute lymphoblastic leukemia (ALL), 13 are Acute Myeloid Leukemia (AML). CALLA +ve B cell ALL were 54, 5 T cell ALL. Total 129 episodes of febrile neutropenia (F.N) observed in 72 patients. 106/129 in ALL, 23/129 in AML. In ALL, F.N episodes commonly observed in Consolidation (67.1%) followed by Reinduction- I (22.6%), then in Induction (10.3%). In AML, F.N episodes were commonly observed in 1st and 3rd month (37.5% each) followed by 2nd& 4th month of chemotherapy (12.5% each). Respiratory complaints seen in 40% of episodes followed by Genitourinary (22%) & Gastrointestinal (20%). Fever Without Focus in 18%. Cultures positive in 66 episodes (53.2%). Common site of isolation was Urine (66.6%), followed by Blood (33.3%). Gram negative bacteria commonly seen (86.3%) followed by Gram positive. Escherichia coli was common (67.2% cases) among gram negatives followed by Pseudomonas aeruginosa (20%) & then Klebsiella (12%). Most of them sensitive to amoxyclav, piperacillin tazobactum and carbepenems. In Gram positives, Staphylococcus was common (83%) followed by Pneumococcus (16%). Episodes responded to first line antibiotics 21.9% of times (Cefipime+ Amikacin), 78.1% episodes needed upgradation of Antibiotics. Antifungals used in 40.4% cases, 84% treated empirically & 16 percent had evidence of fungal infection. Mean duration of hospital stay 6.7days. 5 children died in the study, 3 had relapse and 2 due to Febrile neutropenia (2.7%).
Conclusions: Wth good supportive care western protocol can be used in developing countries without increasing febrile neutropenia related mortality and morbidity.

EP-455

VARIED SPECTRUM OF NEUROLOGICAL COMPLICATIONS RELATED TO DISEASE AND THERAPY IN CHILDHOOD MALIGNANCIES

S. siddaiahgari[1], D. makadia[1], L. lingappa[2], N. shah[2], B. jillela[3], R. varma[4]

[1]pediatric hematology- Oncology, rainbow childrens hospital, hyderabad, India; [2]pediatric neurology, rainbow childrens hospital, hyderabad, India; [3]pediatrics, rainbow childrens hospital, hyderabad, India; [4]pediatric neuroradiology, rainbow childrens hospital, hyderabad, India

Objectives: To describe neurological complications in children with cancer and their short term outcome
Methods: Neurological problem as presenting feature or part of therapy related complications in childhood malignancies, identified and reviewed from november 2008 to december 2013,4 years prospective and 14 months retrospective
Pre existing neurological problems, CNS tumors & post chemotherapy cognitive dysfunctions excluded.
Results: Forty-four children, 3 months to 15 years of age had neurological problems. Acute lymphoblastic leukemia (ALL) 20/44, neuroblastoma 9/44 (Opsoclonus Myoclonus syndrome in 4/9). Neurological problems in Ewings/PNET seen in 4. Histiocytic disorder with CNS deposits in 3 cases. Four had Acute myeloid leukemia (AML), one was Hodgkins lymphoma, one was diffuse large B cell lymphoma, one germ cell tumour and one Rhabdomyosarcoma. **Tumor related neurological problems**: seen in 27; 22/**27** directly related to tumor, **4/27** were paraneoplastic Opsoclonus myoclonus secondary to neuroblastoma. Cord compression-12, (NBL-4, Ewings/PNET-4, Germ cell tumor-1, RMS-1, AML-1, Hodgkin Lymphoma-1). Five presented with seizures (ALL-3, AML-1, Histocytosis-1). Two had Encephalopathy with seizure (1 histiocytosis,1 AML). Two had facial nerve palsy with tumor infiltration as presenting feature (one AML/one DLBL). One ptosis (with intracranial neuroblastoma extension) and 1 primary HLH presented with head ache and vomitings secondary to CNS deposits. Therapy related problems seen in 17 ALL cases. Stroke like presentations seen in 7children with Methotrexate. Seizures in 6 (post methotrexate-4/2 with cortical venous thrombosis secondary to PEG Asparganise). One had ventriculitis while on Induction. One child had post MTX chemical meningitis. One had Posterior reversible Encephalopathy syndrome secondary to hypertension (Steroid) and one had vincristine induced acute flaccid paralysis. Two cases in disease related group and 3 in treatment related had mild neurological disability.
Conclusions: Therapy related neurological complications seen only in ALL children. spinal cord compression was common neurological presenting feature. Early recognition of neurological complication either disease or treatment related is essential to control mortality & morbidity.

EP-456

INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH CANCER

G. Sobol-Milejska[1], K. Musiol[1], A. Mizia-Malarz[1], W. Stolpa[1], A. Strek-Cholewinska[1], H. Wos[1]

[1]Department of Pediatric Oncology Haematology and Chemotherapy, Medical University of Silesia Upper Silesia Children's Care Heatlh Centre, Katowice, Poland

Objectives: The assessment of clinical course of IFI in neoplastic children according to the diagnostic and therapeutic difficulties, based on our institution experience.
Methods: To this study were enrolled 28 children with cancers diagnosed as having IFI. We analyzed the clinical course of IFI based of the initial symptoms, diagnostic difficulties, therapy clinical course of IFI, diagnostic difficulties, therapy and treatment results
Results: All of 28 pts developed IFI during deep neutropenia period with characteristic persistent fever. In 28 pts IFI were located in lungs, in 4 pts additionary in CNS, in 1 pt in the liver. Diagnosed fungi patogens were: Candida albicans, Candida tropicalis, Aspergillus, but in 9 pts pathogen was not identified. In all group IFI were diagnosed as a probable (18pts), possible (8 pts) and proven (1pts) infection.
Conclusions: Invasive fungal infections are serious cancer treatment complication because ofthe diagnostic and therapeutic difficulties, and subsequent result as delay in the therapy. Deep neutropenia play the funamental role in the development of IFI.

EP-457

THE COST OF CHIDHOOD CANCER TREATMENT IN AFRICA

D. Stefan[1], A. Van Zyl[1], D. Stones[2]

[1]Paediatrics & Child Health, Stellenbosch University, Cape Town, South Africa; [2]Paediatrics & Child Health, Free State University, Bloemfontein, South Africa

Objectives: Annually more than 50.000 African children will suffer from cancer. Information on the costs of care of childhood cancer in Africa is missing, making it impossible for policy makers to adopt affordable interventions. The aim of this study is to estimate the health systems costs of cancer care in Africa and to propose a more effective approach to investigations and treatment for the most common cancers.
Methods: The costs of cancer were estimated using administrative data for the different period of time (2008-2012) in different African units. We derived direct and indirect financial and economic costs from a health systems perspective. Costs included drugs, personnel and annuitized capital costs. The diseases analysed included nephroblastoma, retinoblastoma, Burkitt lymphoma and HIV associated malignancies (Kaposi sarcoma and NHL).
Results: The cost of treating nephroblastoma varied between EUR 650 for stage 1 and 5 times more for stage 4 (EUR 3325). Treating one patient with nephroblastoma averted more than 32 DALYs. The cost of treating BL was 591 Euros for group B and 2220 for group C. The first line treatment of KS cost EUR 800 and the paclitaxel salvage regimen EUR 1232. The retinoblastoma cost was estimated at less than 1000 EUR for advanced disease.
Conclusions: Treating childhood cancers in Africa is cost effective. Key policy points from our research are the need for 1) recognition of childhood cancer as a health problem by African governments 2) improving awareness and early diagnosis 3) adapted protocols for local resource limited conditions 4) affordability of treatment.

EP-458

BLOODSTREAM INFECTIONS AND PREDICTORS OF MORBIDITY AND MORTALITY AMONG CHILDREN LIVING WITH CANCER IN RURAL SETTINGS IN UGANDA

J. Suvada[1], M. Meciakova[1], M. Bartosova[1], C. Kiyaga[2], R. Iriso[3], E. Namagala[4], N.H. Russel[5], E. Kaiserova[6], V. Kr cmery[7]

[1]HIA Health Care Project St. John Paul II., St. Elizabeth University of Public Health and Social Science, Kampala, Uganda; [2]Dept. of Microbiology, Central Public Health Laboratories, Kampala, Uganda; [3]Pediatric department, Baylor's College of Medicine, Kampala, Uganda; [4]Children Care, Ministry of Health, Kampala, Uganda; [5]Hope Ward, International Hospital Kamapala, Kampala, Uganda; [6]Children Hematology and Oncology, Children's Teaching Hospital, Kampala, Uganda; [7]Clinical Microbiology, St. Elizabeth University of Public Health and Social Science, Bratislava, Slovakia

Objectives: Bloodstream infections (BSI) are a common cause of admission, morbidity and mortality among pediatric patients with malignancy worldwide. The impact of antibiotic resistance and other co-infection (e.g. HIV infection, TB) on treatment outcomes in many rural developing settings are not well known.
Methods: We conducted prospective multicenter study to evaluate the incidence of BSI and risk factors among children treated due to cancer in 6 rural settings in Uganda. There were observed 176 consecutive admissions of children with signs of systemic infectious disease. Blood was taken for serological tests, culture and malaria microscopy, when indicated. There were recorded data on clinical findings, underlying diseases, antimictobial drug used before and on admission, microbial agent findings and outcome.
Results: The incidence of laboratory confirmed bloodstreem infection was 37% from admitted children with systemic infectious sings. More than 96% of the patients received during prior admission at least one course of antimicrobial therapy and 58% antimarial therapy, prior a blood culture. The most frequent isolates were Klebsiella spp., E. coli, Salmonella, enterococci, Staphylococcus aureus, Streptococcus spp. 16% of the pediatric patients had a malaria, 21% HIV infection and 4% Tubercuosis. 34% of the children with laboratory confirmed bloodstream infection died in comparison to 72% of those with clinical +/-lab presentation of infection from files evaluation. 43% of the microbial agents had confirmed resistance at least to one of the common antibiotic agents.
Conclusions: Bloodstream infections were less common than malaria in our settings but were responsible for more death among children with cancer. The frequent use of antimicrobial drugs prior blood culture may have crucial impact on detection of the micro-organism,

antibiotic testing and susceptibility to commonly used antibiotics. The findings that antimicrobial resistance, co-infection and malnutrition predict fatal outcome calls for renewed efforts and recommendations on national but also local level.

EP-459

EFFECTIVE MODES OF FINANCIAL AIDS FOR SUPPORTING THE TREATMENT OF PEDIATRIC CANCER PATIENTS IN RESOURCE POOR SETTING

D. Thakkar[1], N. Radhakrishnan[1], M. Kalra[1], A. Gupta[1], A. Sachdeva[1]

[1]Pediatric Hematology-Oncology and BMT Unit, Sir Ganga Ram Hospital, New Delhi, India

Objectives: Treatment of any form of cancer in children poses a significant financial burden on the family in resource poor countries like India. In these circumstances, abandonment of treatment is a common event. Financial aid from the Government as well as Non-Government Organizations (NGO) help such patients to complete treatment. We attempted to analyse the effectiveness of various modes of financial aids available to the families that helped them to continue with the treatment.
Methods: A retrospective analysis of patients with Acute Lymphoblastic Leukemia (ALL) diagnosed at our centre between Jan 2012-Dec 2013 was carried out. All patients were treated as per the BFM 95 protocol. The source of financing the treatment of each patient was assessed by a questionnaire.
Results: During the study period, 71 patients were diagnosed with ALL at our centre. Of these, 4 patients (5.6%) were lost to follow up and 22 patients (30.9%) opted for treatment at an alternate centre. Of the remaining 45 patients, 18 patients (40%) sought financial assistance for the completion of treatment. Of these 18 patients, parents of 12 patients (66.6%) completed treatment of their child with the help of insurance available through their employment agencies. 6 patients (33.3%) sought monetary aid from the Prime Minister's Relief fund (Government Support). They also got support from a NGO in the form of 'free of cost' medicines. Of these 6 patients, 2 patients (11.1%) also received aid from the Support Group formed by the parents of children treated of ALL in the past.
Conclusions: In resource poor country like India, many patients diagnosed with ALL need financial assistance for treatment. For financially constrained families, insurance grant from the parental employment agencies and an ascertained financial aid from the Government play a major role in decreasing the rate of treatment abandonment.

EP-460

FEBRIL NEUTROPENIA IN OUR PEDIATRIC MALIGNANCY PATIENTS

A. Akbarzade[1], G. Tokuc[1], A. Koc[1], B. Yilmaz[1]

[1]Pediatric hamatology and oncology, Marmara University, Istanbul, Turkey

Objectives: The aim of this study was to determine the clinical features, microbiological pattern and antimicrobial suspectibility in febril neutropenia in children with cancer.
Methods: Isolated microorganisms and antimicrobial susceptibilities of all febrile neutropenic episodes in patients hospitalized at Department of PediatricHematology and Oncology between August 2011 –October 2013 were evaluated retrospectively in this study.
Results: In 69 patients, 232 episodes of FN were reported. Primary malignancies wereleucemia in 99 episodes (42.7%) and solid tumors in 133 episodes (57.3%). Mean absolute neutrophil count was $150.86 \pm 156.81/mm^3$, mean duration of hospitalization was 9.25 ± 10.03 days and mean fever time was 3.03 ± 4.69 days. Of the 232 episodes, 50 (21.6%) were microbiologically documented. The most common sites of clinical documentation were the mucosa and skin. Of isolated microorganisms, 53.5% were gram-negative bacilli, 41.9% gram-positive cocci and 4.7% Candidaspp. E.coli (15/27; 55.5%) and Staphylococci (13/14; 92.8%) were the most common isolates among Gram-negative and Gram-positive bacteria, respectively. In antimicrobial susceptibility testing among isolated microorganisms, resistance was found 18.7% (3/16) for piperacillin-tazobactam and 21.4% (3/14) for cefepime that the most frequently used antimicrobial agents in empiric therapy. No cephoperazone resistance was identified.A total of 136/232 (58.6%) febrile neutropenic episodes improved with first-line antimicrobial therapy, while modification was required in 96 episodes (41.4%). In leucemia duration of fever and discharge from the hospital were longer and CRP was higher than in the solid tumors. There were a total of 3 deaths (1.3%).
Conclusions: The most suitable and rationalist approach to decrease the mortality and morbidity is to start rapidly empiric therapy in febrile neutropenic patients according to results of frequencies and susceptibility patterns of isolated microorganisms in local epidemiologic data and if necessary to make modification in therapy according to culture results and clinical situation.

EP-461

INCIDENCE AND SEVERITY OF ADVERSE REACTIONS ASSOCIATED WITH ANTHRACYCLINES IN PAEDIATRIC PATIENTS

J. Vargas Neri[1], O. Castelan Martinez[1], R. Rivas Ruiz[2], G. Castañeda Hernandez[1], P. Clark Peralta[3]

[1]Pharmacology, Centro de Investigacion y de Estudios Avanzados del IPN, Mexico City, Mexico; [2]Clinical Research, Centro Medico Nacional Siglo XXI del IMSS, Mexico City, Mexico; [3]Clinical Epidemiology, Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico

Objectives: To determine the incidence and severity of adverse reactions associated with anthracyclines in paediatric patients.
Methods: A retrospective cohort of patients treated with anthracyclines treated at Children's Hospital of Mexico Federico Gomez and the Pediatric Hospital of Centro Medico Nacional Siglo XXI. To identify adverse reactions, Intensive pharmacovigilance method was performed, analysis of causality was performed using the Naranjo test and severity of adverse reactions was determined according to Official Mexican Standard 220-SSA1-2012 called Installation and operation of the pharmacovigilance.
Results: A total of 33 patients were included in the study. Found total of 431 adverse events which 292 (68%) were associated with anthracyclines. The incidence of adverse reactions associated with anthracyclines was 82%, 79%, 48%, 45%, 30% and 3% for neutropenia and fever, vomiting, mucositis, thrombocytopenia, anemia and cardiotoxicity, respectively. According to the severity of adverse reactions associated with anthracyclines 155 (53%) were severe, 90 (31%) were mild and 47 (16%) were moderate.
Conclusions: Anthracyclines have a high rate of adverse events, some even fatal. Intensive pharmacovigilance is an effective method to determine the incidence of adverse events, which is necessary for the timely identification of potential risks in patients with cancer.

EP-462

THE FIRST PEDIATRIC ONCOLOGY HOSPITAL IN MEXICO A NEW MODEL OF CARE

L. Vega-Vega[1], G. Escamilla[2], A. Ellis-Irigoyen[2], D. Aguilar[2], S. Elizalde[3]

[1]Direccion Medica, Hospital Infantil Teleton De Oncologia, Querétaro, Mexico; [2]oncology, Hospital Infantil Teleton De Oncologia, Querétaro, Mexico; [3]radiology, Hospital Infantil Teleton De Oncologia, Querétaro, Mexico

Objectives: To report the planning and opening of the first hospital specially designed for children with cancer in Mexico
Methods: We review the process of planning and the design of the hospital as a innovative model of care.
Results: The construction of the 17500m2 Hospital Infantil Teleton de Oncología (HITO) started in 2012 and finished by november 2013. The medical model is based in 5 axis: Diagnostic accuracy, modern treatment, prevention of complications, quality of life, housing (Teleton House). Teleton foundation designed this campus with hospital and Teleton house to treat children with cancer in an integrated model of health care exclusively for children suffering cancer.
Conclusions: This is a new model of pediatric oncology care, a proposal for a change in health care with focus in the special needs of cancer patients, expecting solve the main problems that affect results.

EP-463

CHEMOTHERAPY SURVEILLANCE WITH CANCER PATIENTS FROM THE NATIONAL INSTITUTE OF PEDIATRICS, MEXICO

M. Zapata-Tarrés[1], L. Velasco-Hidalgo[1], R. Cárdenas-Cardós[1], D. Guerra-Medrano[1], A. Martínez-Avalos[1], M. Pérez-García[1], R. Rivera-Luna[1]

[1]Oncology, Instituto Nacional de Pediatría, Mexico City, Mexico

Objectives: Chemotherapy surveillance is a fundamental tool in pediatric oncology to evaluate with a long term follow up the efficacy and security of treatments. The aim was to describe the severe adverse events (SAE) secondary to chemotherapy in the oncology department at the National Institute of Pediatrics.
Methods: We realized a prospective study registering all grade 3 and 4 SAE according to the World Health Organization from February 2013 to February 2014. We analyzed diagnosis and outcome according to the Naranjo algorithm.
Results: We included 178 patients who presented 874 SAE. The more frequent was grade 3 and 4 neutropenia (60%), anemia (13%), thrombocytopenia (10%), neutropenic colitis (3%), mucositis (3%), anaphylactic shock (3%). The more frequent diagnosis was acute lymphoblastic leukemia (54%) acute myeloid leukemia (8%), osteosarcoma (18%), Ewing sarcoma (7%), retinoblastoma (5%), medulloblastoma (5%), germ cell tumors (3%). Ifosfamide was the more frequent chemotherapeutical agent associated with SAE. Mortality was 10%.
Conclusions: Chemotherapy surveillance in pediatric oncology must be a systematic action in order to establish causality, assess the security of chemotherapy and generate new strategies to reduce the severity and mortality of SAE.

EP-464

EXPERIENCE WITH HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACQUIRED SEVERE APLASTIC ANEMIA IN A DEVELOPING COUNTRY LIKE INDIA

K. Vipin[1], D. Mayank[1], C. Dharma[1], G. Nitin[1], S. Sanjeev[1]

[1]Haematooncology and BMT, BLK Superspeciality Hospital, Delhi, India

Objectives: To asses the role of Haploidentical Hematopoietic Stem Cell Transplantation (HHCT) for Acquired Severe Aplastic Anemia (SAA) as an alternative to Matched unrelated donor (MUD) transplantation in a resource limited country like India.
Methods
Study design: retrospective study.
Study period: January 2011- February 2014.
Setting:B L Kapur Superspeciality Hospital, Delhi.
Inclusion criteria: Two children aged between 10 to 15 year who showed no response to Immunotherapy were included.
Conditioning regimen included Fludarabine (30 mg/m^2 from day-6 to -2days), Cyclophosphamide (14.5 mg/kg on day -6 and -5), and TBI (200cGy on day-1). Prophylaxis against GVHD was cyclophosphamide (50 mg/kg on days +3 and +4), Tacrolimus (0.06mg/kg), and Mycophenolate Mofetil (10mg/kg q8h).
Absolute Viable CD34 positive Cell Count varied between 3 x 10^6 to 6 x 10^6 per kg of recipient body weight.
Results: One of our patient experienced early graft rejection but she received a second HHCT and achieved sustained engraftment. One of our patient developed acute GVHD grade II which was managed with steroids. Both the children are having sustained complete donor chimerism and normal peripheral blood counts.
Conclusions: HHCT using high-dose post transplantation cyclophosphamide for T cell depletion is a reasonable treatment option for children with acquired SAA and is feasible in developing countries, with limited availability of matched unrelated donors.

EP-465

A SKIN PROTECTANT REGIMEN FOR THE MANAGEMENT OF DIAPER SKIN COMPROMISE IN PEDIATRIC ONCOLOGY PATIENTS

C. Braeutigam[1], A. Pyle[1], C. Baker[1], A. Pearson[1], M. Visscher[2]

[1]Cancer and Blood Diseases Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, USA; [2]Skin Sciences Plastic Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, USA

Objectives: Severe diaper dermatitis is an extremely challenging side effect of treatment among infants with leukemia. It is likely due to multiple factors including chemotherapy leading to chemical burns, hyper hydration with increased urine and stool output, looser stools, with suspected higher concentrations of enzymes, decreased immune function, and decreased healing capacity resulting in severe morbidity. The institutional current practice of a liquid barrier film and a topical barrier cream were not sufficiently effective. The objective was to determine the effectiveness of a regimen consisting of a substantive liquid skin protectant plus a zinc-based ointment with daily sitz baths and frequent diaper changes to minimize/prevent irritant diaper dermatitis throughout multiple chemotherapy cycles.
Methods: Infants receiving high dose chemotherapy (e.g., doxorubicin, cyclophosphamide, vincristine, prednisone, L-asparaginase, intrathecal therapy, and high-dose methotrexate and cytarabine) and diapered patients receiving methotrexate, alkalinization and hyperhydration, were enrolled upon hospitalization in the IRB approved study. The liquid protectant was applied to the diaper regions upon resolution of open wounds, evaluated daily and reapplied as necessary throughout multiple chemotherapy and recovery cycles. The zinc ointment was applied liberally at every diaper change. The skin was assessed for erythema and rash using a validated scale and standardized digital images taken to quantify area of involvement and erythema. Absolute neutrophil counts, urine and stool output and frequency, and medications were tracked with skin grades and images over time.
Results: Twenty patients were enrolled and followed for 7 – 240 days. There was no severe diaper dermatitis and only mild perineal irritation was observed over multiple chemotherapy cycles despite being neutropenic or on multiple antibiotics for fevers. There was no delay in chemotherapy due to severe skin breakdown.
Conclusions: The regimen is effective in delaying and lessening skin compromise among infants receiving chemotherapy relative to the hospital standard of care.

EP-466

DEVELOPING A SERVICE CAPABILITY FRAMEWORK: A GUIDE FOR HEALTH SERVICES PROVIDING CARE TO CHILDREN AND ADOLESCENTS WITH CANCER

C. Williams[1], A. Shelly[1], J. Williamson[1], P. Downie[2], F. Mechinaud[3], G. Wheeler[4], D. Ashley[5], K. Whitfield[6]

[1]Paediatric Integrated Cancer Service, Royal Children's Hospital, Melbourne, Australia; [2]Children's Cancer Centre, Monash Children's Hospital, Melbourne, Australia; [3]Children's Cancer Centre, Royal Children's Hospital, Melbourne, Australia; [4]Paediatrics and Late Effects, Peter MacCallum Cancer Centre, Melbourne, Australia; [5]Cancer Services, Barwon Health, Geelong, Australia; [6]Cancer Reform and Strategy, Victorian Department of Health, Melbourne, Australia

Objectives: Achieving best outcomes in paediatric cancer care requires a coordinated, timely, multidisciplinary approach, with active collaboration between health services. To support this approach, the Paediatric Integrated Cancer Service has developed a Service Capability (SCF) for the State of Victoria, Australia. Its purpose is to define the minimum requirements for providing sustainable, coordinated and safe paediatric oncology care across a variety of health networks including regional and urban settings.
Methods: A literature review was undertaken to gather evidence to guide the rationale and recommendations within the SCF. An expert steering group was established, with wider consultation from other disciplines. The SCF was endorsed by the Victorian paediatric tertiary referral centres, as well as the Victorian State government's Risk Management and Insurance Group
Results: The SCF presents four levels of care for health service participation, including an algorithm of risk factors that may escalate the level of care required. The levels are defined according to complexity of care, patient critical mass and the level of paediatric oncology services available. Services vary across Victoria from outreach centres providing supportive care, through to specialist tertiary/quaternary referral centres. Levels are also defined across critical time points in the patient's care, supporting clinical decision making and referral processes. Each level describes the necessary infrastructure, workforce, education, research, quality, clinical governance and service networking required. The framework also describes minimum requirements in speciality areas such as clinical trials, laboratory services, imaging, multidisciplinary team meetings, nursing, pharmacy, psychosocial and psycho-oncology care, radiation oncology, surgery and management of late effects
Conclusions: The SCF supports health services to plan and develop a paediatric cancer service within an agreed scope of practice. The SCF supports health services to deliver a level of care that meets the needs of their local community whilst maintaining patient safety, efficacy and a confidence in referring shared care.

EP-467

BETA BLOCKER TREATMENT IN HEMANGIOMAS: EXPERIENCE IN 344 CASES IN A SINGLE INSTITUTE

N. Yazici[1], F. Sarialioglu[1], A. Erbay[1], I. Erdogan[2], P. Kiper Misirlioglu[3]

[1]Pediatric Oncology, Baskent University, Adana, Turkey; [2]Pediatric Cardiology, Baskent University, Adana, Turkey; [3]Pediatrics, Baskent University, Adana, Turkey

Objectives: Efficacy and safety of beta blockers, especially propranolol had been approved in infantile hemangiomas. Aim of our study was to analyse efficacy and safety of systemic and topical beta blockers in a large population after preliminary experiences in our institute.
Methods: Between September 2009 and January 2014, medical records of 344 patients diagnosed with hemangioma were retrospectively investigated at Baskent University Department of Pediatric Oncology. Basal complete blood count, serum biochemistry were obtained in all patients with systemic beta blocker treatment. Cardiac evaluation was made to all patiets, with echocardiography in selected ones. Starting dose of propranolol ranged from 2-4 mg/kg/day. Steroid was added to propranolol in majority of cases. Local timolol ointment was used in a minority of cases with tiny cutenous hemangiomas. Treatment response was recorded both by early and late response criteria in both groups. Retrospective records of vital signs during initial treatment and recorded adverse events were examined. Re-growth of lesions and secondary treatment was also evaluated.
Results: There were 244 females. Median age was 4.7 months (0.3-108 months). The gestational age of was under 37 weeks in 22%. Indications for treatment were rapid growth, ulceration, infection, cosmetic issues, bleeding, breathing, feeding and ocular problems and compartment syndrome. Early response was seen in 80.8% of the cases. The response at the end of treatment was 75.3%. Adverse events resulting in interruption or cessation of treatment were detected in 7.8% of cases. Favorable results were obtained in several locations and phenotypic variants of hemangiomas. Local treatment with timolol was of limited use.
Conclusions: Experience in hemangiomas revealed satisfactory results in several cases with specific locations and phenotypic variants. We believe that early use of beta blockers would be associated with less complications in course of a benign disorder.

EP-468

PROPRANOLOL IN TUMORS EXCEPT INFANTILE HEMANGIOMAS: PRESENTATION OF FOUR CASES

F. Sarialioglu[1], N. Yazici[2], A. Erbay[2], S. Demir[3], O. Alkan[3], N.E. Kocer[4], S. Uckan[5]

[1]Pediatric Oncology, Baskent University Faculty of Medicine, Ankara, Turkey; [2]Pediatric Oncology, Baskent University Faculty of Medicine, Adana, Turkey; [3]Radiology, Baskent University Faculty of Medicine, Adana, Turkey; [4]Pathology, Baskent University Faculty of Medicine, Adana, Turkey; [5]Oral Surgery, Baskent University Faculty of Dentistry, Adana, Turkey

Objectives: There is no more debate in use of propranolol in infantile hemangiomas but there is some question in efficacy in some of vascular lesions like tufted angioma, Kasabach Merrit syndrome, and hemangioendothelioma. On the other hand improved survival had been published in adult cancers with incidental use of beta blockers for other indications. Herein four cases with lesions other than infantile hemangiomas were presented with beta blocker treatment with interesting results.

Methods: An 9 year-old female with metastatic hemangioendothelioma to liver and bones; a 2 year-old male with Noonan syndrome and progressive hypothalamic chiasmatic low grade glioma, a 4 month-old female with a giant retroorbital plexiform neurofibroma with neurofibromatosis type 1, and 22 months-old female with recurrent giant cell granuloma of the jaw were presented. The parents of the patients with metastatic hemangioendothelioma and progressive glioma refused standard treatment after relapse. In recurrent giant cell tumor, the lesion was inoperable after three operations and steroid injections and the treatment was offered during the period for the procurement of calcitonin from the health care system. In all patients, propranolol 2-3 mg/kg and prednisolon 1-2 mg/kg were used after informed consents were all obtained. Prednisolon duration was differed between patients.
Results: The patient with metastatic hemangioendothelioma responded well to propranolol and prednisolon with failure free survival of 25 months after relapse. The patient with progressive glioma showed prominent neurocognitive developement and radiological regression of the tumor. In case of plexiform neurofibroma, MRI displayed regression of the retroorbital mass in the first three months of treatment and a stabile course thereafter. Giant cell tumor responded to treatment in approximately three weeks after the third relapse. No side effect was detected with prolonged use.
Conclusions: Anti-angiogenesis is the probable mechanism in four different cases with borderline tumors. Acceptable responses to treatment with propranolol were achieved.

EP-469

ABDOMINAL INFLAMMATORY MYOFIBROBLASTIC TUMORS: GREAT MIMICKER, HOW IMAGING CAN HELP IN DIAGNOSIS

A. Youssef[1], Y. Madney[2], M. EL Wakil[1], M. EL Shafie[3], I.M.A.N. Zaky[4]

[1]Diagnostic Imaging, National Cancer Institute, Cairo University, Cairo, Egypt; [2]Pediaterics, National Cancer Institute, Cairo University, Cairo, Egypt; [3]Surgery, National Cancer Institute, Cairo University, Cairo, Egypt; [4]Diagnostic Imaging, National Cancer Institute, Cairo University, Cairo, Egypt

Objectives: Inflammatory myofibroblastic tumor (IMT), is a quasineoplastic lesion that most commonly involves lung and orbit, but it has been reported to occur in nearly every site in the body. IMT has been reported mainly in the children and young adults. Variations in the clinical presentation of IMT have confounded its diagnosis. Because of IMT's rarity and because the lesions often mimic sarcoma, lymphoma, and metastasis, IMT can often be clinically misdiagnosed as a malignant tumor. The features of IMT on the imaging studies are variable but manifest most often as a soft tissue mass. Our objective is to evaluate the imaging features of the pathologically confirmed ten cases of abdomino-pelvic IMT.
Methods: We retrospectively reviewed imaging studies of ten cases of pathologically confirmed IMT of abdomino-pelvic region.
Results: Ten patients, 7 males and 3 females with abdomino-pelvic IMT were studied, their age ranged from one to 17 years. Mesentery was the commonest location (n _ 5) followed by liver (n _ 4) and urinary bladder (n _ 1). US of all ten patients were reviewed and showed non-specific hypo-echoic soft tissue mass lesion with no definite specific sonographic criteria for IMT. CT of all ten patients were reviewed and showed heterogeneously hypo dense masses with evident enhancement; calcification was encountered in only one case, small cysts were noted within 3 cases. The mesenteric lesions did not cause any secondary effect, i.e intestinal obstructions. MRI was reviewed in 2 cases, one hepatic and the urinary bladder case, the most significant feature was hypointense T2WI signal of the IMT masses.
Conclusions: IMT is a rare and usually benign neoplasm that mimics several malignant tumors both radiologically and clinically. The radiologist should be familiar with this entity and its presentations to facilitate accurate diagnosis and help avoid unnecessary radical surgical resection.

PSYCHOSOCIAL

EP-470

INITIATION AND IMPLEMENTATION OF ART AND CRAFT ACTIVITIES BY CHILD LIFE SERVICES DEPARTMENT FOR UNDERPRIVILEGED PEDIATRIC ONCOLOGY PATIENTS TO IMPROVE QUALITY OF LIFE

S. Ali[1]

[1]Psycho Oncology, Children Cancer Hospital, Karachi, Pakistan

Objectives: Child life services (CLS) is an offshoot of the psycho-oncology department, created in 2013 to improve quality of life of hospitalized children. In view of the parental concerns regarding loss of normalcy in child's life, due to the long hospital stays during chemo and other long-term cancer treatments; an art and craft project was initiated with the children. It is an intervention based on the belief that the creative process involved in the making of art is healing and life enhancing.
Methods: Volunteers were initially trained in the basics of child/client centered therapy and art work. They were then sent to engage children in different art and craft activities i.e. hand and face painting, collage, origami, cut and paste, drawing and coloring. They worked with groups of 8 to 10 children (approx 100 children), age range from 4 to 14 years, in in-patient, out-patient and daycare units. Observational study method was used where volunteers provided their written observations pre and post activity along with the feedback of hospital staff and parents.
Results: Response to intervention was observations by staff, parents and volunteers which yielded similar results. Intervention helped in alleviating the mood and stress of children, it created responsiveness, group work, enthusiasm, interest, sharing and release of boredom. Further it helped in producing compliance with food and medicine and also aids in distraction during invasive procedures.
Conclusions: Emotional health and wellbeing of children suffering from cancer is crucial for child development as well as the treatment itself. Implementing such interventions in an underprivileged, charity organization is a challenge in itself due to the scarcity and limitation of material as well as human resources. Also the family's unswerving and unfounded beliefs on faith healers compounds the problems faced by doctors in treating the patients.

EP-471

QUALITY OF LIFE FROM THE PERSPECTIVE OF PEDIATRIC CANCER PATIENTS AND SURVIVORS: "THERE ARE GOOD THINGS AND THEN THERE ARE BAD THINGS"

S. Anthony[1], E. Selkirk[1], D. Dix[2], R. Klaassen[3], L. Sung[4], A. Klassen[1]

[1]Pediatrics, McMaster University, Hamilton, Canada; [2]Pediatrics, BC Children's Hospital, Vancouver, Canada; [3]Pediatrics, Children's Hospital of Eastern Ontario, Ottawa, Canada; [4]Pediatrics, The Hospital for Sick Children, Toronto, Canada

Objectives: The systematic assessment of quality of life (QOL) is necessary within pediatric oncology research and clinical practice. Research and intervention initiatives require a theoretical framework that is founded on a clearly defined construct of QOL; however, given the multidimensional nature of QOL, it remains unclear which domains and concepts are most important to children with cancer. The purpose of our study was to inform the theoretical underpinnings of QOL from the perspective of pediatric cancer patients and survivors through a qualitative study, guided by interpretive description.
Methods: Study participants were recruited from four Canadian academic pediatric hospitals. Data collection was completed through in-depth, one-on-one, semi-structured interviews. Transcripts were examined line-by-line for common themes and patterns and reviewed continuously as interpretative understanding was considered within the context of clinical practice and current knowledge in the field. Themes were refined through team consensus until saturation was reached.
Results: A total of 37 children participated (19 female; 51%) who were diagnosed with varied cancer types or identified as a cancer survivor (median age 13; range 8-18 years). Participants acknowledged the presence of positive and negative aspects within their cancer experience and expressed that it was necessary to take 'the good with the bad'. This perspective was illuminated across three prominent themes: 1) Doing what one is able, but not always what one wants; 2) Feeling isolated within a new closeness of family and friends; and, 3) Developing positivity amidst anger, sadness, and lingering worry.
Conclusions: Exploration of these themes highlighted the participants' interwoven experience of QOL and demonstrated its potential to be dynamic within contextual variables. Future steps include considering whether QOL instruments are a representative assessment of how QOL is experienced within a pediatric population with cancer. A developing theoretical framework will be refined within the context of current findings.

EP-472

LONGITUDINAL CHANGES IN HOPE IN PARENTS OF CHILDREN WITH CANCER OF POOR PROGNOSIS: THE EFFECT OF DIAGNOSIS

A. Di Battista[1], L. Beaune[2], E. Buffet[3], D. Nicholas[4], M. Barrera[1]

[1]Psychology, The Hospital for Sick Children, Toronto, Canada; [2]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [3]Pediatrics, The Hospital for Sick Children, Toronto, Canada; [4]Faculty of Social Work, University of Calgary, Edmonton, Canada

Objectives: To date, no studies have used standardized instruments to prospectively document parental hope when a child is treated for cancer with poor prognosis. Objectives: To use a standardized instrument to longitudinally examine parental hope over the first year post-diagnosis and the effect of cancer diagnosis on hope.
Methods: Thirty-five parents of children diagnosed with cancer of poor prognosis in a large pediatric cancer centre participated. Institutional approval was obtained for the study and participants signed consent to participate. Parents completed the Hearth Hope Index (HHI), in reference to their child's condition, upon enrollment (3 months post diagnosis, T1), 3 months (T2), six months (T3), nine months (T4) and 12 months (15) later. HHI was standardardized with adults with chronic or advanced disease. Based on the child's diagnosis, parents were stratified into three groups: leukemia/lymphoma (LL; 41%), solid tumors (ST; 31%) and brain tumors (BT; 28%). For analyses, repeated measures ANOVAs and t-tests were conducted. Effect sizes are presented.
Results: Overall, parents' scores of hope were significantly higher than normative data at each of the time intervals assessed (T1: $d = 1.21$; T2: $d = 1.28$; T3: $d = 1.39$; T4: $d = 1.07$; T5: $d = 1.11$). At T3 there was significantly more hope in the BT group than the ST ($d = 0.74$) and in the LL group compared to the ST group ($d = 0.60$). In the BT group, parental hope

significantly increased from T2 to T3 ($d = -0.62$). In the ST group, hope significantly decreased between T1 and T3 ($d = 0.60$). Hope did not alter over time in the LL group.
Conclusions: Fluctuations in parental hope over time seem to be related to their child's diagnosis, likely depending on the child's response to treatment. These results suggest the importance of addressing parental hope during the child's treatment as part of psychosocial care.

EP-473

TO ASSESS THE CONTINUED IMPACT OF THE HOLISTIC CARE, PROVIDED AT ST. JUDE INDIA CHILDCARE CENTRES, ONCE THE CHILD RETURNS HOME AFTER TREATMENT

T. Bilgrami[1], B. Sanadhya[2]

[1]Development, St. Jude ChildCare Centres, Mumbai, India; [2]Former Development Manager, St. Jude ChildCare Centres, Mumbai, India

Objectives: To understand the impact that St. Jude has had on the quality of life of the patient-families, analyze the problems that families face at home. To measure the impact of these families as "change agents" in their communities and to use the findings to further support these families, and improve our model.
Methods: A pilot study was conducted with 30 families at the Centre to establish the parameters of the study. A random selection of 37 families who have returned home, who agreed to participate in the study were interviewed, photographs of the home and complete checklist completed of items observed.
Results: There is a change for the better for the entire family, when the daily routine, cleanliness of the home, eating habits change. More than 70% of the families have managed to keep their houses clean. Children learn these good habits and pass them on to others in the family. Many families have tried to improve the way they live at home. Some have renovated their homes to provide proper facilities, Out of the 13 (or 34.21%) of the 37 families have relocated for better homes and schools. The conditions at their home differ substantially from those at the centre. Tables show somedetails of our findings.

TABLE 1: Family Income

Range (per month)	No. of Families	%
500-3000	27	72.97
3000-6000	6	16.22
6000 +	4	10.81
Total	37	100.00

TABLE 2: Type of house

Types	No	%
Apartment	5	13.51
Cemented old homes	11	29.73
Standalone pucca homes	6	16.22
Mud house	5	13.51
Chawl	5	13.51
Brick house thatched roof/temporary	5	13.51
Total	37	100.00

Conclusions: All the families agreed that they have learnt: cleanliness, discipline, control over daily life, to live harmoniously in a community, positive thinking and a feeling of empowerment and confidence.

EP-474

EXPLORATION OF PSYCHOSOCIAL ASPECTS OF PAEDIATRIC ONCOLOGY: PERSONALIZED LIFEBOOKS INITIATIVE ILLUSTRATING PSYCHOSOCIAL EXPERIENCES OF PATIENTS AND FAMILIES WITH PAEDIATRIC CANCER IN SINGAPORE.

J. Choo[1], P. Tan[1], A. Choo[2], C.M. Ho[3], Y.L. Chiu[4], T.C. Quah[5]

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; [2]Raffles Institution, Raffles Institution, Singapore, Singapore; [3]Department of Psychological Medicine, National University of Singapore, Singapore, Singapore; [4]Department of Social Work, National University of Singapore, Singapore, Singapore; [5]Division of Paediatric Haematology-Oncology, National University Hospital, Singapore, Singapore

Objectives: Lifebooks, as a therapeutic tool, have been reviewed in elderly with dementia and the terminally ill, but not yet in children. The process of exploring experiences and their meaning facilitates reflection and holds potentially tremendous psychosocial benefit. This is especially pertinent in acute lymphoblastic leukemia patients and families, who, despite the increasing rates of remission (>90%), still face many psychosocial challenges. Lifebooks also serve as an inspiration, provide advice to others, and help as a coping mechanism for families should their child not survive.
Methods: Patients and families are recruited based on their willingness to have a lifebook. Informed consent was done. Formal open-ended interviews are conducted, audiotaped and transcribed. Transcripts are re-organized into smooth-flowing storylines. Patients and families are involved as much as possible, encouraged to contribute content and design ideas, and provide any materials like photos. Drafts are created with a publishing company, reviewed with the families, doctors-in-charge, and social workers. Complimentary printed copies are given to patient and family.
Results: The production of lifebooks is a long-term ongoing project. Current recipients and healthcare professionals found it very beneficial and therapeutic. Children's Cancer Foundation (CCF) Singapore – a key non-profit organization supporting children with cancer and their families – is supporting this project. We aim to eventually benefit all National University Hospital (NUH) paediatric oncology patients and families.
Conclusions: Besides being therapeutic, the full spectrum of experience narrated in lifebooks uniquely supplement the perspectives of healthcare professionals. Future directions include compiling an advice booklet, publishing a compiled lifebooks coffee-table book, creating a lifebooks library in NUH wards/clinics and launching a lifebooks online platform. Our project is promising in shedding light on how to improve paediatric oncology psychosocial care in the Singapore and Asian setting.

EP-475

HELP CANCER SURVIVORS TO REGAIN THEIR WELL-BEING BY FACING THE CHALLENGE OF A THERAPEUTIC ADVENTURE EXPEDITION

M. Leblanc[1], F. Dufour[1]

[1]Expeditions, On the Tip of the Toes Foundation, Chicoutimi, Canada

Objectives: The adolescents living with cancer are not only threatened in their physical integrity, but they are often affected in their self-esteem, their quality of life and their relationship with family and friends. Since 1996, On the Tip of the Toes Foundation is organizing outdoor therapeutic adventures for young cancer survivors from 14 to 20 years old from all across Canada. Our mission is to help those young people living with cancer to regain their well-being by overcoming new challenges, by being in contact with nature and being part of a group with individuals who has been through the same problematics. The purpose of this presentation is to explain the approach of On the Tip of the Toes Foundation. With their specific program objectives, they help the participants to surpass themselves, to become aware of their strength, to develop their sense of autonomy and responsibility, to create an experience based on social inclusion after going through the sickness and treatments. This adventure programming allows an holistic healing process in the remission period.
Methods: A Powerpoint will be used to present the organization, the program and the results. Some pictures of the trips and a short video will be presented.
Results: The preliminary result of the five years study of The impact of the therapeutic expedition on the quality of life of adolescents living with cancer (PAQUETTE L., University of Quebec in Chicoutimi) will be presented.
Conclusions: The presentation will give a better understanding of the approach and the program developed by On the Tip of the Toes Foundation and the results on adolescents.

EP-476

BALANCING GRIEF AND SURVIVAL: EXPERIENCES OF CHILDREN WITH BRAIN TUMOURS AND THEIR PARENTS

C. Eaton Russell[1], E. Bouffet[2], J. Beaton[3], S. Lollis[3]

[1]Max & Beatrice Wolfe Children's Centre Temmy Latner Centre for Palliative Care, Mt Sinai Hospital, Toronto, Canada; [2]Neuro-Oncology, The Hospital for Sick Children, Toronto, Canada; [3]Family Relations and Applied Nutrition, University of Guelph, Guelph, Canada

Objectives: While researchers have explored many important aspects of living with childhood cancer, including the multitude of strains on family members and their reactions, very little is known about the experiences of children with brain tumours and their parents. To this end, our research team conducted a qualitative study guided by grounded theory methods to explore the unique and shared elements of the experiences of childhood brain tumours, from the perspectives of these children and their parents.
Methods: Semi-structured interviews were conducted with twelve children with brain tumours who were between the ages of 6 and 14 years, and one of each of their parents, for a total of 24 participants.
Results: Woven throughout their stories were expressions of grief and uncertainty related to the tumour and its effects on their lives. Children and parents described efforts and strategies that they used to try to maintain a positive outlook and a sense of normalcy, in order to cope and to adapt to the struggles and the changes in their lives.
Conclusions: A substantive theory of Balancing Grief and Survival was developed, offering a lens through which to view the children's and parents' complex experiences, struggles and

coping strategies as integrated, dynamic processes. This presentation will introduce participants to this theory, illustrated by quotes and insights shared by the children and their parents. Implications for future research and clinical practice will also be discussed.

EP-477

SINGLE SESSION GROUP INTERVENTION FOR GRIEVING RELATIVES

J. Espinosa[1], L. Fuentes[1], L. Marroquín[1]

[1]Psychology, Unidad Nacional de Oncología Pediátrica, Guatemala, Guatemala

Objectives: The purpose of this intervention is to giveemotional tools and strategies to the participants for a healthy elaboration oftheir grief process.
Methods: For this intervention, 39 relatives of 16 patients whodied because of an oncological disease were gathered at the National Unit of PediatricOncology (UNOP) to take part in a series of activities led by thePsychology department and with the aid of Social Work, Child Life and PaliativeCare. These group activities are focused in the development of emotional skillsfor the participants to cope with the loss of someone close.
Results: At the end of theactivity, the participants had a secure environment for the emotional catharsisand can name at least 4 conducts they can introduce into their everyday lifefor the appropriate grieving process.
Conclusions: This semi-annual interventionoffers an opportunity for the participants to guide their own emotionalresources to a healthy resolution of their grieving process.

EP-478

COGNITIVE FUNCTION OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA UNDERGOING CHEMOTHERAPY: DEVELOPING COUNTRY PERSPECTIVE

V. Gupta[1], A. Singh[1], T.B. Singh[2], S.K. Upadhyaya[1]

[1]Pediatrics, Banaras Hindu University, Varanasi, India; [2]Division of Biostatistics, Banaras Hindu University, Varanasi, India

Objectives: There are few studies on cognitive function of patients of acute lymphoblastic leukemia (ALL) while on therapy. Majority of the studies have focused on long term survivors. Data from developing countries is even scarcer as the emphasis is still on cure rather than quality of life after completion of therapy. Present study was carried out to assess cognitive function of children with ALL who were still on treatment.
Methods: Cognitive function of30 children with ALL during maintenance phase of chemotherapy was assessed using Malin's Intelligence Scale for Indian children, an adaptation of Weschler Intelligence scale. Children were divided into standard and high risk groups based on age at diagnosis, initial white cell count, immunophenotyping and cytogenetics. High risk group received more intensive chemotherapy including cranial irradiation. 40 children with non-hematologic chronic disease served as controls.
Results: Median age of patients was 9 years. 15 of 30 (50%) children with ALL scored an IQ of less than 90 as against 6 of 40 (15%) in the control group. Mean IQ score was 89.7 ± 7.93 and 95.9 ± 5.86 in study and control groups respectively ($p < 0.001$). Patients had poor scores in all areas but it was statistically significant in areas of information, comprehension, arithmetic, digit span, picture completion, block design and coding. In subgroup analysis, mean IQ score in high risk and standard risk group was 86.5 ± 7.07 and 93.8 ± 7.23 respectively ($p < 0.01$). High risk patients scored lower in comprehension, arithmetic, block design, object assembly and coding.
Conclusions: Children with ALL undergoing chemotherapy had lower scores on verbal, performance and overall IQ. The difference was more marked in the high risk group. Early identification of at risk patients for poor neuro-developmental outcome will help in better rehabilitation of these patients.

EP-479

PSYCHOLOGICAL PROBLEMS OF HEALTHY SIBLINGS IN PEDIATRIC ONCOLOGY

M. Guseva[1], E. Barchina[2], G. Tseitlin[3]

[1]Rehabilitation, Autonomous Non-government Non-profit organization for rehabilitation of children with cancer "Children", Moscow, Russia; [2]Psychotherapy, Institute of Practical Psychology and Psychoanalysis Moscow Russia, Moscow, Russia; [3]Rehabilitation, Dmitry Rogachev Federal Research Centre of Pediatric Hematology Oncology and Immunology, Moscow, Russia

Objectives: Childhood cancer significantly affects the entire family making considerable impact on daily functioning, emotional condition of healthy siblings who are particularly vulnerable to competently deal with the family crisis. The study purpose is to explore psychological problems, Self-concept and coping resources of healthy siblings. Participants comprised 35 children aged 7 to 17. 15 were pediatric oncology patients in remission; 20 - their healthy siblings, 4 of them grieving the loss of elder sisters from leukemia.
Methods: The study was conducted in rehabilitation camp and city family club for two years, including diagnostics and therapy, individually, in sibling pairs and in groups. Diagnostic projective tests: "House-Tree-Person", "My family". Diagnostic and therapy methods: guided phantasy after V. Oaklander; play therapy after T.D. Zinkevich-Evstigneeva; Sandplay.
Results: Outcomes revealed that healthy siblings have no less but often more long-lasting emotional and behavioral problems than their sick brothers/sisters. Self-concept of healthy siblings: low self-appreciation, diffidence, passive vital position, high or lack of self-control, early "adult status". They feel flooded with complicated emotions: anger, offence, fear of death, jealousy, guilt, sadness, abandonment, coexisting with care and concern for the sick, which leads to emotional conflict and high anxiety. In response siblings demonstrate behavior and syndromes known as defense mechanisms, or maladaptive coping: autoaggression, closeness, acting out, dependent/deviant behavior, hyperactivity or retardation, school failure, psychosomatic disorders, depression etc. Healthy siblings suffer losses which could not be openly acknowledged and mourned: parents' love and safety, confidence in the future, usual way of life etc. – up to possible loss of a cancer sibling.
Conclusions: Healthy siblings should be involved in rehabilitation programs right after cancer is diagnosed in the brother/sister. Family system therapy is the core element of rehabilitation program. Families can help their healthy children cope, sharing with them information, feelings, care for the sick, love, attention.

EP-480

REHABILITATION CAMP PROGRAM.

M. Guseva[1], G. Tseitlin[2]

[1]Rehabilitation, Autonomous Non-government Non-profit organization for rehabilitation of children with cancer (ANO) "Children", Moscow, Russia; [2]Rehabilitation, D. Rogachev Federal Research Center of Pediatric Hematology Oncology and Immunology, Moscow, Russia

Objectives: Russian camp program has been conducted in Moscow twice a year since 2006 by ANO "Children" with scientific and methodological support from D. Rogachev Federal Research Center of Pediatric Hematology, Oncology, Immunology. The purposes are to attain psycho-social rehabilitation and adaptation of disabled children and healthy siblings, to help them overcome social deprivation, to promote the family's effective social integration.
Methods: Over 400 children aged 6 to 18 received care within the program - 20% siblings, 5% receiving maintenance chemotherapy. Our camp program is based on the following principles: siblings are accepted during hospital treatment of their brothers/sisters; there are no restrictions on the number of arrivals; when a child is 18, he (she) can work as a camp leader assistant; children are co-authors of the program; individual and group psychotherapy is the core element of camp program. Multidisciplinary specially educated team of oncologist, psychologists, art therapist, teachers and camp leaders work in the camp.
Results: Camp program for children with cancer is a highly effective rehabilitation technology in pediatric oncology. Its long-lasting rehabilitation effects depend on the several conditions: camp is not independent, but complimentary program with a city family club; children should be involved for the long period in both programs with the same staff.
Conclusions: Camp program is an essential element of rehabilitation system for children with cancer, parents, healthy siblings and the entire family. Our experience shows that permanent development of the camp program is a result of effective collaboration of a non-profit organization, parents' club, Federal Center and commercial structures.

EP-481

CROSS-SECTIONAL ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN SURVIVORS OF CHILDHOOD CANCER: A STUDY FROM TURKEY

V. Hazar[1], A. Erol[2], S. Guney[2]

[1]Pediatric Hematology/Oncology and BMT Unit, Istanbul Medipol University Faculty of Medicine, Istanbul, Turkey; [2]Department of Pediatrics, Akdeniz University Faculty of Medicine, Antalya, Turkey

Objectives: To evaluate the health related quality of life (HRQoL) in Turkish childhood cancer survivors and assess the influence of demographic and medical characteristics on HRQoL.
Methods: This cross-sectional study was conducted with 76 cancer survivors whose ages were between 3 and 18 at the beginning of their treatments and their treatments were stopped at least 5 years ago and 138 healthy controls with the same characteristics in terms of age, gender and socio-economic conditions. While "Pediatric Quality of Life Inventory (PedsQL) 4.0 TM, Generic Core Scale" was used for survivors aged 8-18 years and their parents, "WHO Quality of Life-BREF Survey" was applied for the survivors over the age of 18.
Results: Comparison of total scores between survivors and controls of 8-18 age revealed lower points in HRQoL scores of survivors ($p = 0.04$). Survivors who were older than 8 years at the time of diagnosis had reported significantly worse HRQoL scores ($p < 0.01$) than controls. Survivors of 8-18 age group had worse scores of HRQoL in physical and social subscales ($p = 0.02$ and $p < 0.01$, respectively). Evaluating physical subscale, the scores of the

survivors among the parameters for "walking" ($p = 0.01$)," running" ($p < 0.01$), "exercising" ($p < 0.01$), "daily house work" ($p = 0.04$) and "fatigue" ($p < 0.01$) were found to be lower than those of the control group. Similarly, scores of survivor group among social parameters for "others not wanting to be friend" ($p = 0.04$)," "not able to do things that others can do" ($p < 0.01$), "keeping up when playing with other kids" ($p = 0.04$), were found to be lower than those of control group. "Working capacity" and "concentration" scores were worse in survivors who are older than 18 years old than control group ($p < 0.01$ and $p = 0.03$, respectively).
Conclusions: Our study provides crucial clues on the HRQoL in pediatric cancer survivors. These clues should be leading in post-treatment rehabilitations.

EP-482

THE JORDAN RIVER VILLAGE: CAMP PROGRAM FOR CHILDREN WITH CANCER IN ISRAEL

G. Hertzel[1], Y. Shternin[2], Z. Zihar[2], O.Z. Mordechai[3], M. Ben Arush[3]

[1]Pediatric Hematology Oncology, Haemek Medical Center, Afula, Israel; [2]Jordan River Village, Jordan River Village, Galil, Israel; [3]Pediatric Hematology Oncology, Rambam Health Care Campus, Haifa, Israel

Objectives: Cancer diagnosis and treatment causes significant stress leaving the children at increased risk of psychological problems. The Jordan River village-the 14th and newest member of the Newman chain of camps is located in the Lower Galilee region of Israel and is the only camp of its kind in the Middle East.
Methods: The Jordan River village seeks to be play-land for kids with chronic illnesses in the broader Middle East and to enrich the lives of Jewish, Muslim and Christian children in the region.
Results: The village opened two years ago, 1736 children with chronic diseases came from Israel and Palestine without their parents, 296 diagnosed with cancer (19%) age 9-18 years old (mean 13 years). The staff included volunteers physicians, nurses, therapists, counselors, clowns and social workers. The program offered 24-hour medical supervision during a week of swimming and drama, sports and arts in a 61-acre setting in the Upper galilee. The children are under constant supervision, with one counselor (Arabic and Hebrew language) assigned to every two campers, attending to their needs during the day and sleeping in the same room at night, and with specially trained staff overseeing each of the daily activities. Staff doctors and nurses, as well as many volunteer medical personnel, provide the necessary medical supervision. Leading hospitals and voluntary disease-oriented organizations have partnered with the Jordan River village recognizing the importance of such a village and its benefit to thousands of children.
Conclusions: By creating free, fun- filled, memorable and medically safe camping experiences, the Jordan River village is one of the best model of therapeutic recreation programs for children with cancer giving them an opportunity for independence independently of their cultural differences.

EP-483

RECENT EMPLOYMENT TREND OF CHILDHOOD CANCER SURVIVORS IN JAPAN: A CROSS-SECTIONAL SURVEY

Y. Ishida[1], M. Hayashi[2], F. Inoue[3], M. Ozawa[4]

[1]Pediatric Medical Center, Ehime Prefectural Central Hospital, Matsuyama, Japan; [2]Vice-director, Herat Link Working Project, Niigata, Japan; [3]Member, Herat Link Working Project, Chiba, Japan; [4]Pediatrics, St. Luke's International Hospital, Tokyo, Japan

Objectives: Previous research has shown that some adult childhood cancer survivors (CCSs) have experienced employment difficulties. However, the actual employment status of CCSs in Japan has not been studied.
Methods: The participants were selected from the membership directory of Heart Link mutual-aid health insurance and recruited by the Childhood Cancer Patients' Network. We conducted a cross-sectional survey (a self-rated questionnaire on employment) via postal mail or an e-mail communication with a link to an Internet website. We explored the association between the characteristics of CCSs who require disability qualification and having experienced unemployment. The adjusted odds ratios (ORs) for the factors with an outcome of interest were estimated with logistic regression analysis.
Results: In total, 44 CCSs indicated that they had a disability qualification. The significant independent factors related to needing a disability qualification were late effects [OR 12.3; 95% confidence interval (CI) 3.37–45.2], brain tumors (OR 9.55; 95% CI 1.90–48.0), and being a high school graduate (OR 9.86; CI 2.67–36.4). The unemployment rate was 15.9% among CCSs, excluding homemakers and students. Approximately 70% of unemployed CCSs had some late effects and reported having experienced some job difficulties because of childhood cancer; independent factors related to unemployment were late effects (OR 6.22; 95% CI 1.80–21.40), dropping out of school (OR 8.46; 95% CI 1.66–43.10), and brain tumors (OR 2.73; 95% CI 0.83–8.96). Seventy four% of the unemployed CCSs reported wanting to work if their employers understood CCSs better.
Conclusions: The unemployment rate is not high in Japan, but some CCSs need extended disability qualification. The independent factors related to unemployment were late effects and dropping out of school. Most unemployed CCSs were likely to seek work, despite their health problems.

EP-484

FATHER AND SUVIVOR RETREAT: EXPLORING FATHER/SURVIVOR ROLES, COMMUNICATION AND RELATIONSHIPS IN THE AYA BRAIN TUMOR COMMUNITY

W. Iwata[1], S. Wagner[1]

[1]Social Work, Children's Brain Tumor Foundation, New York, USA

Objectives: While research has indicated that the father's also experience increased distress levels both during treatment and in survivorship (Sloper, 2000), there have been few clinical interventions designed to address distress. The father's level of distress has a greater impact on the vulnerability a child feels than a mothers distress level has on the child (Robinson et al, 2007). Fathers of survivors are less likely to be connected to others in a similar situation than mothers. Peer mentoring and community building have been shown to reduce distress.
Sloper, P. (2000). Predictors of distress in parents of children with cancer: A prospective study. *Journal of pediatric psychology*, *25* (2), 79-91.
Robinson, K. E., Gerhardt, C. A., Vannatta, K., & Noll, R. B. (2007). Parent and family factors associated with child adjustment to pediatric cancer. *Journal of Pediatric Psychology*, *32* (4), 400-410.
Methods: To address the relationship and communication issues for fathers and survivors, a pilot weekend intervention was explored. Father focus groups were conducted to determine program objectives, which indicated concerns around communication and age appropriate developmental markers (careers, relationships, independence). Survivors were also surveyed on interests. Both fathers and survivors indicated a desire for team building activities. Activities and discussion groups were created to meet both the researched and identified needs.
Results: Families were recruited from the tri-state area with twelve brain tumor survivors and their fathers' attending a three day retreat. Increased levels of communication between father and survivor was seen and an increase in father involvement at community events held by Children's Brain Tumor Foundation.
Conclusions: This poster will discuss program creation, implementation and outcomes of our retreat. The impact on father/survivor relationships and communication will be looked at as well as future implications and further steps to evaluate the effectiveness of this intervention.

EP-485

PEDIATRIC ENHANCING CONNECTIONS: AN PARENTING INTERVENTION FOR MOTHERS OF CHILDREN WITH CANCER

B. Jones[1], F. Lewis[2], F. Phillips[1]

[1]School of Social Work, UT Austin, Austin, USA; [2]School of Nursing, University of Washington, Seattle, USA

Objectives: Parents of children with cancer face incredible demands including disruption in normal functioning, anxiety, trauma, depression and other negative psychosocial outcomes. Therapeutic interventions are needed to help parents cope with the ongoing stresses and enhance their resilience in response to their child's diagnosis. The purpose of this study was to evaluate the feasibility of adapting the Enhancing Connections program, a multi-component, manualized educational counseling program for mothers with breast cancer and their school age children to a **Pediatric** Enhancing Connections (PEC) program for mothers and children during the acute phase of the child's cancer diagnosis and treatment.
Methods: Qualitative in-depth semi-structured interviews were used to inquire about how the modified intervention resonates with mother's ($n = 7$) experiences with their child's cancer. The thematic analysis of the data involved identification of common threads that represented participant's experiences. Themes were identified that describe reactions of the mothers to the intervention materials, and how they perceive the intervention as meeting the needs of their family.
Results: Results indicated a desire for support specific to the unique experience of parenting a child with cancer. Mothers described the availability of psychosocial support for their children, but a lack of support for their own emotional needs, specifically parenting concerns. Mothers described feeling guilt and lack of confidence in their parenting skills in regards to their child's illness. Mothers expressed a desire for other parents in similar situations. Finally mothers described barriers faced in relation to self care.
Conclusions: Mothers of children with cancer have clear suggestions for adaptation of this evidence-based intervention to meet their needs. Findings suggest a need for parenting interventions for mothers faced with childhood cancer.

EP-486

CANCER IN CHILDREN AND THE SOCIOECONOMIC RESOURCES OF PARENTS. HOW CAN NON GOVERNMENTAL ORGANIZATIONS SUPPORT FAMILIES?

I. Kebudi[1], H. Akcay[2], E. Aysoy[3], S. Gonen[4], R. Kebudi[5]

[1]Student Hisar Schools, Volunteer in Childhood Cancer Love and Solidarity Society (COKSEV), Istanbul, Turkey; [2]BT Director Fleet Corp., Volunteer in Childhood Cancer Love and Solidarity Society (COKSEV), Istanbul, Turkey; [3]Vice President, Volunteer in Childhood Cancer Love and Solidarity Society (COKSEV), Istanbul, Turkey; [4]Secretary, Volunteer in Childhood Cancer Love and Solidarity Society (COKSEV), Istanbul, Turkey; [5]Pediatric Hematology - Oncology, Istanbul University Cerrahpasa Medical Faculty and Oncology Institute President of COKSEV, Istanbul, Turkey

Objectives: Cancer in children influence the entire family. Parent's work situation may be affected.
Methods: Parents of 50 children with cancer were evaluated in regard to number of siblings, the living environment, parental employment. All hospitalization and medication of all children were reimbursed by the government.
Results: Ten families did not have a home in Istanbul. They stayed in the houses of their relatives, so that two or three families lived in the same house, most of the time having two rooms per house. Twenty families had two or more siblings. Twelve fathers did not have a regular job, they were either unemployed, or had to quit their job to care for their child. Thirty had a very low income. Most mothers were housewifes. About 30% tried to gain some income for the family by doing housework such as cleaning. All hospitalization and medication of all children were reimbursed by the government. Nevertheless, the family had extra financial needs for transportationto and from the hospital, food and clothing.
Conclusions: In addition to the psychological burden of cancer in children, poor socioeconomic resources of the family increase the burden of the family. Non governmental organizations (NGO) may provide some support for these families.

EP-487

DEVELOPMENT OF PEDIATRIC PSYCHO ONCOLOGY IN AN ENVIRONMENT WITH LIMITED RESOURCES

Z. Ke cman[1]

[1]BMT Unit with Laboratory for Cryobiology and the Department for the Treatment of Hematological and Oncological Diseases, Mother and Child Health Care Institute of Serbia "Dr Vukan Cupic", Belgrade, Serbia

Objectives: In Serbia around 350 children are diagnosed with cancer yearly. Moste of them are treated at the Hemato-oncology Department at The Mother and Child Health Care Institute of Serbia 'Dr Vukan Cupic' (MCHCIS). In Serbia there is no formal education program, nor hospital volunteering for psycho-oncologists. Great support in this matter is given by local Childhood Cancer Parent Organization 'Zvoncica' (CCPO), where my professional practice started from. Before my introduction to the Hemato-oncology Ward in July 2013, there were several unsuccessful attempts and during that period it is recognized that psycho-social needs of children and families were not adequately met.
Methods: Psychological support has been provided in the form of individual interviews with children and families, play therapy, medical play and psychological counseling and psychotherapy.
Results: Approximately six hundred psychological interventions were provided to approximately one hundred children in first six months. Children's and families' feedback shows that such help was necessary and that their life quality was improved during long term hospitalization and treatments.
Conclusions: Experience shows that pediatric psycho-oncology support should continue to exist. Our future efforts will be to develop and provide better professional support, to improve professional skills in order to meet children's and families psychological and social development. Our goals are: contributing to children's recovery, preserving of patient's and families mental health, helping them to get through all the challenges of cancer treatment in order to continue their lives once the hospitalization is over. With the medical staff recognition of the necessity of professional psychological support and close cooperation with CCPO, we are on the right track to achieve this.

EP-488

DEVELOPMENT AND IMPLEMENTATION OF THE PSYCHO-ONCOLOGY DEPARTMENT IN CHILDREN CANCER HOSPITAL USING INTEGRATIVE MEDICINE:A MULTIDISCIPLINARY APPROACH

E. Khan Ghazi[1]

[1]Psycho-oncology, Children Cancer Hospital, Karachi, Pakistan

Objectives: In order to meet the psychosocial needs of the pediatric population of Children Cancer Hospital, the Psycho-oncology department was started in January 2013 which included Child Life and Spiritual Counseling services.
Methods: The Psycho-oncology model of care by the Government of Western Australia, Department of Health was used as a benchmark for practice. For assessment the Distress Thermometer, Cross-Cutting Symptom Measure (DSM-5), Human Figure Drawing test and a comprehensive interview schedule are used. Tiered intervention model (Hutchison, Steginga and Dunn, 2006) is used for individual and group therapy. SPIKE protocol for delivering unpleasant information is employed. Interventions such as play, art, music assisted therapy; integrative medicine practices such as meditation, aromatherapy, reiki, touch, dream work, mindfulness based stress reduction, are used to address distress and cognitive disturbances. The legacy project was initiated to ease the dying process. Condolence visit is arranged to give emotional support to family. Child Life specialists employ art and play therapy to ensure optimum quality of life for patients. The Spiritual Counselor, trained in person-centered and cognitive behavioral therapy addresses the patients' and family's existential crises.
Results: Psychosocial care which is available throughout the cancer journey ensures better quality of life and treatment compliance from the patient through reduction of stress/distress associated with illness. Up till now more than six thousand sessions have been given by the Psycho-oncology department to patients and their families.
Conclusions: Further challenges are resource limitations which include human, space and technological; language barrier, poverty, and lack of education and awareness of the patients and their families regarding the disease and its psychosocial impact. Another challenge is the stigma associated with getting psychological help. Further training is required in the field as there is no specialization in Pakistan pertaining to Psycho-oncology.

EP-489

BENEFITS OF FUNCTIONAL ACTIVITY TOYS IN RECREATIONAL THERAPY FOR CHILDREN WITH CANCER

J. Kopplinger[1], D.A.N. Mornar[2]

[1]Design, Udoo Planet Creations Ltd., Surrey, Canada; [2]Oncology/Hematology/BMT Program, British Columbia Children's Hospital, Vancouver, Canada

Objectives: FUNctional Activity Toys positively effect the patients' quality of life when used in recreational therapy for children with cancer.
Methods: UDOO produces therapeutic play products that are also functional clothing items. NewDo hats simulate the activity of hair styling in a fun and creative way. The fleece dreads can be braided, tied or knotted, and can be worn up or down. The hats come in four (4) different colors that mimic natural hair - blonde, brunette, red and black. A range of hair accessories can be added. BooDo hats make it easy and fun to change and rearrange features on the hat, to express different fantasy faces. PuppMittz are functional mittens that keep hands warm, and have four (4) different characters in each mitten. Children and caregivers can flip the mitt and flop the top, to reveal different looks and emotions. PuppMittz can tell stories, and kids can express experiences and feelings through the characters. FUNctional Activity Toys were used in interactive, live theatre performances at BC Children's Hospital, Vancouver, Canada. FUNctional Activities were also added before and after the shows. Based on the results, UDOO PLANET LTD. created a line of FUNctional Activity products particularly suitable for Recreational Therapy.
Results: The results were very promising; the patients exhibited a high level of involvement with the product, and with their peers. The kids were delighted to play, and to act like just kids. There was a clear positive impact on children who participated; they were more engaged and felt better.
Conclusions: UDOO products were enthusiastically received by a facilitated focus group of twenty children at the BC Children's Hospital in Vancouver. Bright colors and tactile fabrics engage children and encourage creativity.

EP-490

EXPERIENCES OF PARENTS OF PAEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) TWO MONTH AFTER THE COMPLETION OF TREATMENT

S. Lucchetta[1], B. Muskat[1], H. Jones[2], W. Shama[1], S. Zupanec[2]

[1]Social Work, The Hospital for Sick Children, Toronto, Canada; [2]Nursing, The Hospital for Sick Children, Toronto, Canada

Objectives: The completion of pediatric cancer treatment is considered a difficult and anxiety producing time for families. The transition from active to follow-up care is believed to be exceedingly stressful as families have spent years living with the demands and uncertainty of cancer treatment. Despite growing recognition of families' emotional stress, uncertainty, vulnerability and decrease in health related quality of life, there exists a paucity of research about parents' experiences during this crucial time. Further exploration of parents' experiences during this transition was needed. The purpose of this study was to capture the lived experiences of parents of pediatric ALL patients two months after completion of cancer therapy, with an ultimate objective of examining the need for end of treatment and post treatment supports.
Methods: This was an open exploratory study of experiences related to the child's illness and treatment, as well as lingering effects of health care experiences and treatment delivery. Qualitative methodology was employed using McCracken's in-depth interview method as well as an interview guide containing open-ended, semi-structured questions. Interviews were audio taped and transcribed verbatim. Transcriptions were entered into NVivo 9 and analyzed using the long interview method of qualitative data analysis.

Results: Findings from the analysis identified a range of themes including elation to guilt and fear of relapse. A sense of decreasing priority, an abrupt end of treatment, uncertainty, dealing with a new normal, and a lack of preparedness for transitioning from active care to follow-up were also identified. Results suggest that a greater understanding of, and sensitivity to the experiences of these families is essential.
Conclusions: The results of this study highlight the need for significant changes to the current practice for therapy completion, to better promote positive long-term psychosocial coping and adjustment. Next steps are to formulate and implement a consistent and comprehensive end of therapy plan.

EP-491

THE POSITIVE IMPACT OF CANCER SURVIVORS AND THEIR MOTHERS IN PROVIDING SUPPORT TO PEDIATRIC CANCER PATIENTS AND THEIR MOTHERS

S. Makhoul Khoury[1], G. Yaqub[1], O. Polinger[1], R. Gagin[1], M. Ben-Arush[1]

[1]Pediatric Hematology Oncology, Rambam Health Care Campus, Haifa, Israel

Objectives: Research shows that mothers of pediatric cancer patients are more involved on a daily basis with their child's treatment course and therefore have more influence on how he and the rest of the family cope with the illness. (Frank et al, 2001).
Adolescents diagnosed with cancer often lose hope more easily, and a success story of a surviving peer may help improve his mental state and bring hope into his life.
Methods: The research involves qualitative questionnaires that check the positive influence of the support the mothers of children who have survived the cancer give families who are at the first stages of treatment and asks their experience, their feelings, and insights after having met the mothers of surviving children, and how it helped them deal with the ongoing treatment.
Results: Mothers in support of mothers: Up till now there were 20 individual meetings between mothers whose children have recovered and mothers whose children are receiving treatment. Interviews with mothers of children under treatment reported satisfaction from the meetings. They felt encouraged and understood that it was possible to deal with the difficult period of treatment. They also felt the supporting mothers were able to pinpoint their weak spots and empathize with them. Survivors in support of patients: Up till now there were 25 individual meetings between survivors and adolescent patients. In interviews conducted with the adolescent patients they reported feelings of hope and optimism and said that listening to other success stories has given them energy to continue the battle. They felt that the survivors understood them and felt a closeness with them, even more so than than with their peers.
Conclusions: The outcomes of the interviews point out that these projects are important and necessary. They promote feelings of optimism and hope among the patients.

EP-492

MARITAL RESILIENCE OF PARENTAL COUPLES FACING STEM CELL TRANSPLANTATION (HSCT) IN CHILDREN WITH CANCER

J. Martin[1], M. Duval[1], M.F. Vachon[1], S. Sultan[1]

[1]Hemato-Oncology, CHu Sainte-Justine, Montreal, Canada

Objectives: Research on the effects of childhood cancer on the parental couple has showed conflicting results with negative and positive effects being described. In order to articulate previous results, we focus on a new model on marital resilience combining the two core elements of common couple's identity and collaborative behaviors. Such a model is necessary to help reinforce parental couples in order to support future family rehabilitation. The purpose of this study is to describe the experience of couples facing HSCT and the cancer of their child, in order to identify perceived factors of couples' resilience.
Methods: We collected cross-sectional qualitative data in twelve couples who experienced HSCT of their child following cancer. Parents were asked to talk about their couple in general and how they both reacted as a marital unit to the cancer and the HSCT of the child. Interviews were video-recorded and coded with an open coding agenda grouping concepts retrieved in previous researches on the subject, and the We-ness Coding Scale, usually used in couple therapy to measure in each partner their individual sense of identity to their couple. They also coded their sense of intimacy on the Inclusion of Other in the Self Scale.
Results: Parents identified several factors of major importance for their marital resilience, including cohesion within their couple, capacity to work as a team when facing adversity, and open communication. The results support the idea that experience of we-ness is a major predictor of resilience.
Conclusions: The importance of collaboration within well-adjusted couples, and especially the maintenance and development of communication and emotional support between parents, suggests that resilience could be encouraged. The results can be translated into a set of recommendations to apply into practice by transplantation teams to strengthen parental couples.

EP-493

PSYCHOSOCIAL RISK IN BRAZILIAN FAMILIES OF CHILDREN WITH CANCER: TWO MOMENTS OF THE TREATMENT

A. Motta[1], F. Caprini[1], T. Genelhu[2], T. Bortolini[3]

[1]Post-Graduation Program of Psychology, Federal University of Espirito Santo, Vitória, Brazil; [2]Social and Developmental Psychology Department, Federal University of Espirito Santo, Vitória, Brazil; [3]Onco-Hematology Service, Hospital Estadual Infantil Nossa Senhora da Glória, Vitória, Brazil

Objectives: Psychosocial risks associated with the cancer diagnosis must impact on adjustment of children and adolescents to the treatment, besides their future adaptation. This research aimed to describe the psychosocial risks of families of children with cancer in the moment of the diagnosis (Time 1 = T1) and after two months from the beginning of the treatment (Time 2 = T2).
Methods: Nine patients aged 6-12 years (M = 7,8) attending in the Onco-Hematology Service of a Children hospital in Espirito Santo, Brazil, were included in the study. Their parents provided information about psychosocial risk through the Portuguese language version of Psychosocial Assessment Tool (PAT) and about their social economic level (Brazilian Economic classification criteria). Clinical characteristics were obtained from the patient medical documents. Data were analyzed by descriptive statistics, and considering the tool standards.
Results: Most of the patients received the diagnosis of Leukemia (55.5%) and Lymphons (33.3%) and presented high risk gravity of cancer (55.5%). The socioeconomic level of the families were C2, indicating vulnerability in this aspect. The patients families maintained the psychosocial risk classifications in the levels Clinical (T1 = 66.7% and T2 = 55.6%) and Targeted (T1 = 22.2% and T2 = 44.4%), and in T2 any family exibited the Universal classification. The subscales analysis showed that Family Problems (T1 = 0.50 and T2 = 0.35) and Problems with the Children (T1 = 0.50 and T2 = 0.40) were highlights as source of risk, but in T2 the domain of Stress Reactions showed the greated average risk (M = 0.41).
Conclusions: The psychosocial risk found in T1 remained after two months, showing that these families are under the impact of cancer diagnosis even when the treatment goes on. It is recognized that these families must be assessed during the recent diagnosis and continuously over time, directing intervention proposals that promote adaptative outcomes over the cancer course and in the children's survival.

EP-494

PARENTAL SUPPORT REQUIRED BY HEALTHY SIBLINGS OF PEDIATRIC CANCER PATIENTS

A. Nagao[1], M. Ozawa[2], Y. Ogawa[3], Y. Takei[4], E. Takeuchi[3], A. Manabe[2], S. Suzuki[3]

[1]Department of Preventive Psychiatry/Department of Research Management, Graduate School of Medicine Tohoku University/St. Luke's International Hospital, Sendai, Japan; [2]Department of Pediatrics, St. Luke's International Hospital, Tokyo, Japan; [3]Graduate School of Human Sciences, Waseda University, Saitama, Japan; [4]Faculty of Medicine/Department of Research Management, University of Miyazaki Hospital/St. Luke's International Hospital, Saitama, Japan

Objectives: Siblings of pediatric cancer patients have a higherrisk of developing emotional problems. Especially during the patients' hospitalization, the siblings would receive less attention from their mothers. We investigate thesupport by mothers to the siblings and further identify the support required bythe siblings.
Methods: The participantswere 20 mothers of pediatric cancer patients and the patients' siblings and 11siblings. The mothers were asked to complete the support scalewhich measures how much support the mothers provided to the siblings. Thesiblings answered another support scale which measures how muchsupport they received from their mother.
Results: A chi-square test indicated that there were significant differencesbetween the mother and thesiblings about 'telling the siblings by the mother which treatmentwill work for the patient' ($\chi^2 = 5.77$, $p \leq .05$) and 'going on a holiday with their mother' ($\chi^2 = 7.37$, $p \leq .05$).
Conclusions: The results suggest thatthe siblings require the information about the patient's treatment.

EP-495

THE PAIN MAY BE SINGULAR, BUT THE SUFFERING IS PLURAL: A QUALITATIVE ANALYSIS OF THE IMPACT OF CHILDHOOD CANCER ON THE SENEGALESE FAMILY

S. Ndiaye[1], S.M. Ndiaye[2], A.C. Dieng[1], M.T. Sagna[1], C. Moreira[1], M.N. Diouf[1], F.B. Diagne[1]

[1]Pediatric Oncology, University Hospital Aristide Le Dantec, Dakar, Senegal; [2]Psychiatry, Hopital Principal de Dakar, Dakar, Senegal

Objectives: It is assumed that the diagnosis of childhood cancer will agitate the family. We aim to explore numerous families' testimony to understand their experience and find out how they undergo it.
Methods: This is a qualitative analysis of thirty focus groups with 387 parents of hospitalized children. We address their journey before they reach the only pediatric oncology unit, the

hardships during hospitalization, the strain on the family equilibrium, and we discuss the resources they mobilize to manage the cancer experience.
Results: Parents report delays in diagnosis because they have wasted time seeking traditional treatment and were not suitably referred in the medical system. They discussed the financial burden of treatment fees but mostly the struggle to balance the cost of living in the hospital with the expenses at home. Parents report feelings of powerlessness and frustration when not informed sufficiently by the medical team or when their child's health degrades. Mothers testify being distressed by the lack of understanding from their spouses or in-laws who blame them of voluntarily staying in the hospital. Regardless, parents are grateful for the quality of care and the reassuring improvement of their child's health. They also value the support from other parents and from some medical team members. Mostly, they are impressed by their own strength and the emotional resources they mobilize for their children and never knew they possessed.
Conclusions: The intrusion of cancer in a child disturbs the family's homeostasis. Parents are fragile since they are separated from their supporters, they have to reorganize their structure and mobilize sparse resources. They report a highly stressful period in which they must be resilient and perseverant to support their children when they are themselves overwhelmed and lonely. Yet they fight, for giving up on their child is never an option.

EP-496

A NORDIC PLATFORM FOR CLINICAL ETHICS IN PEDIATRIC ONCOLOGY

P. Pergert[1], T. Brøner[2], A. Castor[3], S. Tóroddsdóttir[4], P. Wendtland Edslev[2], H. Glosli[5], H. Frøland Hauge[5], S. Lehtinen[6], G. Petersen[7], L. Törnudd[8], o.b.o.t. NOPHO/NOBOS Working Group on Ethics[9]

[1]Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; [2]Pediatric Department, Aarhus University Hospital, Aarhus, Denmark; [3]Department of Pediatric Oncology/Hematology, Skane University Hospital, Lund, Sweden; [4]Department of Pediatric Oncology/Hematology, Childrens Hospital, Reykjavik, Iceland; [5]Department of Pediatric Medicine, Oslo University Hospital, Oslo, Norway; [6]Department of Pediatrics, Oulu University Hospital, Oulu, Finland; [7]Department of Pediatrics and Adolescent Medicine, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark; [8]Pediatric Clinic, University Hospital of Linköping, Linköping, Sweden; [9]Nordic Society of Pediatric Oncology Nurses (NOBOS), Nordic Society of Paediatric Haematology and Oncology (NOPHO), Nordic countries, Sweden

Objectives: The purpose of this presentation is to present the development, activities and achievements of the NOPHO/NOBOS Working Group on Ethics (WGE) 2008-2013.
Methods: A joint working group on ethics, consisting of pediatric oncology nurses and physicians, was constituted during the NOPHO/NOBOS Annual Meeting in 2008. The intention was to create a Nordic competence group addressing ethical questions within pediatric oncology. The WGE has 14 members (7 nurses and 7 physicians) with at least two representatives from each of the Nordic countries. The group meets yearly at two 1-day-meetings and one 3-day-workshop. Meetings are organizational and educational. Members are educated through international courses and conferences in clinical ethics, and are trained facilitators in moral case deliberation.
Results: All WGE members participate in, or have initiated, formalized clinical ethics projects at their pediatric departments, hospitals, regions or countries. Most clinical projects provide deliberation on ethically difficult cases on a regular basis as an integrated part of daily work in pediatric oncology. Ten members are active in local clinical ethics committees. Two members have initiated or supervise research projects on ethical matters. Two members teach ethics to nursing or medical students. One is a board member in a national society for clinical ethics.
Conclusions: To the best of our knowledge, WGE represents the first specialized working group on ethics within the framework of an international study group for pediatric oncology (NOPHO) and the first joint working group of NOPHO and NOBOS. It has proved beneficial to combine pediatric oncology nurses and physicians from different countries for this work. Through collaboration and education we have created a common Nordic platform for developing clinically applied ethics. Importantly, the WGE has inspired and enabled all members to initiate or engage actively in projects locally, regionally and nationally, thus increased the focus on clinical ethics.

EP-497

CAREGIVER SELF-ADMINISTERED FINANCIAL EXPENDITURES (C-SAFE) FOR PEDIATRIC CANCER: ADAPTING AN ESTABLISHED INSTRUMENT

J. Pole[1], C.J. Longo[2], A. Zuk[1], L. Sung[3]

[1]Research Unit, Pediatric Oncology Group of Ontario, Toronto, Canada; [2]DeGroote School of Business, McMaster University, Hamilton, Canada; [3]Haematology/Oncology, Hospital for Sick Children, Toronto, Canada

Objectives: To adapt the Caregiver Self-Administered Financial Expenditures (C-SAFE) instrument for use in the pediatric cancer context. The C-SAFE will be used to measure the longitudinal financial burden among caregiver's of pediatric cancer patients and to identify the characteristics of those financial burdens.
Methods: Focus group methodology was used to evaluate the face validity and understandability of C-SAFE in pediatric cancer. 16 individuals were invited to review the current C-SAFE instrument in a face-to-face meeting. Participants included a diverse group of health care professionals and parents of children diagnosed with cancer. In advance of the focus group, participants evaluated each item with regard to importance of each item related to costs; and understandability. During the focus group, an independent facilitator worked question-by-question probing participants with regard to the essential nature of the concept, understandability, face validity and appropriate use of examples. The revised C-SAFE was provided for additional comments to participants.
Results: All 16 invited participants provided pre-meeting evaluations of the C-SAFE. A total of 9 participants attended the face-to-face meeting. The focus group responses provided clarity in three main areas: recall timeframe, concept clarity and the need for more overall explanation and specific examples. The C-SAFE was then restructured. An introduction that describes the focus of each section along with definitions used throughout was generated. Each question was revised to focus recall to the past 4 weeks. The format, wording and examples for each question were revised based on feedback.
Conclusions: Utilization of a multi-disciplinary focus group to help in the adaptation of an established instrument for a new, but unique, population provided invaluable insight. The focus group participants drove a thoughtful re-design of the instrument, ultimately resulting in an instrument that is more focused, easier to understand and provides clear instruction and examples.

EP-498

MEASURING LEVELS OF MEDICAL TRAUMATIC STRESS IN PARENTS OF CHILDREN WITH CANCER WHO HAVE RECENTLY COMPLETED TREATMENT

S. Quinn[1], A. Gozman[1], V. Kanwar[1]

[1]Pediatric Hematology Oncology, Albany Medical Center, Albany, USA

Objectives: The transition to off-therapy follow-up is a stressful event for parents and/or primary caregivers (henceforth referred to as parents) of children with cancer. The psychosocial needs of parents after therapy have received limited attention in the United States with only 3 published quantitative studies, the largest with 35 parents, and as a small academic center without a formal off-therapy program we wanted to investigate and address these needs. We recruited a transition care coordinator (TCC) to quantitatively screen parents at end of therapy and to develop supportive interventions.
Methods: After informed consent, a standardized questionnaire, the Psychosocial Assessment Tool (PAT) was administered to parents at therapy completion (T1) and 6 months later (T2). The TCC provided "universal " intervention to all families with an end of therapy binder containing a treatment summary, follow-up roadmaps, information on late effects, and survivor scholarships. Based on their PAT scores, some parents were provided intervention specific to symptoms (targeted intervention) or referred to a behavioral health specialist (clinical intervention).
Results: PAT was administered to 14 parents; at T1 women ($n = 10$) scored 54% higher than men ($n = 4$). Parents experienced worry and anxiety (71%) and sadness/depression (50%). In addition, they reported post-traumatic stress symptoms of re-experiencing (29[v1]%) and hypervigilance (36%) [v2]. A substantial proportion (29%) were found to warrant targeted or clinical intervention for psychosocial need, facilitated by the TCC.
Conclusions: This pilot study was initiated in October 2013 at a small academic center using a TCC and PAT screening tool. Emerging statistics suggest greater stress on mothers after therapy, and that a substantial proportion of parents have symptoms of PTSS after therapy. We anticipate gathering data on 40 parents to confirm these findings.

EP-499

LINKING COMMUNITY RESOURCES TO SUPPORT ADHERENCE TO TREATMENT APPOINTMENTS AND REDUCE ABANDONMENT IN CHILDHOOD CANCER IN EL SALVADOR

N. Rossell[1], C. Salaverria[1], A. Hernandez[1], S. Alabi[1], R. Vasquez[1], M. Bonilla[2], C. Lam[2], R. Ribeiro[3], R. Reis[4]

[1]Oncology Department, Benjamin Bloom Children's Hospital, Santa Tecla, El Salvador; [2]International Outreach Program, St. Jude Children's Research Hospital, Memphis, USA; [3]Department of Oncology, St. Jude Children's Research Hospital, Memphis, USA; [4]Department od Public Health and Community Care, Leiden University Medical Center, Leiden, Netherlands

Objectives: Abandonment of treatment is a major cause of treatment failure and deaths for children with cancer in developing countries. Our purpose was to gain insight into reasons of Salvadoran parents for missed appointments and abandonment to be able to establish their need for support. The study formed part of a newly introduced tracking system for early detection and improvement of adherence to treatment appointments, which resulted in a substantial decrease of abandonment rates.
Methods: Nearly 500 patients who missed one or more appointment were tracked and qualitative data were gathered through 374 interviews varying from short phone conversations to semi-structured interviews at the hospital.

Results: Most of the reasons for absences were practical, and local resources such as health clinics and municipalities in the patient's community were contacted, to assist in supporting the families to adhere to treatment. This consisted mostly of money or transportation for attending appointments. This confirms that parents' decision making is not only dependent on medical considerations regarding risks and benefits of the treatment, but also on practical resources. We also asked parents' experience of the support they received. Their answers suggest the added importance of socio-emotional benefits of both the tracking and the interventions resulting from it. Giving practical support in the direct daily environment of patients reduced feelings of isolation and helplessness and thus had a positive influence on the predisposition of parents towards the treatment of their children.
Conclusions: The hospital can reach the patients' community and have an impact on decisions about treatment by putting together resources ready to be used in the patients' daily environment. The participation of community institutions brought economic relief to the families and to the cancer program. We propose that unexpected social emotional benefits helped enhance the effects of the intervention.

EP-500

IN THEIR OWN WORDS: AN ANALYSIS OF WEBLOGS POSTED BY PARENTS OF CHILDREN WITH CANCER

K. Ruccione[1], J. Gilberto[1], S. Gantan[1], A. Gordon[2]

[1]Division of Hematology Oncology and Bone Marrow Transplantation, Children's Hospital Los Angeles, Los Angeles, USA; [2]Institute for Creative Technologies, University of Southern California, Los Angeles, USA

Objectives: To identify psycho-educational needs of parents of children with cancer distilled naturalistically from blogs posted on the Internet.
Methods: Blog posts were identified using StoryUpgrade, a program that searches weblog posts using a fictional prototype story. We sought posts from 3 time points: diagnosis, active treatment, and after treatment completion. Using the Family Adjustment and Adaptation Response (FAAR) model as a conceptual framework, a team of 3 content experts independently reviewed blog entries, coding them into themes/sub-themes. Reviewers' coding differences were resolved through discussion to achieve consensus.
Results: Through analysis of 90 posts on 40 blogs, key themes previously identified in focus groups and structured interviews (Patterson et al. 2004; Miedema et al. 2010) were verified. Strains most often noted were illness related to treatment (*cancer-related*), strong emotions and loss of normal life/activities (*child*), strong emotions and loss of normal family life (*family*). Resources most frequently mentioned were child's strengths (*child*), religious beliefs, parental competence and extended family support (*family*), support from parents' friends/co-workers (*community*), competent/caring doctors and support from nurses/social workers (*health care system*). Coping strategies most often cited were being positive/maintaining hope, religious faith, pride in child/strength from child, and living and focusing on the present (*appraisal-focused*); being normal/seeking normality, balancing family needs, advocating for child, being organized/planning ahead, seeking information about cancer (*problem-focused*); and humor/fun/celebrating, seeking/giving support (*emotion-focused*). Blog analysis also discovered several themes not previously identified: cancer-related pain (strains); gratitude, altruism (coping); and general community support, tangible support (resources).
Conclusions: Weblog analysis yielded confirmatory and new evidence of parents' psycho-educational needs, supporting use of the Internet for such research. Findings may be useful in guiding clinical care and fostering access to vetted e-health resources (e.g., searchHOPE.chla.org) based on parents' collective lived wisdom.
Acknowledgements: Partial funding support provided by the Chase Family Foundation.

EP-501

EXPERIENCE OF USING SICK CARD AND OTHER PATIENT EDUCATION MATERIAL TO IMPROVE OUTCOME OF CHILDHOOD CACRES

R. Seth[1], R. Seth[1], A. Singh[1], T. Thomas[1], A. Srivastava[1], B. Singh[1]

[1]Pediatrics, ALl India Institute of Medical Sciences, Delhi, India

Objectives: Parents of children undergoing treatment for childhood cancers are under stress and extreme anxiety. Many of them are from distant places. The aim was to provide details of disease, side effects of treatment, information on care of children with cancer, opportunities available from government and non governmental sources for treatment to the families. We have also constructed a sick card which carries all information regarding the patient's disease, the medications for common ailments with doses and first line management for febrile neutropenia. This is made in the local language too besides English.
Methods: A questionnaire to 25 parents was provided based to assess their understanding of the patient education material
Results: Parents were aware of various forms of patient education materials prepared for them. Details of them will be provided. This helped in their ability to understand disease better. Details of various laboratories and investigation rooms will be provided. They found the sick card particulrly useful as it carries informationof intravenous drugs that may be used as first line treatment for febrile neutropenia, out telephone contact number, e mail of the support group that is made for parents of children undergoing cancer treatment. Details of support group'Sambhav 'will e diacussed
Conclusions: Patient education material plays an important role towards impoved treatment outcomes.

EP-502

CAMP TRILLIUM – CANCER CAMP FOR CHILDREN WITH CANCER AND THEIR FAMILIES IN ONTARIO, CANADA

M. Shea-Perry[1], A. Martiniuk[2]

[1]Executive Director, Camp Trillium, Hamilton, Canada; [2]Faculty of Medicine, University of Sydney, Sydney, Australia

Objectives: For over 30 years Camp Trillium has been providing camp experiences for children with cancer and their families. Both summer and year-round camping programs are very popular for children with cancer and their families in Ontario. Recent findings suggest camping programs help children and families cope with childhood cancer and help improve quality of life. We aim to describe the scope of the programs and number of campers attending the programs offered by Camp Trillium and to increase the awareness of its existence. Camp Trillium has been considered a leader in oncology camping and has been actively involved in collaborating with national and international programs to enhance the cancer camp experience.
Methods: A qualitative approach was taken including: gathering historical and current documents about Camp Trillium and interviewing current staff and board members of Camp Trillium.
Results: In the summer of 2013, 587 families participated in camp programs. Of these families 24% of were on active cancer treatment, 68% were off cancer treatment and 8% were bereaved families. Camp Trillium works with all 5 pediatric treatment centres. Of the 587 summer families in 2013 38% were patients at the Hospital for Sick Kids in Toronto, 17% were patients of Children's Hospital of Western Ontario, London, 18% from McMaster Children's Hospital, Hamilton, 18% from the Children's Hospital of Eastern Ontario, Ottawa, 7% from Kingston Regional Cancer Centre, Kingston and 2% unknown clinics. Interactions with board of directors and year staff conclude that the mission of Camp Trillium has demonstrated positive impacts to families of children with cancer.
Conclusions: This abstract aims to raise awareness of Camp Trillium and oncology camping programs which supports children with cancer and their families.

EP-503

A CANADIAN MODEL: THE CANCER CAMP MOVEMENT – NATIONAL COLLABORATION OF ONCOLOGY CAMP BEST PRACTICES

M. Shea-Perry[1], A. Robertson[2]

[1]Treasurer, Canadian Association of Pediatric Oncology Camps, Hamilton, Canada; [2]Chair, Canadian Association of Pediatric Oncology Camps, Toronto, Canada

Objectives: The Canadian Association of Pediatric Oncology Camps, was formed in 2006 to ensure that the cancer camps pediatric oncologists were referring their patients to were safe. The clinic directors from across Canada (C17) encouraged leaders in cancer camps to examine all oncology camp programs in Canada. As a result a set of guidelines were adopted and developed as a baseline for best and standard practice. The implementation of an annual standards review process has led 13 member camps across Canada being given the Gold Star for practicing at the highest level.
We aim to describe the evolution and role of the Canadian Association of Pediatric Oncology Camps (CAPOC) and to increase the awareness of its existence and need for best practices in camping programs.
Methods: A qualitative approach was taken including: gathering historical and current documents about CAPOC and interviewing current board members of CAPOC.
Results: Together with its board of directors, medical committee, CAPOC has worked to develop a comprehensive set of guidelines for oncology camps. Several resources and networking opportunities already exist including peer – peer visits that occur every three years resulting in Gold Star Membership. These visits allow other members to see camp in action, to share ideas and verify the camps commitment to safe camp operations.
Conclusions: This abstract aims to raise awareness of CAPOC and therefore, enable future work around the development of pediatric oncology camping guidelines, resources and sharing of best practices world-wide. The oncology camper requires attention and expert knowledge about their needs, prior to, during and after the camp experience. The safest cancer camps consider the medical and psychosocial supervision and supplies that are needed to care for a sick child, as well as the meeting or exceeding of the provincial camp standards to ensure camp contributes to a positive experience for the child.

EP-504

ADDRESSING THE PSYCHOSOCIAL NEEDS OF THE HOSPITALIZED CHILD: THE ROLE OF THE CHILD LIFE PROGRAM

A. Sievert-Fernandez[1], N.S. Jose[1]

[1]Child Life Program, Kythe Foundation Inc, Quezon CIty, Philippines

Objectives: Kythe Foundation Inc., a Philippine based organization, established hospital-based child life programs (CLP) to address the psychosocial needs of chronically ill patients, providing developmentally appropriate interventions that minimize the stress and anxiety experienced and assuring continued optimal growth and development. Kythe undertook this study to look into the role the CLP plays in lowering the negative emotions experienced by chronically ill children.
Methods: The study was conducted at the Hematology and Oncology Department if the Philippine Children's Medical Center that adapted the CLP in December 2012. As evidence of the value of the CLP, children's drawings through the Child Drawing: Hospital (Clatworthy, 1999), an instrument designed to measure the emotional status of hospitalized children, were obtained from 30 hema-onco pediatric patients, ages 6-13 years old, prior to the implementation of the CLP. The same instrument was administered six months into the implementation of the CLP to ascertain whether changes in the children's drawings were seen. A statistician was hired to analyze the data.
Results: Results show a significant difference in the scores between the pretest and posttest drawings, indicating an alleviation of the negative emotions experienced by the children.
Conclusions: Child life programs are integral in the hospital setting as these focus on the social and emotional impact of illness and hospitalization on children and strive to promote a positive hospital experience for them. The goal is to minimize the stress and anxiety as much as possible and to provide an environment where children can gain a better understanding of the hospital, their illness and medical treatment.

EP-505

WORKING WITH TEENAGERS AND YOUNG ADULTS (TYA) WITH CANCER TO DEVELOP BETTER APPROACHES TO CARE: A CO-CREATION APPROACH

M. Stevens[1], A. Cameron[2], J. Cheshire[1], P. Spencer[1], P. Beynon[1], E. Fynn[1], C. Neck[1], J. Cargill[2]

[1]On Target, Bristol Royal Hospital for Children, Bristol, United Kingdom; [2]TYA Cancer Service, University Hospitals Bristol NHS Trust, Bristol, United Kingdom

Objectives: Service user questionnaires, used for clinical service evaluation/improvement, often represent the knowledge/insights of professionals who construct them. Responsibility for solutions also tends to lie with professionals so that services are re-designed around, rather than with patients. Co-creation methodology shifts the focus from professionals delivering care to one in which patients become central not only to the re-design of services but also in continuous development, to co-create better health experiences/outcomes. The likely success of this approach in a TYA population was unknown.
Methods: A convenience sample of patients attending a regional TYA centre was invited to participate in exploratory work based around the development of a patient questionnaire: 27 expressed interest and 7 (26%) fully engaged. A combination of techniques (1:1 interviews, email exchanges, focus group) was used over a period of several months to ascertain views about the construction of a questionnaire (content, design/face validity, communication preferences) for distribution to a larger patient cohort. Respondent validation ensured congruence between team records and patient experience/perspective.
Results: Unanimous agreement was reached about areas for inclusion: Physical wellbeing/health; Peer support; Information provision; Psychological/emotional support; Family/friends; Education/employment; Education/training about TYA cancer for others; along with design suggestions and ideas for ongoing communication with TYA patients. The questionnaire was subsequently distributed to 108 TYA patients with whom the team had had no prior contact: 42/108 (39%) were returned; 28/42 (66%) indicated an interest in continuing to work with the team.
Conclusions: Using co-creation, patients engaged creatively in the development of a TYA friendly questionnaire with satisfactory response rates. Subsequent work has involved TYA in prioritising themes for service development interventions based on the questionnaire findings. Their participation has included: agreeing content and delivery of wellbeing days; selection of mentors for a work mentoring programme; and defining content, design and functionality of a psychological support website.

EP-506

BENEFIT-FINDING IN ADOLESCENTS WITH CANCER: A SIX MONTHS FOLLOW-UP STUDY DURING THE FIRST YEAR AFTER DIAGNOSIS

E. Sulkers[1], J. Fleer[2], A. Brinksma[1], P.F. Roodbol[1], W.A. Kamps[3], W.J.E. Tissing[3], R. Sanderman[2]

[1]UMCG School of Nursing and Health, University of Groningen University Medical Center Groningen, Groningen, Netherlands; [2]Department of Health Sciences Health Psychology Section, University of Groningen University Medical Center Groningen, Groningen, Netherlands; [3]Department of Pediatric Oncology/Hematology Beatrix Children's Hospital, University of Groningen University Medical Center Groningen, Groningen, Netherlands

Objectives: Despite the fact that benefit-finding (BF) has been promoted as one of the potential mechanisms underlying resilience in adjustment to pediatric oncology, few studies have examined BF in youth with cancer. Furthermore, research on BF during the early phase of the cancer trajectory is almost absent. This study aimed to investigate (1) the temporal dynamics (time of onset, pattern of change over time), and (2) impact of BF on psychological outcomes in adolescents with cancer during the first year post-diagnosis.
Methods: Thirty-three newly diagnosed adolescents with cancer (mean age = 14.1, SD = 1.7; 55% female; all types of cancer; 88% >60% chance of survival) completed measures of BF, anxiety, depression and quality of life at 6 and 12 months post-diagnosis.
Results: Six months post-diagnosis (T1) all adolescents experienced BF at least to some degree. BF at T1 ($M = 34.5$, $SD = 5.5$) did not differ significantly from BF at 6 months follow-up (T2) ($M = 35.2$, $SD = 6.7$, $t\ (29) = 0.64$, $p = <.05$). BF at T1 was significantly positively associated with the physical functioning quality of life subscale at T1 and T2, but not with anxiety, depression or other aspects of quality of life. BF at T2 was unrelated to all outcomes (all p's>.05).
Conclusions: The finding that patients report a similarly high level of BF at both assessment points suggest that BF already occurs within the first 6 months after diagnosis. Future research with a longer follow-up should determine whether levels of BF remains stable or decrease during the (long-term) survival phase. BF was not associated with any of the psychological outcomes measured in this study. Thus, the question whether BF is adaptive for youth with cancer requires further investigation.

EP-507

PREDICTORS OF BACTERIAL INFECTION AMONG PEDIATRIC CANCER PATIENTS AND SINGLE CENTER EXPERIENCE

J. Suvada[1], M. Plesko[2], E. Kaiserova[2], L. Perdochova[3], M. Zuzulova[4], N. Kulkova[5]

[1]Children Hematology and Oncology, St. Elizabeth University of Public Health and Social Science, Bratislava, Slovakia; [2]Children Hematology and Oncology, Children's Teaching Hospital, Bratislava, Slovakia; [3]Clinical Microbiology, HPL, Bratislava, Slovakia; [4]Dept. of Biochemistry and Immunology, Oncology Insitute of St. Elizabeth, Bratislava, Slovakia; [5]Dept. of Microbiology, St. Elizabeth University of Public Health and Social Science, Bratislava, Slovakia

Objectives: Children with cancer undergoing chemotherapy develop many common complications. A bacterial infection (BI), especially blood stream infection (BSI) is usually commonly observed during treatment course. Presentation can be different from case to case, with or without neutropenia, fever and clinical signs of sepsis.
Methods: We conducted a prospective, single-center study to identify predictors for invasive bacterial infection or culture negative sepsis in children cancer patients in Slovakia. There were enrolled 140 patients who met inclusion criteria. It was taken sample for investigation of bacterial inflamation e.g. IL-6, IL-10, TNF alpha, procalcitonin, C-reactive protein and presepsin. Independent predictors at clinical presentation were analyzed using multiple regression models.
Results: Patient's median age was 7.24 years; 62% had an underlying diagnosis of leukemia. Independent predictors of bacterial infection were ANC less than 500, temperature at presentation $\geq$39.0˚C, central venous catheter insersion and underlying diagnosis of ALL. All markers except CRP and procalcitonin correlated with predicting of bacterial infection. The highest values were observed among those who developed blood stream infection or serious bacterial invasive infection. More common were hospital-aquired infection (83%).
Conclusions: This study identifies predictors of infection/complications and confirmed predictive value of new markers in pediatric patients with bacterial infection. This work highlights the importance of the new inflamation markers whoch can be successfully used in different cancer pediatric patients. These prediction models warrant prospective validation.

EP-508

EXPLORATION OF THE PSYCHOSOCIAL ASPECTS OF PAEDIATRIC ONCOLOGY: A QUALITATIVE STUDY OF THE PSYCHOLOGICAL, SOCIAL AND EMOTIONAL EXPERIENCES OF PATIENTS WITH PAEDIATRIC CANCER IN SINGAPORE

P. Tan[1], J. Choo[1], A. Choo[2], T.C. Quah[3], C.M. Ho[4], Y.L. Chiu[5]

[1]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; [2]Raffles Institution, Raffles Institution, Singapore, Singapore; [3]Division of Paediatric Haematology-Oncology, National University Hospital, Singapore, Singapore; [4]Department of Psychological Medicine, National University of Singapore, Singapore, Singapore; [5]Department of Social Work, National University of Singapore, Singapore, Singapore

Objectives: Acute lymphoblastic leukemia (ALL) – the commonest childhood cancer – had dismal 10-20% survival rates in the 1960s. However, with extensive biomedical advances, >90% now enter complete remission and 80-90% are cured. Yet, with countless physical, emotional and psychosocial implications of childhood cancer, the question of whether quality matches up to quantity of life remains unanswered. This study aims to identify, collate, analyze and classify significant psychosocial issues from patients to improve the holistic care, patient-family education, and lay down a good foundation for further research.
Methods: Seventeen semi-structured 1-3-hour-long interviews were done with 17 pairs of caregiver and patient. Interviews were kept open-ended and conversational using Seidman interviewing techniques. Audio-recordings were transcribed and analyzed using Smith's interpretative phenomenological analysis (IPA). All subjects had no relapses/transplants, and were under Ma-Spore ALL 2010 protocol.

Results: An organized over-arching hierarchy was conceptualized to logically encompass the wide-range of psychosocial issues raised by subjects. Out of many themes and subthemes, significant ones were: Adverse impact on academic pursuits; Deteriorating relationships with peers and siblings; Fear of medical settings, personnel and procedures attributable to impressions from caregiver and healthcare professionals; and Increased maturity of child.
Conclusions: Important psychosocial issues highlighted by this study will help guide healthcare professionals in providing psychosocial care to patients and caregivers. Further research could delve deeper into reasons and ramifications of these issues, and their exact significance to quantifiable health-related quality of life.

EP-509

DECISION-MAKING FOR CHILDREN FOLLOWING A CANCER DIAGNOSIS– PRELIMINARY FINDINGS FROM A QUALITATIVE STUDY WITH PARENTS AND ONCOLOGISTS

D. Badarau[1], A. Colita[2], M. Dragomir[3], B. Elger[1], T. Kuehne[4], I. Miron[5], F. Niggli[6], K. Ruhe[1], T. Wangmo[1]

[1]Pediatric Ethics, Institute for Biomedical Ethics, Basel, Switzerland; [2]Pediatric Oncology, Fundeni Clinic Institute, Bucharest, Romania; [3]Pediatric Oncology, Prof Dr. Al. Trestioreanu Oncology Institute, Bucharest, Romania; [4]Pediatric Oncology and Haematology, University Children's Hospital, Basel, Switzerland; [5]Pediatric Oncology, Sf. Maria Clinic Emergency Hospital, Iasi, Romania; [6]Pediatric Oncology, University Children's Hospital, Zürich, Switzerland

Objectives: To investigate decision making processes for children undergoing curative cancer treatment from the perspective of parents and oncologists.
Methods: Semi-structured interviews were conducted separately with 12 dyads of parents and oncologists in Switzerland and Romania. The study was approved by Research Ethics Committees in both countries and written informed consent was obtained from each participant before starting the interview. Participants were asked to discuss their experiences at the time of their child's cancer diagnosis and treatment. Interviews were transcribed verbatim and thematic coding with MAXQDA was used to elicit major topics.
Results: Parents describe the time of their child's diagnosis as overwhelming and catastrophic. They identify a myriad of constraints that limit their ability to make decisions regarding treatment: their lack of medical knowledge and understanding, time pressure, unfamiliarity with the hospital setting, information overload, and emotional turmoil. Hence most of the time they follow physicians' lead in decision making but feel equally responsible for the decision. Parents highlight a loss of control that is somewhat regained by focusing on starting treatment immediately. Physicians report to grapple with this need by gearing discussions towards starting treatment while also customizing information to parents' reactions. In interactions with parents, physicians tend to seek compliance to treatment which they perceive as following the best interest of the child.
Conclusions: Decision making in pediatric oncology around the time of diagnosis is a complex and partially understood process. A better understanding of parents' needs in these difficult situations can facilitate communication at diagnosis and address constraining factors impinging on decision making.

EP-510

PERCEPTIONS OF YOUNG ADULTS WITH CANCER OF THE "VENTURING OUT PACK PROGRAM " AS A SOURCE OF TANGIBLE SUPPORT

L. Wazneh[1], A. Tsimicalis[2], C.G. Loiselle[3], M. Purden[2], D. Edward[4]

[1]Ingram School of Nursing, McGill University, Montreal, Canada; [2]Ingram School of Nursing Faculty of Medicine, McGill University, Montreal, Canada; [3]Christine and Herschel Victor/ Hope & Cope Chair in Psychosocial Oncology Department of Oncology and Ingram School of Nursing, Jewish General Hospital & McGill University, Montreal, Canada; [4]Adolescent and Young Adult (AYA) Oncology, Venturing Out Beyond Our Cancer Foundation, Montreal, Canada

Objectives: Within the cancer community, young adults (YAs) with cancer have been increasingly recognized as a distinct group with unmet supportive care needs. 'Venturing Out Beyond Our Cancer' is a non-profit community agency committed to providing YAs with tangible support services to address their cancer-related needs. One of these services, called the 'Venturing Out Pack (Vo-Pak) Program', provides backpacks containing three resource kits to help YAs throughout their cancer journey. The study objectives were to: (a) explore the needs of YAs newly diagnosed with cancer; (b) discuss with them the extent to which Vo-Pak helps them meet their practical, psychosocial and informational needs; and (c) explore with them how the Vo-Pak could be further enhanced.
Methods: A qualitative descriptive study was conducted with a purposive sample of 12 YAs treated for cancer at a university-affiliated tertiary hospital in Montreal, Quebec, Canada. One-time, audio-recorded, semi-structured interviews were conducted, transcribed, coded and thematically analyzed.
Results: Overall, YAs positively perceived the Vo-Pak as a welcoming, ready-to-use, timely package to meet their cancer-related needs. The Hospital Comfort Kit was seen as a 'hands on' resource that helped in comforting them during their hospital stay. The Venturing Out Kit was viewed as a catalyst for connecting with similar others and offering them 'guilt-free' complimentary outings. The Friends of Lara Information Kit was commended for its relevance as a dispatcher to important support resources. Participants recommended delivery of the Vo-Pak two month after diagnosis and broader awareness and dissemination of the program.
Conclusions: Enhancing the Vo-Pak program by increasing awareness and promoting networking among YAs with cancer is critical in meeting their needs. More systematic dissemination of programs such as this one would add to the overarching goal of providing comprehensive person-centered cancer care to an underserved segment of the cancer population.

EP-511

EXISTENTIAL ANXIETY AND GROWTH IN CHILDREN WITH CANCER

R. Woodgate[1], C. West[1], K. Tailor[2]

[1]Faculty of Nursing, University of Manitoba, Winnipeg, Canada; [2]Counselor Education & Counseling Psychology, Marquette University, Milwaukee, USA

Objectives: To date, there has been minimal research that details the experience of children diagnosed with cancer in their existential predicament. The purpose of this presentation is to describe findings that speak to the existential challenges experienced by children living with cancer.
Methods: An interpretive, descriptive qualitative research design was used. Thirteen children (8-17 years) undergoing treatment for cancer participated in the study. Two main sources of data collection were utilized. First, children had the opportunity to journal their experiences via a computer diary created by the first author. Additionally, the computer diary had a drawing tool for children to express how they were feeling. The second source of data involved children taking part in open-ended individual interviews. Data analysis occurred concurrently with data collection using the constant comparative method of data analysis.
Results: Within the cancer world children moved between feelings of anxiety (generated by existential worry, existential longing, and the existential vacuum) and existential growth. As children worked within the drawing tool, a portal to their inner worlds was opened, which allowed them to explore their anxiety through drawings. In many of the children's drawings the intimate connection between the physical symptoms and the emotions that defined their existential challenges were clearly evident. connection between the physical symptoms and the emotions that defined their existential challenges were clearly evident.
Conclusions: This research provides evidence that the active engagement of children's imaginations through the use of a computer-drawing tool may have significant therapeutic value for assisting children with cancer to explore, understand, and manage their physical suffering, as well as the associated anxiety they live with. The use of symbolic forms of communication including drawing, offer health-care professionals new possibilities for enhancing the therapeutic conversations and interactions they have with ill children and their families.

RARE TUMOURS

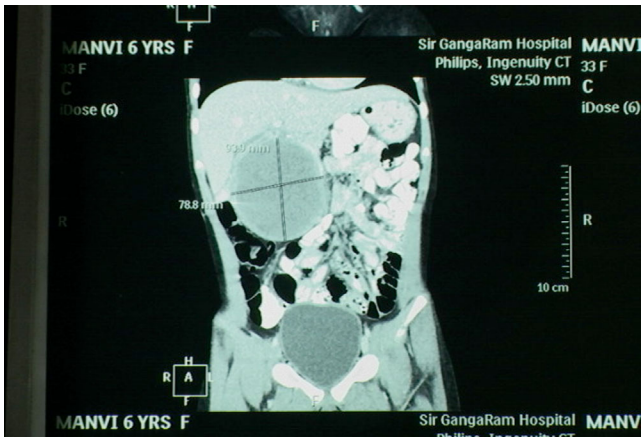
EP-512

CASE REPORT OF MALIGNANT SMALL ROUND CELL TUMOUR OF UNKNOWN HISTOGENESIS: A DIAGNOSTIC DILEMMA

S. Agarwal[1], D. Thakkar[1], D. Taringini[1], N.I.T.A. Radhakrishnan[1], A. Sachdeva[1]

[1]Pediatric Hematooncology, Sir Ganga Ram Hospital, Delhi, India

Objectives: Malignant small round cell tumors with extensive necrosis such that its histogenesis could not be delineated are rare lesions which have occasionally been reported from India. The exact incidence, etiology and histogenesis of such tumors are unknown because of its rarity
Methods: We report a patient of abdominal mass in whom despite a comprehensive evaluation no tumor defining histopathologic, immunocytochemical, ultrastructural, cytogenetic, features could be identified.
Results: A 6 years old female presented with fever- 6 days duration and a mass per abdomen-4 days with difficulty in breathing-1 day. USG showed a large retroperitoneal heterogeneous mass lesion with areas of hypoechogenicity suggestive of necrosis. CECT showed a hypo-dense mass in C loop of duodenum, head of the pancreas not defined from the lesion. For further evaluation PET scan was done, revealed a large lobulated FDG avid peripherally enhancing solid cystic mass lesion with hyper-dense areas suggestive of hemorrhage, abutting the liver, gall bladder and duodenum. She underwent exploratory laparotomy, frozen sections on histopathology were found to be necrosed and no viable tumor cells were available for reporting. Repeated attempts to obtain the tissue also revealed only necrotic tissue, which was verified at multiple centers in INDIA. IHC - low Ki 67 activity and negative for LCA, Synaptophysin, CD 99, MPO, CK and PLAP. She was given VAC regimen following which the tumor shrunk in size making it amenable for surgical resection. She underwent Whipple's procedure (Isolated loop) which again revealed extensive ischemic necrosis with outlines of round cell tumor. However the patient is stable without recurrence on 6 months of follow up.



Conclusions: This diagnostic nightmare due to non availability of viable tumour was a peculiar finding in our case. However she responded to standard treatment modality. The exact nature of the tumor is still a mystery and can be a spectrum of yet unidentified category of tumors.

EP-513

SYSTEMIC SYMPTOMS OF ANGIOMATOID FIBROUS HISTIOCYTOMA ARE CAUSED BY EWS-CREB1 FUSION-INDUCED EXCESSIVE IL-6 PRODUCTION

M. Akiyama[1], M. Yamaoka[1], J. Yoshizawa[2], M. Ikegami[3], K. Matsumoto[4]

[1]Pediatrics, The Jikei University School of Medicine, Tokyo, Japan; [2]Pediatric Surgery, The Jikei University School of Medicine, Tokyo, Japan; [3]Pathology, The Jikei University School of Medicine, Tokyo, Japan; [4]Allergy and Immunology, National Reserch Institute for Child Health and Development, Tokyo, Japan

Objectives: Angiomatoid fibrous histiocytoma (AFH), a rare soft tissue neoplasm with intermediate biologic potential, often arises in the extremities of children and young adults. However, the etiopathogenesis of AFH remains unclear. In this study we describe a 7-year-old Japanese female with a tumor of the left upper extremity which appeared on magnetic resonance imaging as a heterogenous lobulated mass (low intensity on T1-weighted images, high intensity on T2-weighted images, and low enhancement with contrast) measuring 55 x 41 x 28 mm. Moreover, the patient had systemic symptoms such as weight loss continued intermittent fever. Laboratory data showed anemia, thrombocytosis, and high level of inflammatory reactive markers. After complete resection of the tumor, both the patient's general condition and the laboratory data markedly improved. We studied the molecular etiopathogenesis of AFH.
Methods: The resected tumor was studied immunopathologically and molecular genetically. Blood samples obtained before and after the operation were subjected to cytokine analysis by using Bio-Plex multiplex assay (Bio-Rad laboratories).
Results: The tumor was diagnosed as an AFH on the basis of pathological findings and *EWS-CREB1* fusion gene detected with fluorescent in-situ hybridization and reverse-transcriptase polymerase chain reaction (RT-PCR). Direct sequencing of the RT-PCR-amplified product showed that exon 7 of the *EWS* gene was fused on exon 7 of the *CREB1* gene. The cytokine profiles of serum samples demonstrated postoperative decreases in interleukin-6 (IL-6), MIP-3a (CCL20) and the chemokine superfamily fractalkine. Immunopathological study showed that the resected AFH cells were positive for IL-6 and phosphorylated STAT3 (Tyr705).
Conclusions: The *EWS-CREB1* fusion gene leads to continuous activation of the *CREB1* gene, resulting in IL-6 production. Excessive production of IL-6 might play a pivotal role in the etiopathogenesis of AFH. Our results, therefore, provide the rationale for the development of IL-6 target therapies for AFH.

EP-514

OLFACTORY NEUROBLASTOMA IN CHILDHOOD

C. Akyuz[1], H. Susam Sen[1], B. Aydin[1], A. Varan[1], B. Yalcin[1], T. Kutluk[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: Olfactory neuroblastoma (estesioneuroblastoma) is a rare, slow growing and locally aggressive tumor derived from olfactory neuroepithelial tissue. Symptoms are not prominent before tumor reaching bigger size. Total surgical resection is the mainstay of the treatment. But literature supports the combined treatment approaches with surgery, neoadjuvant chemotherapy and radiotherapy. In this study, it was aimed to evaluate clinical characteristics and treatment results of patients diagnosed with olfactory neuroblastoma in our department.
Methods: Olfactory neuroblastoma (estesioneuroblastoma) is a rare, slow growing and locally aggressive tumor derived from olfactory neuroepithelial tissue. Symptoms are not prominent before tumor reaching bigger size. Total surgical resection is the mainstay of the treatment. But literature supports the combined treatment approaches with surgery, neoadjuvant chemotherapy and radiotherapy. In this study, it was aimed to evaluate clinical characteristics and treatment results of patients diagnosed with olfactory neuroblastoma in our department.
Results: Three patients aged 3, 9 and 13 were diagnosed as olfactory neuroblastoma. All had nasal obstruction at diagnosis. All three tumors were at sinonasal region. Bone destruction, intracranial or intraorbital extension was also present. Patients had stage III disease according to Kadish staging system. Endoscopic tumor excision was performed in 2 patients after neoadjuvant chemotherapy. First patients died due to metastatic disease. Second patient have been followed up in remission for 3 years. Third patient had craniotomy and partial tumor excision craniotomy adjuvant radiotherapy and chemotherapy for third patient; he has been followed up in remission for 6 years.
Conclusions: The best treatment approach is surgery in olfactory neuroblastoma however it is difficult to perform total resection because of the tumor localization. Literature supports the chemosensitivity of the tumor. Combining surgery with neoadjuvant chemotherapy and radiotherapy might increase the resectability and outcome.

EP-515

HISTIOCYTIC SARCOMA IN A 15 MONTHS-OLD FEMALE: A CASE REPORT

A. Bastandji[1], F. Bernard[2], M. Yaiche[1], N. Bouchair[1], S. Kharoubi[3], J. Donadieu[4], J.F. Emile[5]

[1]Clinique Médicale Infantile Ste Thérése, C.H.U Ibn Rochd Annaba, Algérie; [2]NBK Hospital, Koweit City, Koweit; [3]Service ORL CHU Dorban, Annaba, Algérie; [4]Service d'Hémato_oncologie Pédiatrique, Centre de référence des Histiocytoses, Hopital Trousseau Paris, France; [5]Service de Pathologie, Hôpital Universitaire Ambroise Paré, Paris, France

Objectives: Histiocytic sarcoma (HS) is an exceedingly rare tumor especially in children and an aggressive malignant neoplasm showing morphologic and immunophenotypic evidence of histiocytic differentiation. The vast majority of previously reported HSs are recognized to be initial misdiagnosis.
Methods: We describe a pediatric patient with HS who presented with lymphadenopathies and pulmonary nodules. Her tumor progressed during chemotherapy designed for Langerhans' cell histiocytosis (LCH) and sarcoma.
Results: A healthy 15 months-old female experienced isolated fibroelastic lymph nodes in the left inguinal region. Most lymph nodes measured less 10 mm, the largest measuring 27 by 21 mm. A biopsy was made and the results were suggestive of LCH. Node volume quickly increased and evolved to a large vascularized swelling bleeding on contact. LCH-based therapy was started. Because her condition was deteriorating a new biopsy was performed. Morphological and immunohistochemical alterations were compatible with HS. Immuno-phenotyping confirmed the histiocytic lineage by positive expressions of the CD 163, CD68 and lysozyme, and negative for CD1a, CD3, CD20, CD30, and Melan A, EMA, ALK. Chemotherapy according to MMT98 sarcoma protocol was started. Under treatment CT scan showed evolution with mediastinal lymph nodes and pulmonary nodules. Because of disease spread and poor response to therapy the patient received ICE chemotherapy. Condition deteriorated and the child died.
Conclusions: Few reports of bona fide HS exist, mostly involving adults. We describe an unusual clinical presentation. The diagnosis is mainly based on immunohistochemical techniques and on molecular genetic methods excluding other malignancies with epithelial, melanocytic and lymphoid phenotypes. Poor prognosis is a common finding (because of disease spread and poor response to therapy). We report a similar poor response to LCH- and sarcoma-based chemotherapy. The rarity of HS continues to make its management and recommended therapy challenging for young children.

EP-516

MALIGNANT SOLID TUMORS IN CHILDREN WITH DOWN SYNDROME: REPORT OF THREE CASES AND DISCUSSION

J.M. Eguiguren Leon[1], G. Sanchez[2], E. Villanueva[2], J. Acebo[2], E. Dueñas[2], M. Eguiguren[3], M. Egas[2], C. Vicuña[2]

[1]Pediatrics, Hospital Metropolitano y SOLCA Universidad San Francisco de Quito e Internacional del Ecuador, Quito, Ecuador; [2]Pediatrics, Hospital SOLCA Quito, Quito, Ecuador; [3]Pediatrics, St. Joseph's Children's Hospital, Paterson, USA

Objectives: Children with Down syndrome (DS) have decreased incidence of solid tumors. We report three patients, two with rhabdomyosarcoma and one with periosteal osteosarcoma.
Methods: Description of three recent cases with DS seen at SOLCA Hospital: AE, a 5 years-old male with trisomy 21 and metastatic embryonal rhabdomyosarcoma in relapse, refered from another hospital two years after diagnosis. He had a history of hematuria and a bladder tumor; received chemotherapy and relapsed during treatment. In our hospital we found pelvic and bladder tumors, pulmonary and hepatic metastasis. He received second-line chemotherapy, developed renal failure and tumor progression, and went into palliative care.

AM is an 18 moths-old male with DS and agenesis of the right kidney. He presented at 13 months of age with pedunculated perianal lesions, the largest was 9 x 6 cm in diameter. He also had inguinal metastasis. The biopsies confirmed an embryonal rhabdomyosarcoma. He is undergoing chemotherapy with frequent infectious complications. YN, 12 years-old female with DS and a 24 months history of a slowly growing left tibial mass. MRI of left leg showed a 13 x 5.4 cm tumor with soft tissue involvement. CT scan of thorax disclosed multiple metastasis. Bone biopsy was diagnostic of periosteal osteosarcoma. She received two cycles of cisplatin and doxorubicin with resolution of lung metastasis. Local therapy was not accepted by the parents and abandoned therapy.
Results: Occurrence of solid tumors, specifically rhabdomyosarcoma and osteosarcoma, is very unusual in patients with DS. Only few reports of embryonal and bone tumors have been recorded in the medical literature
Conclusions: It is speculated that tumor supressor genes, increased levels of S-100 b protein and decreased hormone and endostatin serum levels protect children with DS against solid tumors. Treatment related toxicity constitutes a formidable challenge in these cases.

EP-517

BILIARY RHABDOMYOSARCOMA, A RARE TUMOR IN CHILDHOOD - A CASE REPORT

D.G. Gasperini[1], R.Z.M. Silva[1], N.L.G. Suarez[1], C.E.B. Cavalcante[2], E.C.A. Silva[3], L.F. Lopes[4]

[1]Oncology pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Radiologist oncology pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [3]Pathologist oncology pediatric, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [4]Phd Medical Director, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil

Objectives: Rhabdomyosarcoma is a malignant tumor of mesenchymal origin, most often occurs in children and adolescents, corresponding to 4% of cancers in children. Common sites are the head and neck, genitourinary tract and retroperitoneum. Biliary location is rare (0.8%), but is the most common cause of malignant obstructive jaundice in this age group. The average age of presentation is 3 years. They can present obstructive jaundice in 60-80% of cases and they can be accompanied by fecal acholia and hepatomegaly. Pain, nausea, vomiting and fever are uncommon. The histology of the biliary tract is only the embryonic type. Current treatment includes surgical resection, radiotherapy and chemotherapy, usually a highly chemosensitive tumor and commonly used medications are: actinomycin, vincristine, cyclophosphamide or ifosfamide with or without doxorubicin.
Methods: Because of this rarity we report the case of a child, male, 2 years and 11 months old, who was admitted to abdominal distension, jaundice, acholic stools, choluria and hepatomegaly. With hyperbilirubinemia, elevated liver enzymes, negative hepatitis serology and normal Alpha-fetoprotein. Abdominal ultrasound and TC scan of the adbomen showed a large mass liver heterogeneous, well-defined limits, located on segments III, IVa, IVb, V and VIII, involving portals and hepatic vessels, causing mild dilatation of bile ducts, measuring 7.0 x 8 6 x 5.9 cm. Percutaneous biopsy and histological examination showed biliary embryonal rhabdomyosarcoma. Immunohistochemical examination positive vimentin, Alfa1T, S100, HHF35, desmin, myogenin and C99 confirmed the diagnosis.
Results: Chemotherapy with vincristine, dactinomycin and cyclophosphamide was made. After week 5 patient developed progression of disease, even with chemotherapy rescue with irinotecan and vincristine the tumor was refractory and the patient died.
Conclusions: In conclusion, our patient had an unfavorable outcome compared to the few reports in the literature.

EP-518

CERVICAL SPINE RHABDOID TUMOR: CASE REPORT AND LITERATURE REVIEW

I. Chabchoub[1], M. HAJ MANSOUR[1], A. Gargoura[1], F. Zairi[1], I. Ayadi[2], I. khanfir[2], N. Bouaouina[3], S. Ben Ahmed[1], H. krifa[4], M. Frikha[2]

[1]Medical Oncology, Farhat Hached, Sousse, Tunisia; [2]Medical Oncology, Habib Bourguiba, Sfax, Tunisia; [3]radiotherapy, Farhat Hached, Sousse, Tunisia; [4]neurosurgery, Sahloul, Sousse, Tunisia

Objectives: To report a retrospective case of an atypical spinal malignant rhabdoid tumor (MRT) in a 14 years old female.
Methods: A retrospective case report of spinal pediatric rhabdoid tumor (SPRT) in a 14 years old female with a family past history of a first degree consanguineous marriage.
Results: The patient presented first with cervicobrachial neuralgia that rapidly progressed into tetraparesis. The MRI showed a right latero-vertebral tumor localized in the right scalenus lodge at the level of C5, with vertebral invasion and spinal canal extension. Surgery was performed with residual disease. In immunohistochemistry, the tumor cells were positive for EMA, Pan CK, vimentin, CD99 and NSE, and negative for LCA, desmin and myogenin. INI1 was not practiced (not available). Despite postoperative radiotherapy followed by chemotherapy, we only obtained the stabilization of the tumor then the patient died 11 months after initial diagnosis.
Conclusions: The prognosis of PSRT remains poor. More cases are needed to determine effective treatment.

EP-519

SUCCESSFUL LONG-TERM USE OF SORAFENIB IN PROGRESSIVE PULMONARY METASTASES IN PEDIATRIC PAPILLARY THYROID CARCINOMA

S. Heine[1], N. Graf[1], T. Rohrer[2], N.N. N.N.[3]

[1]Dept. Pediatric Oncology/Hematology, University Children' s Hospital Pediatric Oncology, Homburg, Germany; [2]Dept. Pediatric Endocrinology, University Children' s Hospital Pediatric Oncology, Homburg, Germany; [3]Dept. Radiology, University Hospital Radiology, Homburg, Germany

Objectives: Sorafenib has been studied in adult patients with advanced thyroid cancer and prolonged their progressive-free survival. Reports on the use of this substance in the pediatric population are scarce. Our objective ist to present a young female with progressive pulmonary metastases due to RAI-resistant PTC who achieved stable disease with few side-effects with long-term use (3 years so far) of Sorafenib in the adult dose (2 x 400 mg).
Methods: A twelve year old female had been diagnosed with PTC 6 years previously. (TNM 2002) pT3N1bpM1 (pul). She underwent thyreoidectomy, neck dissection, and 8 courses of radioactive iodine, the final 3 courses after retinoids. But pulmonary metastases progressed, thyreoglobulin increased and signs of pulmonary insufficiency developed. Off-label use of Sorafenib was initiated in 5/2011, 200 mg once daily and step-wise increased to twice 400 mg after 6 months. Hematologic side-effects were minimal, also cutaneous side-effects were mild (grade 1 hand/foot syndrome). Due to cramping, diarrhea and weight loss, therapy was decreased to once daily 400 mg after a year and increased again to the full dose after 5 months. Therafter minor reductions of the dose were necessary for a further few months, but for one year now the patient has tolerated the full dose of 2 × 400 mg with hardly any side-effects. Thyrotropin-suppressive therapy, calcium and calcitriol therapy were continued as before.
Results: One month after initiation of sorafenib the extensive pulmonary metastases showed a mild reduction, therafter no futher decline was observed with MRI and CT, but also no progression. Thyreoglobulin levels and thyreoglobulin antibodies have remained elevated without significant decrease due to fluctuating values (thyreoglobulin 200 ng/ml-75 ng/ml).
Conclusions: In a case of pediatric PTC with progressive pulmonary metastases and no further RAI option Sorafenib can help to stabilize the disease and can be given in the adult dose of 2 x 400 mg without severe side-effects.

EP-520

CHILDREN WITH RET PROTOONCOGENE CODON 634 MUTATION

D. Ince[1], B. Kadioglu[2], E. Buke[3], Y. Oymak[2], H. Unver[4], O.Z. Karakus[5], F. Hazan[6], E. Ozer[7], K. Mutafoglu[3], N. Olgun[3]

[1]Pediatric Oncology, Dokuz Eylul University Institute of Oncology, Izmir, Turkey; [2]Pediatric Hematology&Oncology Clinic, Dr Behcet Uz Children Hospital, Izmir, Turkey; [3]Pediatric Oncology, Dokuz Eylul University Insitute of Oncology, Izmir, Turkey; [4]Pediatric Endocrinology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [5]Pediatric Surgery, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey; [6]Genetic, Dr Behcet Uz Children Hospital, Izmir, Turkey; [7]Pathology, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

Objectives: We would like to present our treatment experience in children with RET protooncogene codon 634 (c634) mutation.
Methods: Medical records of patient is summarized.
Results: A 7 years old female admitted to our center without any complaint. Her medical history was unremarkable. Her mother was 30 years old and had 3rd pregnancy. Mother had been diagnosed as medullary thyroid carcinoma (MTC), and treated six years ago. Heterozygous mutation of the RET proto-oncogene at c634 (c.1901 G>T) had been detected in her mother. There was no history of malignancy in mother's family. Her father and 9 years old sister were healthy. The RET protooncogene analysis was normal in 9 years old sister. The RET protooncogene analysis showed heterozygous mutation at c634 (c.1901 G>T) also in our patient. Physical examination was unremarkable. Thyroid ultrasonography revealed no abnormalities Thyroid function test resulted in normal fT3: 4,12pg/mL (2.5-3.9) fT4: 0.96pg/mL (0.50-1.51), TSH: 0.73(IU/mL (0.34-5.6). Serum levels of antimycrosomal and antithyroglobulin antibodies were normal (Anti-TPO: 0,2 IU/mL (0-35), Anti TG <0,9 IU/mL (0-40). Serum calcitonin level was found minimal elevated at two times (Calcitonin: 37.9 pg/mL, and 26,2 37.9 pg/mL (0-11.5). Parathormone (PTH: 52,4 pg/mL) and carcinoembrionic antigen (CEA:2,21 ng/mL) levels were normal. Prophylactic thyroidectomy and sampling of cervical lymph nodes were performed. Histopathologic examination of thyroid revealed hyperplasia in C cells, and examination of lymph nodes revealed reactive lymphadenopathy. There was no MTK.
Conclusions: The risk of MTC has been reported 100% through the life for patients who had RET proto-oncogene mutation, and prophylactic tyhroidectomy is proposed for these patients. It has been reported that particularly patients with c634 mutation had more risk for occurence

of metastatic and progressive/recurrent MTC, rather than patients who had c804, v618, c620 mutation. Prophylactic thyroidectomy and cervical lymph node dissection before 5-years-of-age should be proposed for patients with c634 mutation.

EP-521

PRIMARY PULMONARY PNET/EWING'S SARCOMA WITH ADRENAL METASTASIS

B. Jindal[1], B. Dubashi[2], B. Naredi[1], S. Raju[3], A. Ramesh[4], D. Halnayak[5]

[1]Department of Pediatric Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India; [2]Department of Medical Oncology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India; [3]Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India; [4]Department of Radiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India; [5]Department of Nuclear Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

Objectives: Extraskeletal Ewing sarcomas are exceptionally rare tumors and primaryextraskeletal Ewing sarcoma/PNET of the lung is even rarer and very few caseshave been reported in the literature. Retrospective study of extraosseous PNET from 2009-2013 and describe a case of primary pulmonary PNET lung with adrenal metastasisin an 11 year female child.
Methods: To study with the clinical, pathological and radiological profile of a primary pulmonary PNET and review the literature
Results: Of the total 5 cases of Extraosseous Ewing sarcoma, treated between 2009-2013 only one case of Primary pulmonary PNET was detected with adrenal and bony metastasis
Conclusions: Primary pulmonaryPNET is a very rare tumor with usually a very poor outcome especially in cases where it presents with metastasis and emphasises the importance of early evaluation of any metastasis.

EP-522

SURGERY OPTIONS AND RESULTS OF TREATMENT OF CHILDREN WITH SOLID PSEUDOPAPILLARY TUMORS OF THE PANCREAS

P. Kerimov[1], D. Rybakova[1], A. Kazantcev[1], M. Rubansky[1]

[1]Children Oncology, Federal State Budgetary Institution «N.N. Blokhin Russian Cancer Research Center» Under The Russian Academy of Medical Sciences, Moscow, Russia

Objectives: Solid pseudopapillary tumor (SPT) of the pancreas are rare neoplasms with low malignant potential, first described by Franz in 1933 and less than 3% of the tumors. It is extremely rare in children.
Methods: In scientific research institute of Children's oncology and hematology from 2005 to 2012 9 children with the diagnosis a solid pseudo-papillary tumor of a pancreas are operated. We analysed clinicodiagnostic data, operation volumes, and results of treatment and observation time.
Results: All patients were females age from 9 to 15 years (a median 13y.o.). As a rule, the disease is asymptomatic and discovered incidentally, but the two children experienced pain in the epigastric region, 1 patient had nausea and vomiting. According to the study at 4 patients the tumor was located in the tail of the pancreas, 2 - in the body, and 3 - in the head. The maximum size of the tumor was 8.3 × 7, 4 × 8, 5 cm and was located in the head of the pancreas. In 4 children underwent laparoscopic distal pancreatectomy, 2 - gastro-pancreatoduodenal resection, and 1 case performed distal subtotal resection of the pancreas, enucleation of the tumor resection wall duodenum, resection of the body of the pancreas. Complications occurred in 5 patients: in 2 cases - postoperative pancreatonecrosis, in the other - pancreatic fistula, bleeding from the pancreatic branch of the splenic artery and pneumonia. The observation period of the patients was from 1 month to 6 years. All patients are alive without evidence of disease recurrence.
Conclusions: Solid pseudopapillary tumor (SPT) of the pancreas is a rare disease in children, which usually occurs in females of pubertatny age. The main method of treatment is surgery, however there is a high risk of complications because of tumor localization.

EP-523

SURGICAL TREATMENT OF PANCREATIC TUMORS (ONE CENTRE EXPERIENCE)

I. Shchepotin[1], G. Klymnyuk[2], A. Lukashenko[1], A. Ijovskyi[2]
[1]Abdominal oncology, National Cancer Institute MPH of Ukraine, Kiev, Ukraine; [2]Pediatric Oncology, National Cancer Institute MPH of Ukraine, Kiev, Ukraine

Objectives: Solid pancreatic tumors are the rare pathology at the young age. The surgical treatment for this group of patients is technically complicated. A surgical treatment experience is not sufficiently advanced in a modern literature.
Methods: 10 patients (9 females and 1 male) were given the surgical treatment of pancreatic tumor for the last 15 years. The average age of patients was 10.7 years (children from 1 till 15 years old). The following operations were carried out: one patient received pancreatic tumor enucleation, two patients – splee-preserving distal pancreatomy, four patients – radical antegrade modular pancreatosplenectomy, one patient – radical antegrade modular pancreatosplenectomy with left adrenalectomy, two patients – pancreaticoduodenectomy with duct-to-mucosa pancreatojejunostomy and author's method of totally isolated Roux-en-Y pancreaticobiliary tract reconstruction with microjejunostomy and microgostomy (patient age was 1,10 year old).
Results: Pathology conclusion of operation materials shown as follows: in four cases tumor was verified as a solid pseudopapilloma pancreas cancer (all female patients), three cases - a malignant neuroendocrinological tumors (G3), one case - a malignant paraganglioma (G3), next one - as an adenocarcinoma and another one - as a mature teratoma with involving to a head of pancreas. The average time of surgery is 250 min., the average hemorrhage was 156 ml (max was 300 ml). During the postoperative period one patient had an abscess which was success treated via US drainage. Three patients have been treated with adjuvant chemotherapy. One patient died because of metastatic recurrent, nine patients - still alive, without signs of disease.
Conclusions: Surgical treatment of solid pancreatic tumors is a complicated method that provides long term survival.

EP-524

ALPHA-FETOPROTEIN PRODUCING RIGHT ADRENOCORTICAL ADENOMA IN A TEN-YEAR OLD BOY: CASE REPORT

M. Migita[1], T. Watanabe[1], K. Sato[1], M. Ono[1], M. Takahashi[1], M. Takahashi[1], T. Takezoe[1], T. Shimizu[1], Y. Fuchimoto[1], Y. Kanamori[1], T. Mori[2]

[1]Pediatric Surgery, National Center for Child Health and Development, Tokyo, Japan; [2]oncology, National Center for Child Health and Development, Tokyo, Japan

Objectives: We report a case of adrenocortical adenoma with an elevated level of serum alpha-fetoplotein (AFP)
Methods: Case report
Results: The patient was a ten-year-old male. He consulted a family doctor because of diarrhea and abdominal pain, and incidentally a right adrenal gland tumor was diagnosed by ultrasonography. He was referred to our hospital for further treatment. The adrenocortical function was normal by blood test, and all tumor markers were negative except for serum AFP (234 ng/ml). Abdominal CT showed the tumor mass in the right upper retroperitoneum. The size of the tumor was 36 x 48 x 52 mm with homogeneous texture (CT index was low, around 40-50). Radiological findings strongly suggested the tumor to be an adrenocortical carcinoma. The patient underwent right adrenectomy. No lymph node swelling around the tumor was detected. The final pathological diagnosis was adrenocortical adenoma. Serum AFP decreased to the normal level after the operation.
Conclusions: Adrenocortical tumor is rare in children. Furthermore AFP producing adrenal tumor was extremely rare, only one adult case had been reported before in English literature. This is a first pediatric case of AFP producing adrenocortical adenoma.

EP-525

MALIGNANT ATYPICAL RHABDOID TUMOR OF PELVIS: CURE IS STILL A DISTANT DREAM

R. Mohammed[1], C. Yogiraj[1], K. Satyendra[1], S. Arvind[1], M. B.K[1], Y. Satya Prakash[1]

[1]Pediatrics Hematology Oncolgy and BMT Unit, Fortis Memorial Research Institute, Gurgaon, India

Objectives: Extra renal extra cranial malignant rhabdoid tumor is highly lethal, rare tumor with poor prognosis with an incidence of 0.15 per million in children. No definite treatment has been defined. Here we describe course and outcome of malignant atypical rhabdoid tumor (MATRT) in a child.
Methods: A seven year old female was admitted with us in view of bleeding per vaginum for 2 weeks duration. Her rest general and systemic examination was normal. On further evaluationMRI of pelvis showed a mass of 65 x 43 x 45 mm in the pelvis without any metastasis, suggestive of rhabdomyosarcoma. Histopathological report of transrectal trucut biopsy of mass showed high grade poorly differentiated malignant tumor of pelvis. Immunohistochemical stains were positive for vimentin but negative for desmin and myogenin. Finally diagnosed as MATRT. A PET-CT scan showed an FDG avid heterogeneously enhancing cystic mass localized topelvis withno other FDG avid distal metastasis.
Results: Repeat MRI of whole abdomen with contrast after 6 weeks of VAC (Vincristine, Actinomycin and Cyclophosphamide) showed a mass of almost same size. She underwent surgery with gross total resection and colostomy. Histopathology and immunohistochemistry was compatible with viable MATRT (expressed EMA and vimentin but negative for desmin and myogenin). She received 6 courses of alternating VDC/IE chemotherapy (vincristine, doxorubicin, cyclophosphamide, ifosphamide, etoposide) with concomitant radiotherapy (50.4 Gy) after 3 courses of IE/VDC. Repeat MRI and PET scan showed no evidence of disease. After six cycles of mentioned chemotherapy, spino-meningeal relapsed occurred. She was given high dose methotrexate (5gm/m2) and cyclophosphamideto relieve her symptoms. She was planned for autologous stem cell transplant but finally died at home.
Conclusions: Cure is still a distant dream for ATRT. A newer and aggressive multimodality approach is required in near future to cure this fatal disease.

EP-526

NEONATAL SOLID TUMORS. 5 YEARS EXPERIENCE IN THE RICARDO GUTIERREZ CHILDREN HOSPITAL ONCOLOGY DEPARTMENT

M. Nana[1], M. Garcia Lombardi[1], R. Rohr[1], P. Robledo[1], D. Detoni[1], G. Rey[1]

[1]Oncology, Hospital de Niños R. Gutierrez, Ciudad Autónoma de Buenos Aire, Argentina

Objectives: Neonatal solid tumors (NST) are rare neoplasms in children: 0.5% to 2%. Their histology, low incidence, tumor behavior and response to treatment differ from tumors found in older children. To describe clinic and epidemiological features, histological type, treatment and outcome of NST.
Methods: Retrospective descriptive study of patients (p) with NST admitted in the Oncology Department of Ricardo Gutierrez Children Hospital between 2008 and 2014.
Results: n: 27 p, histology: benign 40% (11p), malignant 60% (16p). Prenatal ultrasound diagnosis 22% (6p). Signs and symptoms at birth: 26% (7p). Tumor types: neuroblastoma (NBT) 26% (7p), 4s 2p; low grade fibrosarcoma 3.5% (1p); myofibromatosis 7.5% (2p); retinoblastoma (RTB) 11% (3p), bilateral 2p; hepatoblastoma 3.5% (1p); mesoblastic nephroma 3.5% (1p); primitive neuroectodermic tumor 3.5% (1p); teratoma 19% (5p), 4 mature, in central nervous system (CNS) 1p, sacrococcigeal 3p; other CNS tumors: anaplastic ependymoma 1p, low grade glioma 3p, papyloma 1p; adrenocortical tumor 3.5% (1p). Diagnosis: 70% (19p) required biopsy; 4 NBT clinic and image diagnosis, all RTB with ocular fundus and 1 brainstem glioma with image. Metatatic at diagnosis: 15% (4p), 3 NBT and 1 myofibromatosis. Treatment: 44% (12p) received chemotherapy and 85% (23p) require surgery, 12p alone and the rest combined with other therapy. 2p with RTB received local radiotherapy. 63%% achieved complete remission. Only 1p relapsed (bilateral RTB). 4p (15%) died: 1 NBT due to surgery complication and the rest for tumor progression. Sequelae: 22% (6p)
Conclusions: The majority of p evaluated had malignant disease (the most frequent tumor type was NBT), a quarter of the p presented symptoms at birth and few prenatal diagnosis. The surgery was an important mainstay of treatment. High rate of complete remission was observed and low relapse rate and mortality. The data obtained were similar to those reported in the world literature.

EP-527

A NOVEL ALK REARRANGEMENT A2M-ALK IN A NEONATE WITH FETAL LUNG INTERSTITIAL TUMOR

T. Onoda[1], M. Kanno[1], H. Sato[1], N. Takahashi[1], H. Izumino[1], H. Ohta[2], T. Emura[2], H. Katoh[2], H. Ohizumi[2], H. Ohtake[3], H. Asao[4], L.P. Dehner[5], A.D. Hill[6], K. Hayasaka[1], T. Mitsui[1]

[1]Department of Pediatrics, Yamagata University Faculty of Medicine, Yamagata, Japan; [2]Second Department of Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan; [3]Department of Pathology, Yamagata University Faculty of Medicine, Yamagata, Japan; [4]Department of Immunology, Yamagata University Faculty of Medicine, Yamagata, Japan; [5]Department of Pathology and Immunology and Pathology in Pediatrics, Washington University in St. Louis, St. Louis, USA; [6]Division of Pathology, Children's National Medical Center, Washington DC, USA

Objectives: Fetal lung interstitial tumor (FLIT) is a recently-reported pathological type of congenital lung lesion comprising solid and cystic components. The pathological features include unique interstitial mesenchyme-based cell proliferation, and differ from other neoplasms represented by pleuropulmonary blastoma or congenital peribronchial myofibroblastic tumor. FLIT is extremely rare and its gene-expression profile has not yet been reported. Here we first report a novel chromosomal rearrangement resulting in (-2-macroglobulin (*A2M*) and anaplastic lymphoma kinase (*ALK*) gene fusion in a patient with FLIT.
Methods: Surgically-resected tumor specimen was reviewed pathoimmunohistochemically and examined to identify the tumour specific translocation using fluorescence *in situ* hybridization (FISH) and 5'-rapid amplification of cDNA ends (5'-RACE).
Results: The tumor cells contained the t (2;12) (p23;p13) translocation and were mesenchymal in origin (e.g., inflammatory myofibroblastic tumors), suggesting the involvement of *ALK* in this case of FLIT. Break-apart FISH demonstrated chromosomal rearrangement at *ALK* 2p23. Using 5'-RACE, we further identified a novel transcript fusing exon 22 of *A2M* to exon 19 of *ALK*. The corresponding chimeric gene was subsequently confirmed by sequencing, including the genomic breakpoint between intron 22 and 18 of *A2M* and *ALK*, respectively.
Conclusions: Discovery of *A2M* as a novel *ALK* fusion partner, together with the involvement of ALK, provides new insights into the pathogenesis of FLIT, and suggests the potential for new therapeutic strategies based on ALK inhibitors.

EP-528

EXTRARENAL RHABDOID TUMOR: "RARE BUT CLINICIANS SCARE"

S. Pai[1], S. Qureshi[2], N. Singhal[3], S. Banavali[1], M. Ramdwar[4], G. Chinnaswami[1], M. Prasad[1], T. Vora[1], B. Aurora[1], G. Narula[1]

[1]pediatric oncology, TATA Memorial Hospital, Mumbai, India; [2]pediatric surgical oncology, TATA Memorial Hospital, Mumbai, India; [3]surgical oncology, TATA Memorial Hospital, Mumbai, India; [4]Pathology, TATA Memorial Hospital, Mumbai, India

Objectives: Malignant rhabdoid tumors are rare. The central nervous system is the commonest extra renal site reported, while extra renal and extra cranial sites are extremely rare with few isolated case reports in literature. Keeping this scarcity of literature in to prospective we report our experience as a case series with an aim of providing greater insight in to management of this rare entity.
Methods: A retrospective audit of all the patients with histologically confirmed diagnosis of extrarenal rhabdoid tumor presenting to the pediatrics division of our hospital in the year 2013 was done. Only patients with complete follow up details and who were treated at our hospital were included in this review.
Results: There were 5 patients in our study, of which 3 were males and other 2 were females. The site of origin included axilla, cervicothoracic, liver and groin. All the patients were less than 10 year age at the time of diagnoses. Loss of INI1 was found in our all cases on IHC. Vincristine and Adriamycin based chemotherapy was given to all of our patients and was not found to be very effective. None of our patients benefitted from radiotherapy. Two of our patients had succumbed to their disease within 6 months of the diagnoses, while one patient had a recurrent disease at local site post treatment and died within 2 months of disease recurrence. Two of our patients are alive with disease and are on metronomic therapy.
Conclusions: Rarity of these tumors makes it impossible for any institute to gain solid experience and formulate management guidelines, thereby making it imperative for the clinicians to review the literature available in form of case series and derive appropriate inferences to guide treatment and improve the dismal prognosis of these rare but scary tumors.

EP-529

USE OF VANDETANIB IN METASTATIC MEDULLARY CARCINOMA OF THYROID IN A PAEDIATRIC PATIENT WITH MULTIPLE ENDOCRINE NEOPLASIA 2B

M. Ronghe[1], V. Narayanan[2], F. MacGregor[3], N. Bradshaw[4], R. Davidson[4], N. Reed[5], G. Shaikh[2]

[1]Paediatric Oncology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [2]Paediatric Endocrinology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [3]Paediatric ENT, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [4]Medical Genetics, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [5]Clinical Oncology, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom

Objectives: We aim to present the first case of a paediatric patient with multiple endocrine neoplasia (MEN) 2B and unresectable metastatic medullary carcinoma of thyroid (MTC) treated with vandetanib, together with a positive response to treatment. Vandetanib is a novel tyrosine kinase inhibitor selectively targets transfection (RET) gene, vascular endothelial growth-factor receptors 2 and 3, and epidermal growth-factor mediated signalling.
Methods: A 12 year old male presented with locally advanced and metastatic inoperable MTC associated with MEN2B. Genetic studies confirmed mutation of rearranged during transfection (RET) gene. He was started on vandetanib, 100 mg daily.
Results: He has demonstrated a good clinical response with a fall in calcitonin levels from 15,400 ng/l to 1,200 ng/l within 2 months and a reduction in size of the primary thyroid malignancy, lymph nodes and pulmonary metastases on repeat CT scan. He has now been on vandetanib for over 18 months with stable disease and calcitonin levels.
Conclusions: Vandetanib has a role in the treatment of patients including children with inoperable locally advanced and metastatic medullary carcinoma of thyroid. More information is needed on its use in children and long term outcome.

EP-530

NASOPHARYNGEAL CARCINOMA IN CHILDHOOD. REPORT OF THREE CASES AND DISCUSSION

G. Sánchez[1], J.M. Eguiguren[1], E. Villanueva[1], J. Acebo[1], A. Carrión[1], M. Egas[1], V. Vicuña[1]

[1]Pediatrics, SOLCA HOSPITAL, Quito, Ecuador

Objectives: During the past seven years we treated three adolescents with Nasopharyngeal Carcinoma (NPC) in the Service of Pediatric Oncology. This tumor is rare in children; therefore the management is derived from adult treatment protocols.
Methods: Review of medical records of three patients with NPC treated from 2007 to 2012 and analysis.
Results: A 17 years-old male presented with cervical pain, fever, weight lost and dysphagia. The CT scan reported a 7.3 cm mass obliterating 80% of the nasopharynx. A non-keratinizing NPC Stage III was diagnosed. He received Radiation therapy (RT) (66.6 Gy), chemotherapy with 5-fluorouracil and cisplatin. He relapsed after 5 years; received second line chemotherapy with gemcitabine and carboplatin and is in complete remission. The second

patient is a 16 years-old male who presented with weight loss, fever and bilateral cervical and supraclavicular lymphadenopathy. CT scan showed a mediastinal mass, initially misdiagnosed as germ cell tumor received BEP with excellent response; after pathological review a NPC Stage IV was confirmed and started 5-fluorouracil and cisplatin. He had progressive disease and a partial response was obtained with second-line chemotherapy. The third patient is 10 year-old male with a 5 months history of cervical lymphadenopathy and suspicion of tuberculosis. The biopsy reported NPC Stage III. He received radiotherapy 66.6 Gy, eight cycles of chemotherapy with 5-fluorouracil and cisplatin and remains in remission 8 months after completion of therapy. These results evidence male predominance, advance stages and systemic symptoms such as weight loss and fever. The diagnosis was established by lymph node biopsies. Initially, two patients had a complete response followed by relapse, the three patients are alive.
Conclusions: Nasopharyngeal carcinomas are rare in children. There is a male sex predominance, which cannot be completely explained by known risk factors. A cooperative study is needed in order to standardize the treatment options.

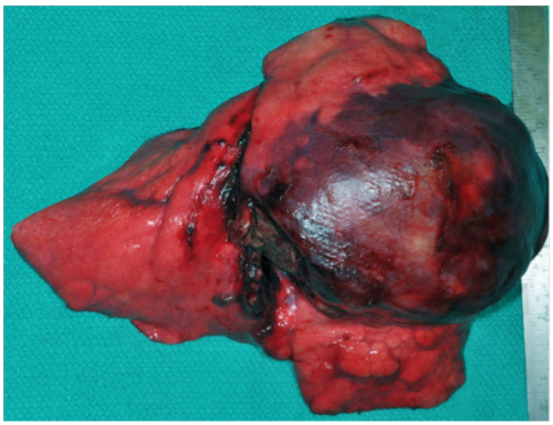
EP-531

MALIGNANT PLEURAL MESOTHELIOMA IN A CHILD

J. Scharf[1], G.M. Lees[1], C.M. Sergi[2]

[1]Surgery, University of Alberta, Edmonton, Canada; [2]Pathology, University of Alberta, Edmonton, Canada

Objectives: Herein, we describe successful treatment of malignant pleural mesothelioma in a child. There is a scarce body of literature pertaining to childhood mesothelioma, and most practices are guided by data from adult literature. Our objective is to add to the paediatric literature in order to improve outcomes in the treatment of the childhood entity.
Methods: An eight year old child found to have a right sided chest mass measuring roughly 11 x 8 x 8 cm is the basis of our report. After an inconclusive needle biopsy, an open lung biopsy was done. Unfortunately, frozen section specimens were inconclusive, and were further reviewed in Boston and Vancouver. A diagnosis of malignant pleural mesothelioma - epithelioid type - was made. We decided to surgically resect the tumour, and intra-operatively found that the tumour appeared to originate from the visceral pleura of the horizontal or oblique fissure. It extended into the lung parenchyma to involve all three lobes of the right lung. Right pneumonectomy was performed. Unfortunately, the child developed a right chest wall recurrence and the chest wall, including ribs four through eight were resected. Following surgery, the child underwent 8 cycles of chemotherapy with Pemetrexed and Cisplatin.



Results: The child is now 20 months from pneumonectomy and 14 months from chest wall excision. There appears to have been complete response to therapy with no definite recurrence of disease. Functionally, the child is well and able to attend school.
Conclusions: Childhood malignant pleural mesothelioma is an extremely rare tumour in the paediatric population that caries a dismal prognosis. Although additional work is needed to develop a standard of care for the disease, we have documented successful treatment with pneumonectomy followed by chest wall excision, and chemotherapy with Pemetrexed and Cisplatin.

EP-532

AMG 900, AN AURORA KINASES INHIBITOR, ENHANCES THE CHEMOSENSITIVITY TO TOPOISOMERASE II INHIBITORS AND MODULATES GENE EXPRESSION IN H295A ADRENOCORTICAL TUMOR CELL LINE

C.A. Scrideli[1], K.S. Borges[2], A.F. Andrade[2], V.S. Silveira[1], D.A. Marco Antonio[3], E.J.R. Vasconcelos[4], S.R.R. Antonini[5], C.E. Martinelli Jr[5], M. Castro[6], L.G. Tone[5], C.A. Scrideli[5]

[1]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [2]Genetics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [3]Bioinformatics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [4]Seatle Biomedical Research Institute, Seatle Biomedical Research Institute, Seatle, USA; [5]Pediatrics, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil; [6]Internal Medicine, Ribeirão Preto School of Medicine - University of São Paulo, Ribeirão Preto, Brazil

Objectives: Pediatric adrenocortical tumors (ACT) are rare malignancies and in advanced disease the treatment has a small impact on overall survival. Previous study from our group suggests that AURKA and AURKB overexpression in pediatric ACT may be related to more aggressive disease. These genes are involved in the maintenance of the genome integrity during cell cycle division and they have been considered as new targets to cancer treatment. The present study shows the results of the effects of the new aurora kinase inhibitor AMG 900, associated or not with standard chemotherapeutic agents, on adrenocortical carcinoma cell line H295A.
Methods: Cell proliferation was assessed by Giemsa staining and apoptosis was performed by flow cytometry. Drug combination analysis was made on the basis of Chou-Talalay method. Hormones dosage assay was performed to evaluate the effects of the aurora kinases inhibitor on hormone secretion. Microarray experiments were carried out using the Agilent Human microarray.
Results: Treatment with AMG 900 caused inhibition of proliferation, increased apoptosis and sensitized the cells to topoisomerase II inhibitors (doxorubicin and etoposide) whereas combination with cisplatin led to an antagonistic response. Additionally, the AMG 900 reduced hormone synthesis and modulated the expression of genes involved in this activity. Finally, aurora kinases inhibition altered the expression of genes associated with G1 cell cycle phase regulation and affected the Notch signaling pathway target genes.
Conclusions: These data suggest that aurora kinase inhibition by AMG 900 may be a new therapeutic approach to adrenocortical carcinoma treatment.

EP-533

EXTRA-CRANIAL MALIGNANT RHABDOID TUMOR IN CHILDREN: A SINGLE INSTITUTE EXPERIENCE

H.Y. Shin[1], C.R. Hong[1], H.J. Kang[1], H.Y. Ju[1], J.Y. Lee[1], H. Kim[1], K.D. Park[1], H.S. Ahn[1]

[1]Pediatrics, Seoul National University Children's Hospital, Seoul, Korea

Objectives: Malignant rhabdoid tumor (MRT) is a rare and highly aggressive tumor that affects young children. Due to its' extreme rarity, most of the available data is based on retrospective case series. To add to the current knowledge of this disease, we reviewed the patients treated for extra-cranial MRT in our institute.
Methods: A retrospective medical record review was done on children treated for pathologically confirmed extra-cranial MRT at Seoul National University Children's Hospital between January 2003 and May 2013.
Results: Eleven children (7 males, 4 females) were diagnosed with extra-cranial MRT at median age of 9 months old. Six patients (55%) had renal MRT, and 5 (45%) had soft tissue MRT in submental, paraspinal, retrosternal or coccygeal area. Ten patients were evaluated for loss of *INI1* and 9 patients (90%) had loss of *INI1* staining. The 1 patient whose specimen had retained *INI1* staining was showed late presentation during adolescence. Five patients (45%) had metastasis at diagnosis. The entire cohort (100%) received chemotherapy, and 4 patients (36%) underwent additional high dose chemotherapy with autologous stem cell rescue (HDCT & ASCR) with melphalan, etoposide, and carboplatin (MECb). Eight patients (73%) had surgery, and 6 patients (55%) received therapeutic radiotherapy. Five patients (45%) progressed or relapsed. The overall survival of the cohort was 51.9% with median follow-up duration of 17.8 months (range, 2.3 to 112.3 months), and the event free survival was 50.0% with median follow-up duration of 11.9 months (range, 0.9 to 112.3 months).
Conclusions: Extra-cranial MRT is still a highly aggressive tumor in young children. But the improved survival of our cohort is promising. Surgical resection, therapeutic radiotherapy, and HDCT & ASCR with MECb may be promising treatment options.

EP-534

COLORECTAL CARCINOMA IN CHILDREN AND ADOLESCENTS, SINGLE CENTER EXPERIENCE

D. Sumerauer[1], K. Svojgr[1], D. Kodetova[2], A. Puchmajerova[3], L. Pos[4], M. Kyncl[5], Z. Linke[6], M. Zapotocky[1], J. Stary[1]

[1]Department of Pediatric Hematology and Oncology, Faculty Hospital Motol, Prague 5, Czech Republic; [2]Department of Pathology and Molecular Medicine, Faculty Hospital Motol, Prague 5, Czech Republic; [3]Department of Biology and Medical Genetics, Faculty Hospital Motol, Prague 5, Czech Republic; [4]Department of Pediatric Surgery, Faculty Hospital Motol, Prague 5, Czech Republic; [5]Department of Radiology, Faculty Hospital Motol, Prague 5, Czech Republic; [6]Department of Oncology, Faculty Hospital Motol, Prague 5, Czech Republic

Objectives: Colorectal carcinoma (CRC) is one of the most common tumors in adults, but is extremely rare in childhood. This study retrospectively reports on a group of six patients <

18 years old, treated at the Department of Pediatric Hematology and Oncology, Prague, Czech Republic between 1993 and 2013.
Methods: There were 3 females and 3 males among the children/adolescents with CRC (median age 15.8 years, range 12.9-17.6), all had unfavorable CRC histiotypes (Signet cell or mucinous adenocarcinoma) and all had advanced disease (1x stage IIB, 1x stage IIIB, 4x stage IV) at the time of disease onset. Initial surgical resection was complete in 3/6 cases, 5 patients received postoperative chemotherapy (Xelox, Folfox) with/without targeted therapy. Tumor predisposition syndrome was confirmed in two patients (Lynch sy., CMMR-D sy.).
Results: Four patients had tumor progression or relapse and all died of their tumor, overall survival (OS) was 21% at 5 years. Two patients are alive, one with stage IIB CRC is a long term survivor, now over 19 years from the time of disease diagnosis.
Conclusions: This study confirms the rarity, advanced stage, aggressive biology and poor prognosis of CRC in children and adolescents, Surgery remains the mainstay of treatment, chemotherapy with targeted therapy had no impact on disease control in metastatic childhood CRC.
"Supported by the "Project for Conceptual Development of Research Organization 00064203"

EP-535

PEDIATRIC MALIGNANT SOLITARY FIBROUS TUMOR OF KIDNEY: CASE REPORT AND REVIEW OF THE LITERATURE

D. Tugcu[1], F. Akici[1], O.F. Atay[2], G. Aydogan[2], Z. Salcioglu[2], M. Gokce[2], G. Keskindemirci[2], H. Sen[2], U. Guvenc[3], S. Sander[3], S. Dervisoglu[4]

[1]Pediatric Hematology-Oncology, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey; [2]Pathhology, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey; [3]Pediatric Surgery, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey; [4]Pathology, Istanbul University Cerrahpasa Medical School, Istanbul, Turkey

Objectives: Renal solitary fibrous tumors are unusual spindle cell neoplasms orginating from mesenchymal cells and were orginally discovered in the pleura.
Methods: Ten year old male, previously healthy was admitted to our hospital with macroscobic hematuria and dysuria. He had low grade fever and abdominal pain, without palpable mass and normal blood pressure. Laboratory tests showed mildly elevated white blood cell count and normal renal function tests. Urine analysis showed numerous white and red blood cells, with normal culture results.
Results: Abdomen Ultrasonography revealed well-defined, lobulated soft tissue mass in the right kidney with hyperechoic appearance, measuring 40 × 42 mm. Enhanced CT scan of the abdomen revealed 40 × 42 mm, hyperdense mass, located within the pelvis of the right kidney with focal ectasia. The radical right nephrectomy was performed.
Macroscopically the specimen measured 7 × 6 × 5 cm, located in the pelvis with renal parenchymal infiltration, without hemorrhage and necrosis. Microscopically, the cells and nuclei were from round to oval to spindly, hyperchromatic with eosinophilic cytoplasma and mild coarse chromatin. Tumor cells frequently had mitoses 5–6 or more per 10 high power fields. Tumor was classified as malign group due to hypercellulerity, cytologic atypia and mytotic activity histopathologically. The neoplastic cells were diffusely positive for CD34 and vimentin. They showed rare positivity for SMA and were negative for bcl-2, S-100 protein, EMA, desmin, CD 68 and pancytoceratin. Nuclear positivity with Ki-67 was detected 3-25% of the cells.
Conclusions: After the total resection of the tumor, there wasn't any recurrence or metastasis within the 15 months follow-up without any chemotherapy. In our knowledge, this is the first reported case of malignant solitary fibrous tumor of the kidney in pediatric age. Further clinical trials are needed to follow-up the malignant forms of tumor and clarify the benefit of chemotherapy.

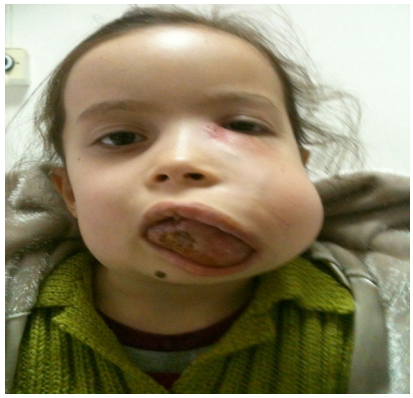
EP-536

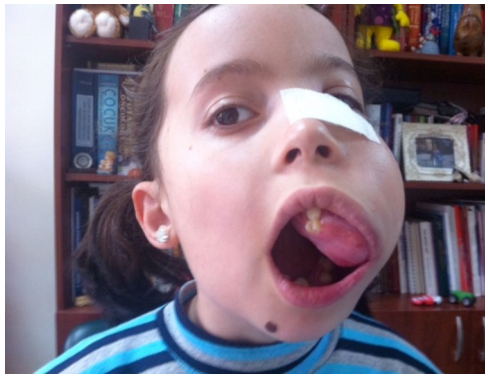
DENOSUMAB TREATMENT OF GIANT-CELL TUMOR OF MAXILLA IN A 9-YEAR-OLD GIRL

G. Yavuz[1], E. Unal Cabi[1], N. Tacyildiz[1], H. Dincaslan[1], E. Pekpak[1], B. Aksoy[1], M. Berberoglu[1], Z. Siklar[1], Z. Gordu[1], F. Asarcikli[1]

[1]Pediatric Hematology-Oncology, Ankara üniversity Faculty of Medicine, Ankara, Turkey

Objectives: Giant-cell tumor of bone (GCTB) is primarily seen in young adults and comprises 5% of primary bone tumors. GCT are rarely seen in childhood, only in 1.7%of all cases of GCTB. It is usually a benign tumor but frequently recurs locally after surgical resection. Metastatic disease at presentation is uncommon. A 9-year-old female presented in March 2010 with a facial mass causing a swelling on her left side. Family history revealed her father being diagnosed as GCTB at 7 years of age. Her brother, was diagnosed as GCT of maxilla at the age of 14, was successfully treated with intralesionar steroids and calcitonin in our center.
Methods: The patient was treated with intralesionar steroids and calcitonin, developed cellulitis, was hospitalized with broad spectrum antibiotics, surgical drainage and curettage. After she was discharged, she was lost to follow up for 3 years, finally she admitted in February 2013 with a left maxillary huge mass completely filling the oral cavity, dacryocystitis and fistula. She was put on subcutaneous IFN-Alpha2A 3million U/m2/d every other day and Imatinib mesylate 400mg/day orally. Two months later she was seen at outpatient clinic, maxillofacial surgeons performed intralesionar steroids/weekly, for a month then every other month. In May 2013, Denosumab treatment was planned because there was no satisfactory regression of the tumor. She was subsequently started on denosumab with induction dosing of 120mg subcutaneously/weekly for 3 weeks, followed by 120 mg denosumab subcutaenously per month.
Results: She is currently 10 months into treatment. The patient has required 4,000 IU/day of oral vitamin D and 40mg/kg/day elementary Calcium supplementation because of developing hypocalcemia from decreased bone turnover during her treatment, her most recent calcium level was 9.1mg/dl. The tumor showed shrinkage, the reconstructive surgery is planned.
Conclusions: She is the first pediatric patient treated with Denosumab for GCTB in Turkey.





EP-537

ARE THYROID CANCERS INCREASING IN YOUNG ADOLESCENTS

E. Unal Cabi[1], N. Tacyildiz[1], G. Yavuz[1], H. Dincaslan[1], G. Tanyildiz[1], M. Berberoglu[1], Z. Siklar[1], A.Y.D.I. Yagmurlu[1], E. Erden[1], M. Kir[1]

[1]Pediatric Hematology-Oncology, Ankara üniversity Faculty of Medicine, Ankara, Turkey

Objectives: We believe that the incidence of a rare tumor, differentiated thyroid cancers in children, are increasing following The Chernobyl Nuclear catastrophe. The most common presenting findings of thyroid cancers are thyroid nodules and cervical lymphadenopathy. Positive family history and neck irradiation are risk factors for development of thyroid carcinoma.
Methods: Between 1990- February 2104, 22 cases of thyroid carcinoma have been diagnosed. Sixteen were females, 6 were males with an age range of 15.8±3.2 years. One had cranial RT for ALL, one had neck irradiation because of HD, one patient who had lived in Kiev, had family history in both parents. Histopathologically 13 cases had differentiated papillary thyroid carcinoma, 7 had papillary thyroid variant, 1 follicular and 1 medullary thyroid carcinoma. In 3 of the cases thyroid nodules were
Results: Following surgery, there was lymph node infiltration in one case, whereas in one, there was distant - lung metastasis. Three patients experienced hypoparathyroidism, in one case there was vocal chord problems. All patients received adjuvant radioactive iodine therapy and were put on thyroid hormone replacement therapy. B-RAF 600 mutation studies were carried out in case of adding targeted therapy i.e sorafenib to metastatic recurrent cases. The patients are monitored by measuring serum human TG levels and by ultrasound for recurrences.
Conclusions: Although the treatment modality in children with thyroid cancers is still controversial, total thyroidectomy together with lymph node sampling / dissection represent

the dominant method of surgical treatment, enabling the success rate of RAI therapy and provide a longer disease free survival.

EP-538

AGGRESSIVE FIBROMATOSIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

A. Varan[1], C. Akyuz[1], B. Aydin[1], F. Yildiz[2], I. Barista[3], B. Yalcin[1], T. Kutluk[1]

[1]Dept. of Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey; [2]Dept. of Radiation Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey; [3]Dept. of Medical Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: To determine the clinical features and treatment results of children with aggressive fibromatosis treated in a single institution.
Methods: The records of11 patients with aggressive fibromatosis treated between 1972 and 2013 were analyzed retrospectively. Demographic characteristics and tumor locations were recorded. If possible, surgery was performed. Radiotherapy (RT) and/or chemotherapy were used for treatment. Tamoxifen, interferon, rocaltrol, vincristin+actinomycin-D+cyclophophamide+adriamycin, or vinblastine+methotrexate regimens were used according to relapsed or disease condition.
Results: There were three males and eight females with a median age of 8 years (range, 4-16 years). Tumors were located in the lower limb (n = 4), upper limb (n = 3), gluteal region (n = 3), and neck (n = 1). The largest tumor diameter ranged from 5 to 20 cm (median 14 cm). Five patients had undergone a subtotal resection at the time of diagnosis, while six had only undergone a biopsy. Seven patients who all had progressive disease were followed-up without any treatment after surgery. Two out of the 11 patients received RT, and they achieved stable disease without need for any further treatment. Two patients received RT and chemotherapy, one with rocaltrol and the other with tamoxifen+vincristin+actinomycin-D+cyclophophamide+adriamycin. These cases also had stable disease and did not require any further treatment. The patients who had progression after follow-up were treated with RT and/or chemotherapy. Three of them were only treated with RT, and one received RT and rocaltrol, two only received rocaltrol, and one received vinblastine+methotrexate. One patient treated with RT + rocaltrol and one with only tretaed with RT achieved stable disease, while another treated with RT alone developed progressive disease.
Conclusions: Agressive fibromatosis is a rare tumor, and treatment can be problematic. Although our series was small; we can conclude that RT may enable a stable disease course in some patients.

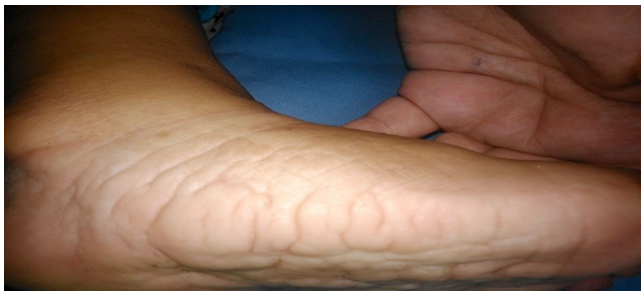
EP-539

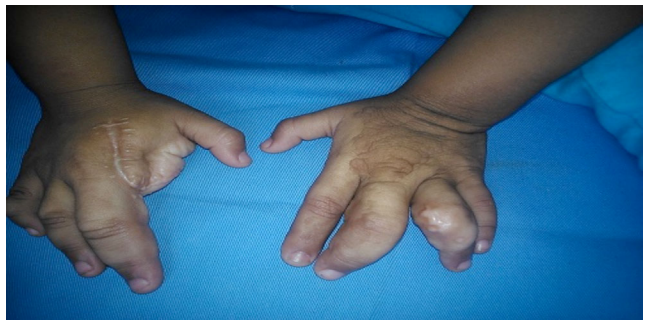
PARAOVARIAN ENDOMETROID CYSTOADENOCARCINOMA IN AN INFANT WITH PROTEUS SYNDROME: A CASE REPORT AND REVIEW OF LITERATURE

L. Vasquez[1], I. Maza[1], M. Oscanoa[1], J. Geronimo[1], M. Tello[1], A. Latorre[2]

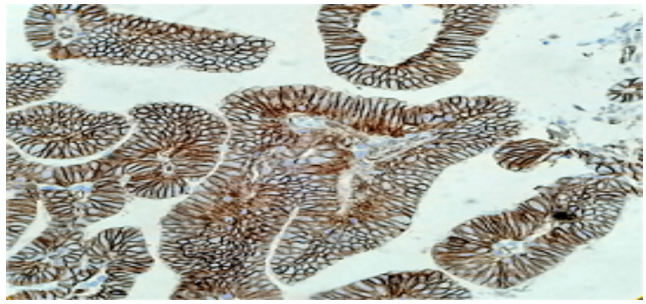
[1]Pediatric Oncology, Rebagliati Hospital, Lima, Peru; [2]Pathology, Rebagliati Hospital, Lima, Peru

Objectives: Ovarian and paraovarian malignant neoplasms are uncommon in children; mainly germ cell tumors and least frequently, epithelial tumors. There is an association between genital tract tumors and Proteus syndrome, a rare, sporadic ad progressive entity, characterized by a postnatal overgrowth of several tissues in a mosaic pattern caused by a mutation in the AKT gene.
Methods: We describe an infant with Proteus syndrome who developed a paraovarian cystoadenocarcinoma. Clinical presentation, histological features and clinical outcome were examined. A PubMed/Medline search was performed to collect all cases of adnexal masses in Proteus syndrome.
Results: A 20-month-old asymptomatic female with Proteus syndrome was diagnosed of an unilateral paraovarian mass in a routine ultrasound. Classical criteria for this syndrome like connective tissue nevus and disproportionate overgrowth of limbs and fingers was found.





There was no evidence of distant metastasis at onset. She underwent complete resection of the tumor, taking samples of omentum, lymph nodes and peritoneum. The pathology was an endometroid cystoadenocarcinoma, stage IC.



She received adjuvant chemotherapy with paclitaxel 175 mg/m2 in a 3h infusion at day 1, 8 and 15 and carboplatin AUC 6 at day 1, for 3 cycles with no evidence of disease after seven months of follow-up. A total of nine patients have been described with tumors of female tract and Proteus syndrome, which mostly includes bilateral ovarian cystoadenomas and other benign masses.
Conclusions: A paraovarian neoplasm is extremely rare in children and could be included as a criterion for Proteus syndrome. This is the youngest patient with this rare syndrome and a malignant adnexal tumor so far reported in the international literature. Staging and treatment of these tumors is not well standardized; however, most authors conclude that these neoplasms must be treated as their ovarian counterparts.

EP-540

SMALL CELL LUNG CANCER IN A 13-YEAR-OLD MALE

M. Yano[1], M. Hebiguchi[1], K. Kodama[1], T. Takahashi[1]

[1]Department of Pediatrics, Akita University Hospital, Akita, Japan

Objectives: Small cell lung cancer (SCLC) is exceedingly rare in children.
Methods: We herein report a pediatric case of extensive-stage SCLC.
Results: A 13-year-old male was admitted to our department with a three-month history of cough. Thoracic CT and MRI showed two large masses, one was a 5.8 × 4.3 × 3.9 cm primary tumor close to the right middle lobe bronchus, and the other was a 2.8 × 4.0 × 4.5 cm subcarinal lymph node. Systemic PET-CT revealed multiple bone metastases. In the serological analyses, the levels of pro-gastrin releasing peptide (pro-GRP) and neuron-specific enolase were high, at 4,075 pg/mL (normal, ≤ 81 pg/mL) and 52.3 ng/mL (normal, ≤ 16.3 ng/mL), respectively. We diagnosed the patient with SCLC based on the histopathological findings of biopsy specimens which were obtained endoscopically from the tumor partially exposed on the bronchial wall. We started treating him with cisplatin and irinotecan (PI), because this combination therapy is one of the recommended regimen for adult patients. After the first course of PI combination therapy, there was both a reduction in the tumor volume and a decrease in the levels of some biomarkers. Therefore, we plan to administer several courses of PI therapy.
Conclusions: The long-term prognosis of adult SCLC patients is generally poor, even if desirable initial treatment responses are obtained. In order to improve their prognosis, new trials with other anti-cancer agents, such as topotecan and amrubicin, should be performed. Bevacizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody which is effective against non-SCLC, is an intriguing candidate molecular target drug that should be evaluated for SCLC. Because the value of VEGF in the present patient's plasma was high, we consider that early administration of bevacizumab in combination with the effective PI therapy may be an intense treatment for the patient, and may improve his prognosis.

EP-541

A PEDIATRIC NEUROENDOCRINE TUMOR WITH HEPATIC METASTASES

S. Yesil[1], C. Bozkurt[1], G. Tanyildiz[1], H. Kirimlioglu[2], S. Tekgunduz[1], O. Candir[1], G. Sahin[1]

[1]Pediatric Oncology, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey; [2]Pathology, University of Acibadem, Istanbul, Turkey

Objectives: Neuroendocrine tumors (NETs) are heterogeneous group of malignancies that arise from neuroendocrine system. NETs in pediatric population are extremely rare and primarily involve the gastrointestinal tract and lungs. These tumors can be either non-functioning tumors with symptoms related to mass effects and malignant tumor disease or functioning tumors with specific hormones secreted to induce specific clinical syndromes. Although the majority of tumors are malignant, they are relatively slow-growing neoplasms and most of NETs classified as well-differentiated tumors due to tumor's histology. Metastatic tumors are more frequent than localized NETs and often they present with liver metastasis. In this paper we aimed to present a pediatric NET with hepatic metastases at initial diagnosis.
Methods: Thirteen years old male admitted with the complaint of abdominal pain. On physical examination he had erythematous eruption on the face, neck and trunk. Also he had epigastric mass. Radiological examinations revealed solid masses in all segments of the liver which had cystic and necrotic components. Pathological report of tru-cut biopsy of liver revealed diagnosis of well-differentiated neuroendocrine tumor, WHO Grade 2. The level of 5-hydroxyindoleacetic acid in 24-hour urine collection was elevated. Gastrointestinal system endoscopy and biopsies were normal. Somatostatin receptor scintigraphy revealed only the liver lesions. Octreotide and everolimus treatment were given for one year. Severe tricuspid valve regurgitation developed and treatment was discontinued. Somatostatin receptor-targeted radionuclide therapy administered two months ago and any side effects were observed.
Results: Systemic treatment options for a child with neuroendocrine liver metastases who is not a candidate for surgical resection were rather limited. Our patients' symptoms resolved and liver lesions regressed with the combination of somatostatin analogs and everolimus. But we had to terminate this therapy because of severe cardiac side effects due to everolimus.
Conclusions: Somatostatin receptor-targeted radionuclide therapy offers a promising treatment option for NETs in children.

EP-542

MANAGEMENT CHALLENGES IN A YOUNG CHILD WITH THREE CO-EXISTING TUMORS: A COMPLEX CASE OF LI-FRAUMENI SYNDROME

A. Zanette[1], D. DeAngelis[2], T. Gerstle[3], G. Somers[4], D. Malkin[1]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Opthalmology, The Hospital for Sick Children, Toronto, Canada; [3]General Surgery, The Hospital for Sick Children, Toronto, Canada; [4]Pediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, Canada

Objectives: Li-Fraumeni-Syndrome (LFS) is an autosomal dominantly inherited cancer predisposition syndrome associated with heterozygous germline mutations in the *TP53* gene. LFS-related cancers generally occur in children or young adults and survivors have an 80-fold increased risk for multiple primary cancers. Knowledge of the genetic status of the *TP53* gene in these patients is critical not only due to the increased risk of malignancies, but also because of the therapeutic implications, since a higher rate of radiation-induced secondary tumours in these patients has been observed.
Methods: We describe a 2 year old child with LFS harbouring a maternally inherited heterozygous *TP53* germline mutation (Glu294fs). who was affected by three synchronous malignancies at the age of 2: an anaplastic alveolar rhabdomyosarcoma (RMS) of the right orbit (diagnosed at age 19 mnths), right adrenocortical carcinoma (ACC) (at age 27 mths) and a right orbit low grade osteosarcoma (OS) (at age 28 mths). Radiological treatments and a surveillance program were adjusted according to recommendations for LFS patients.
Results: He was treated as per Children's Oncology Group (COG) protocol ARST0331 for the RMS. In order to avoid radiation, local control was achieved by an orbital exonteration. During routine LFS surveillance, the ACC and orbital low grade osteosarcoma were diagnosed. Following two cycles of chemotherapy/mitotane as per COG ARAR0332, complete resection of the ACC was achieved. Optimal management strategy of the OS is being evaluated.
Conclusions: Management of tumour treatment options for patients with LFS is complex due to both theoretic and actual risks of treatment-related and de novo secondary tumors. The concurrent presentation of three distinct cancers in our case highlights the challenges of management, the potential for development of cancers even while on therapy, and the importance of surveillance imaging for presymptomatic tumor detection.

EP-543

DESMOPLASTIC SMALL ROUND CELL TUMOR: A CASE REPORT

D. Thakkar[1], N. Radhakrishnan[1], M. Kalra[1], S. Agarwal[1], D. Tarangini[1], A. Sachdeva[1]

[1]Pediatric Hematology-Oncology and BMT Unit, Sir Ganga Ram Hospital, New Delhi, India

Objectives: Desmoplastic Small Round Cell Tumor (DSRCT) is a rare disease in all age groups. Less than 200 cases have been reported worldwide till now. Presentation in infancy is rare. Because of the rarity of this disease, little is known about optimal treatment and outcome. We try to present our findings of the course of the illness of a patient diagnosed with DSRCT at our institute.
Methods: A step wise approach to identify the etiology of the illness was adopted for the patient who presented with symptoms of abdominal distension.
Results: An 8 months old male child, presented with progressively increasing abdominal distension since 1 month. There was no history of altered bowel habits, fever, bleeding, jaundice, loss of weight or hematuria. His β-HCG and AFP levels were normal. CT Scan revealed a retroperitoneal large heterogeneous soft tissue mass lesion. Subsequently, biopsy was done which revealed malignant small round cell tumour (SRCT) but the exact nature of the disease could not be delineated. In view of lack of specific diagnosis, a repeat biopsy was done which showed a malignant round cell tumor with expression of Mic 2, epithelioid markers Cytokeratin, EMA (focal) and an occasional cell expressing desmin. Also, the tumor cells were immunonegative for Synaptophysin, WT-1, LCA and Myogenin, thus confirming it to be DSRCT. After the diagnosis, the child was given Inj Vincristine, Cyclophosphamide and Doxorubicin. However, the response could not be assessed as the parents abandoned treatment post 2 cycles of chemotherapy for the lack of resources.
Conclusions: DSRCT is a rare tumor that requires a high index of suspicion and multidisciplinary approach. Inspite of rarity of the occurrence of such tumors, DSRTC should be kept in mind as a differential diagnosis in an infant presenting with intra-abdominal mass.

RENAL TUMOURS

EP-544

THE PROGNOSTIC SIGNIFICANCE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) EXPRESSION IN WILMS' TUMOR AND ITS RELEVANCE TO WT1 EXPRESSION

D. Abdallah[1], E. Abdelzaher[1], G. Khedr[2], H. Elleithy[2]

[1]Pathology, Alexandria Faculty of Medicine, Alexandria, Egypt; [2]Oncology, Alexandria Faculty of Medicine, Alexandria, Egypt

Objectives: Angiogenesis plays an important role in wilms tumor progression and metastatic spread. Vascular endothelial growth factor (VEGF) is an angiogenic factor found in genitourinary neoplasms. VEGF is a direct, WT1 target gene.
Methods: VEGF and WT1 expression was determined immunohistochemically in 30 Wilms' tumor specimens
Results: All cases (100%) expressed VEGF and WT1. A significant positive correlation was detected between WT1 and VEGF expression and a significant negative correlation was detected between WT1 expression and tumor stage. A significant association was found between poor outcome on one hand and advanced tumor stage and high risk pathological group on the other hand.
Conclusions: WT1 expression, advanced tumor stage and high risk pathological group are poor prognostic factors in Wilms' tumor. VEGF and WT1 significant positive correlation implicate them in tumorogenesis and further support the postulated regulatory influence of VEGF over WT1 expression.

EP-545

NEPHROBLASTOMA INFILTERATION OF TRICUSPID VALVE IN A 4 YR OLD BOY

O.A. Adewuyi[1], S. Mda[1], T. Kyaw[2]

[1]Paediatrics, Medunsa, Pretoria, South Africa; [2]Virology, Medunsa, Pretoria, South Africa

Introduction
Nephroblastoma is the commonest childhood renal cancer and its spread into the heart without pulmonary involvement is unusual.
Methods: A 4yr old male referred with a 2 month history of dyspnoea, progressive abdominal mass, weight loss, anorexia and weakness. No cough or contact with Tb patients. On examination, no dysmorphism, has wasting of muscles with stunted growth (WHZ, HAZ <-2). Dyspnoeic and tachypnoeic, (RR = 48/min), pallor, mild dehydrated, had generalized lymphadenopathy, no splinter haemorrhage; Normal eyes. Temperature 37.2°C, BP 114/74mmHg, HR142/min. There was ascites as well as hepatomegaly (4 cm) with a hard mass in right lumber region crossing the midline and extending superiorly to the right hemi thorax. Normal bowel sound. Apex beat was located at 5th ICS anterior axillary line. PSM 4/6 was audible at LLSB.CXR showed cardiomegaly with >65% cardio-thoracic ratio. Right lower lobe collapse of the lung was also noted. Echocardiogram detected the presence of tricuspid vegetation which extends to the pulmonary valve area. Haematuria (3+) and proteinuria (2+) observed on urine dipsticks. Blood culture for bacteria was negative. Haemoglobin was 7.6 g/dl and ALT was normal (28u/l). Blood urea and creatinine were normal (1.3mmol/l and 26 μmol/l respectively). LDH level was high (3216 u/l). VMA, HVA and NSE were negative. MIBG was negative. CT abdomen revealed a huge right renal mass invading inferior vena cava and Para aortic lymph nodes. Stage IV nephroblastoma diagnosed with tricuspid valve involvement and heart failure. He had pre-op chemotherapy, nephrectomy and got post-op chemo and radiotherapy. Valvular lesions regressed with residual tumor which was planned to be removed by cardiothoracic surgical unit but he collapsed and died while awaiting cardiac operation.

Results: see images
Conclusions: The prognosis of nephroblastoma with cardiac involvement in children appears to be altered negatively especially in poor resource countries.

EP-546

CAN IMPLEMENTATION OF STRONG SOCIAL SUPPORT IMPROVE SURVIVAL OF RENAL TUMORS IN A DEVELOPING COUNTRY? CHILDREN'S HOSPITAL LAHORE EXPERIENCE

A. Ahmad[1], N. Asghar[1], A.W. Rathore[1], M. Faizan[1], S. Mahmood[2], M. Sheikh[3]

[1]Paediatric Oncology, Children's Hospital & ICH, Lahore, Pakistan; [2]Paediatric Surgery, Jinnah Hospital Lahore, Lahore, Pakistan; [3]Paediatric Surgery, Children's Hospital & ICH, Lahore, Pakistan

Objectives: Children's Hospital Lahore is a tertiary government centre receiving over 500 new cancer patients from all over Pakistan and across the border per year. The purpose of this study was to analyze management and outcome of children with renal tumors and to discuss the role of effective social support in improving the survival of these patients.
Methods: Retrospective review of 120 patients enrolled between January 2011-January 2014 was done. Data regarding their age, stage, histopathology, risk stratification, treatment, outcome and impact of social support was analyzed. Patients were treated according to UKCCSG WT 2001 02 protocol.
Results: Total 120 patients with age ranging from < 1 to 10 years (mean age = 3.43) were included. M: F Ratio was 1:1. 101/120 (93%) presented with advanced stage,43/120 (36%) stage IV and 68/120 (57%) stage III and only 9/120 (7%) stage II (p-value = 0.014).105/120 (87%) wilm tumor, 8/120 (7%) CCS, 6/120 (5%) had Round blue cell tumor. Total 50/120 ((42%) have completed treatment, 27/120 (23%) are on treatment, 21/120 (17%) got LAMA and 14/120 (12%) expired due to metastatic and progressive disease. 67/120 (56%) received preoperative chemotherapy and 36/120 (30%) had upfront nephrectomy done and 17/120 (14%) are on preoperative chemotherapy. Four patients (3%) relapsed during their course of therapy. 92/120 (77%) travelled >100 km for day care visits.68/120 (57%) fathers had monthly income <100USD (p-value = 0.050). 75/120 (64%) of moms have had only primary education.67/120 (58%) patients had malnutrition (p-value = 0.013). By providing more social support and patient tracking system LAMA rate decreased from 27% to 17% and treated patients increased from 37% to 42% (comparing the SIOP DATA 2012- PUB 406).
Conclusions: Survival of these patients can be significantly improved by strengthening the social support services and public awareness to seek early and complete treatment. Mortality of 12% can be reduced by early diagnosis and treatment and effective infection control practices. The abandonment rate can be decreased by efficient tracking and follow-up services in the day care center.

EP-547

GROWTH RATE OF RENAL TUMORS IN INFANTS

I. Begun[1], I. Papkevich[1]

[1]Functional Diagnostics, Belarusian Research Center for Pediatric Oncology Hematology and Immunolog, Minsk region, Belarus

Objectives: To establish the growth rates of malignant kidney tumors in infants.
Methods: The twenty infants were surveyed (median age 7.6 months) with malignant tumors of the kidney (established prospectively: nephroblastoma -17, rhabdoid tumor-2, sarcoma-1). The prenatal diagnosis in terms of 32-37 weeks of gestation in fetus and ultrasonography in infants with suspected malignant tumor of the kidney were completed.
Results: There were no patients diagnosed with a kidney tumor by the prenatal diagnosis data. Nevertheless postnatal volume of the tumor was 317 ml (218-498 ml) at the primary diagnosis time point. How can we explain this? Established volume of the tumor 317 ml consists of 30 embryonic of doublings. According to the published data the rate doubling of cell culture of nephroblastoma have 7-8 days. Hence, fetal tumor growth of the visual-detectable volume beginning at 1 ml can be formed during 210-240 days (30.0-34.3 weeks). Given the start time favorite of the excretory system, we can determine the gestational age visualization reference between 33.5-37.8 weeks. However, controversy this findings, we found that in the group of sick infants the tumor grew at least for 2.3-3.5 months, but at different speed. So, the number of doublings for all stages of the tumor was 8.30 (7.70-8.68). But in infants with III-IV stages of disease the doubling time of the tumor was 11.19 days (10.24-23.91) and age of 93 (91-132 days)) that is much less than those in group I-II, V stages (31.42 (24.83-38.11) and 231 (185-303) days) (p <0,05).
Conclusions: The natural history of tumor growth remains poorly understood. It is not possible or possible in isolated cases only to continuously track down the growth of native human tumors. Received data have required to study the pathophysiological aspects of tumor growth and establishment of the screening intervals of ultrasonic testing in infants.

EP-548

APPRAISAL OF EFFECTS OF APPLYING UH-1 CHEMOTHERAPY REGIMENT TO PEDIATRIC TOUGH WILMS TUMOR

Y. Cao[1], J.I.E. Yan[1], H. Wang[1]

[1]Padiatric Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

Objectives: The preliminary effects of applying COG UH-1 chemotherapy regiment to pediatric tough Wilms Tumor in our hospital in recent years were summarized and analyzed.
Methods: In reference to NWTSG standard diagnosis synthetic appraisal by stage and texture pathologicalpattern, preliminary summary and analysis were done of applying COG UH-1 chemotherapy regiment and synthetic radioactive therapy to tough children Wilms' Tumor in our hospital between April 2009 and May 2013.
Results: All the patients who have been kept contact for 5 to 43 months were all survived. The overall survival (OS) rate and disease-free survival rate (DFS) were 100% and 87.5%, respectively. No serious reaction occurred except acute myelosuppression. In comparison with the previous 3-year overall survival rate and 3-year disease-free survival of treatment IV stage of metastasis or recurrent Wilms Tumor, 37.5% and 12.5%, respectively, the 3-year OS and DFS of unfavourable prognosis pathological pattern (UFH+CCSK+RTK) were 77.27% and 59.08%.
Conclusions: Applying UH-1 chemotherapy regiment to pediatric tough Wilms Tumor is safe and significantly effective.

EP-549

MULTILOCULAR CYSTIC NEPHROMA: A RARE BENIGN RENAL NEOPLASM

L. Chen[1], Z. Ling[2], W. Xu[2], G. Wang[2], K. Dong[3]

[1]Pathology, Children's Hospital of Fudan University, Shanghai, China; [2]Department of Urology, Zhongshan Hospital Fudan University, Shanghai, China; [3]Department of Surgery, Children's Hospital ofl Fudan University, Shanghai, China

Objectives: Multilocular cystic nephroma (MLCN) is a relatively rare, benign tumor of uncertain etiology. we have increased the awareness of this type of renal tumor.
Methods: Two 2-year-old children who underwent radical nephrectomy due to left renal mass were presented. The characteristic of imaging, histopathological features, differential diagnosis, and treatment alternatives were discused.
Results: CT scan revealed a well-defined circumscribed exophytic mass consisting cystic elements and contrast holding septations, arising from outer border of left kidney.A radical nephrectomy has been finally performed. On microscopic examination, the cysts are lined by cuboidal epithelial cells arranged in a hobnailed pattern, and they were separated by cellular spindle cell stroma. No adjunct therapy was administered. In our follow-up, the patients were completely asymptomatic and free of recurrence and metastasis.
Conclusions: Most MLCNs have been managed by radical nephrectomy due to the suspicion of renal cell carcinoma, such as in our case. But nephron-sparing surgery should be kept in mind if the mass is solitary, localized, unilateral, and smaller than 4 cm. Also, nephron-sparing surgery becomes more important for the patients who have solitary kidney or contralateral renal pathology.

EP-550

WILMS TUMOUR: A SINGLE CENTRE STUDY IN SINGAPORE

K.T. D[1], M.Y. Chan[1], A.M. Tan[1], S.Y. Soh[1]

[1]Paediatric Haematology and Oncology, KK Women's and Children's hospital, Singapore, Singapore

Objectives: Wilms tumour is the most common malignant renal tumour in childhood. We retrospectively reviewed clinical profile and outcome of Wilms tumour cases in KK women's and Children's hospital (KKH), Singapore.
Methods: The study was approved by Singhealth Centralized Institutional Review Board. We included all patients with malignant renal tumours seen at KKH from 1997 to 2012 (16 years).
Results: There were 21 patients with Wilms tumour in the study period. There were eight males and 13 females; male:female ratio was 1:1.6. The median age at diagnosis was 3.3 years (range 0.25 to 10.8 years). Abdominal mass was the most common presentation (n = 16, 76%), either isolated or together with other symptoms such as abdominal pain, fever, poor feeding, vomiting, hypertension and haematuria. One patient had hypospadias and bilateral cryptorchidism. Two presented with gross painless haematuria only. Two patients had tumour diagnosed on screening – one had underlying aniridia; the other had hemihypertrophy with umbilical hernia. Another child was diagnosed incidentally during workup for diabetic ketoacidosis and fever. All had unilateral disease. One patient had nephroblastomatosis on contralateral kidney. The staging according to NWTS was: seven (33%) stage I, five (24%) stage II, seven (33%) stage III and two (10%) stage IV (with lung metastasis). All were treated by NWTS protocol except one with SIOP. One patient had unfavourable histology (diffuse anaplasia). Median follow up time was 4.7 years. All were alive with no disease recurrence.
Conclusions: Abdominal mass was the most common presentation seen in spectrum of presentation. The survival outcome was excellent even in stage IV disease. Multidisciplinary treatment with standardization of protocol is vital for optimal care.

EP-551

MALIGNANT RHABDOID TUMORS IN CHILDHOOD: REPORT OF 15 CASES TREATED AT A SINGLE INSTITUTION

C. Duan[1], X.L. Ma[1], M. Jin[1], D.W. Zhang[1]

[1]*Heamatology/Oncology, Beijing Children's Hospital, Beijing, China*

Objectives: Malignant rhabdoid tumors (MRTs) are rare high-grade malignancies in the renal or extrarenal organs. MRTs of the extrarenal organs mostly affect the liver, central nervous system, pelvis, soft tissue, and intra-abdominal cavity. The treatment of patients with non-Wilms renal tumors remains challenging.
Methods: Between 2006 and 2014, 15 children with MRTs, aged 9 month to 8 years, were diagnosed at a single institution.
Results: 10 patients were diagnosed as renal MRTs. 5 patient were diagnosed as extrarenal MRTs, including 1 patient of central nervous system MRT, 3 patiens of intra-abdominal cavity MRT and 1 patient of soft tissue MRT. The follow-up time was 1 month to 3.5 years, and the median follow-up time was 6 month. Seven of these patients subsequently received radiotherapy. During follow-up, 9 patients had recurrence of the tumor within 4month to 3.5 years, 6 patients died of progressive disease and one died of operative mortality. The median survival time of all patients was 11 months. One 1 year old male with recurrent soft tissue MRT received aggressive chemotherapy and radiotherapy, and his disease remained stable for 14 month.
Conclusions: Malignant rhabdoid tumors (MRTs) are rare malignant tumors with very worse prognosis. Surgical operation treatment combined with radiotherapy and aggressive chemotherapy may help alleviating the disease.

EP-552

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF UNILATERAL WILMS' TUMOR IN EGYPT, REPORT FROM A PROSPECTIVE COHORT ANALYSIS

M. El-Ayadi[1], W. Zekri[1], M. Zaghloul[2], A. Younes[3], E. El Desouky[4], E. Ebeid[5]

[1]*Paediatric Oncology, National Cancer Institute, Cairo University, Children Cancer Hospital (57357), Egypt;* [2]*Radiation Oncology, National Cancer Institute, Cairo University, Children Cancer Hospital (57357), Egypt;* [3]*Surgical Oncology, National Cancer Institute, Cairo University, Children Cancer Hospital (57357), Egypt;* [4]*Cancer Epidemiology and Biostatistics, National Cancer Institute, Cairo University, Egypt;* [5]*Paediatric Oncology, National Cancer Institute, Cairo University, Egypt*

Objectives: A huge progress has been made in treatment of Wilms' tumor (WT) resulting in an outcome exceeding 85% in the modern era. Our study aimed at evaluating the demographics, disease characteristics and treatment outcome for unilateral WT patients treated at National Cancer Institute, Cairo University and Children Cancer Hospital, Egypt (57357)
Methods: This prospective cohort study included 98 eligible patients with newly diagnosed nephroblastoma during the period from January 2010 to December 2011. Patients were treated according to Unilateral Renal Tumors Protocol "CCHE_RenTUL#7" based on COG Protocols. Patients were followed till December 2013.
Results: Among the 98 patients, 52 were males (53%); mean age at diagnosis was 3.5 ± 2.6 years. 25 patients (25.5%) were metastatic at presentation. Post surgery, 36 patients (36.7%) had a stage III tumor, 29 patients (29.6%) had stage I, and 8 patients (8.1%) had a stage II disease. Anaplasia was seen in 11 patients (11.2%) while all other patients ($n = 87$) had favorable histology WT (FHWT). The median follow up period was 29.3 months (range 0.3 to 46.6 months). The 3-year overall (OS) and event-free survival (EFS) rates in FHWT patients were 83.4% and 64.2% respectively. Patients with anaplastic WT had 3-year OS and EFS rates of 88.9% and 79% respectively. Early tumor stages (I/II) were associated with significantly improved EFS compared to stage III and stage IV (3-Y EFS 83.3% versus 63.8% versus 18.2% respectively, $P < 0.001$). Regarding OS, no statistically significant difference was found between stages (I/II) and stage III, however, it was significantly better compared to stage IV disease (3-Y OS: 95.7% versus 94.7% versus 66% respectively, $P < 0.001$).
Conclusions: In our study, outcome for early stages WT was comparable to results from other western groups, while metastatic WT had a significantly worse outcome compared to other groups.

EP-553

WILMS TUMOR OUTCOME IN ADOLESCENT AND YOUNG ADULT PATIENTS AT ANN & ROBERT H. LURIE CHILDREN'S HOSPITAL OF CHICAGO

C. Higham[1], D. Walterhouse[1], Y. Gosiengfiao[1], J. Reichek[1], E. Morgan[1], E. Perlman[2], J. Woodman[1]

[1]*Pediatric hematology/oncology, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, USA;* [2]*Pathology, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, USA*

Objectives: Historically, adults with Wilms tumor have inferior outcomes compared with pediatric patients. Recent studies suggest that adult Wilms tumor patients when treated on a pediatric protocol fare better than patients who were not treated on a pediatric protocol (5 year event-free survival (EFS): 77% and 24%, respectively). The purpose of this study was to determine outcome of adolescent and young adult (AYA) Wilms tumor patients treated at Lurie Children's and to identify factors, which may affect outcome.
Methods: We performed a retrospective chart review of patients $\geq$10 years old who were diagnosed with and completed therapy for Wilms tumor at Lurie Children's from 1994-2011.
Results: Nine patients aged 10-26 years were identified. Stage distribution was: 1 stage I, 3 stage II, 1 stage III and 4 stage IV. Only 1 patient had unfavorable histology. EFS was 11%, and overall survival was 44% (median follow-up of 40 months). Median time to relapse was 16 months. Second complete response rate was 43%. The median time from presentation to treatment was 13 days with 3 of the 5 deceased patients having 26 or more days from presentation to treatment. All patients who relapsed $>$ 16 months from diagnosis are alive ($n = 3$) while those patients who relapsed prior to 16 months are deceased ($n = 4$). Only one patient had significant delay in treatment due to toxicity. Available tumors were tested for loss of heterozygozity (1p loss ($n = 0$), 16 loss ($n = 1$), and 1q gain ($n = 2$)). The patient with 16 loss and 1q gain is alive without relapse (67 month follow up). The patient with 1q gain died from disease progression.
Conclusions: The outcome for our cohort of AYA patients with Wilms tumor is worse than expected for patients treated with pediatric protocols. Tumor biology does not appear to explain the poorer outcome. Delay in initial referral and start of treatment may contribute to the inferior outcome.

EP-554

RESULTS OF TREATMENT OF CHILDREN WITH BILATERAL NEPHROBLASTOMA

M. Rubansky[1], A. Kazantsev[1], P. Kerimov[1], M. Rubanskaya[1], D. Rybakova[1], A. Hizhnikov[1], O. Kapkova[1]

[1]*Pediatric Oncology, N. N. Blokhin Cancer Research Center Russian Academy of Medical Sciences, Moscow, Russia*

Objectives: To improve the results of treatment of children with bilateral nephroblastoma
Methods: During the period from 1980 to 2011 at the Institute of Oncology and Hematology were examined and treated 75 children with bilateral nephroblastoma. In all patients, the diagnosis was confirmed morphologically. The main peak of incidence of bilateral nephroblastoma accounts for the period from age 3 to 5 years - 41 (54.7%). Surgical treatment was 71 of 75 children. The other four children have not received surgical treatment due to progression of the disease on the background of the treatment. 54 children (76.1%), surgical treatment was carried out in two stages, first at the least affected kidney tumor, then - on the contralateral organ. 17 patients (23.9%), surgery was performed in one step.
Results: Median follow-up of all patients was 28 months, median progression-free survival - 26 months. (10-60 months). In the group of patients who received surgical treatment in two stages (54 patients), the figures were 29 and 28 months respectively. In the group of patients who received surgical treatment in one stage (17 patients), 26 and 25 months respectively. Overall two-year survival of patients with bilateral nephroblastoma was 86.5%. Two-year disease-free survival - 83.6%.
Overall and disease-free two-year survival of children with bilateral nephroblastoma who underwent surgical treatment in two stages, was 91.2% and 88.5%, respectively. In the group of patients in whom surgery was performed simultaneously, the total two-year survival rate was 92%, disease-free - 88.2%.
Conclusions: The correct diagnostic and modern strategy therapy can improve overall survival in children with bilateral nephroblastoma.

EP-555

MANAGEMENT AND TREATMENT OF CHILDHOOD WILMS TUMOR DURING THREE YEARS OF FOLLOW-UP AT A HOSPITAL BASED STUDY

A. Mehrvar[1], M. Tashvighi[1], A.A. Hedayati Asl[1], M. Faranoush[1], N. Mehrvar[2], R. Gholami[3], M. Alebouyeh[1]

[1]*Oncology, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran;* [2]*Research, MAHAK's Pediatric Cancer Treatment and Research Center, Tehran, Iran;* [3]*Medical Unit, Islamic Azad University, Tehran, Iran*

Objectives: Wilms tumor is a curable childhood malignancy that can develop in healthy child too. Since 1980, the five-year survival rate of this tumor has been above 90%. The purpose of this topic is to evaluate the Pediatric Cancer Treatment epidemiology, treatment and follow-up of children with Wilms tumor who referred to MAHAK's and Research Center.
Methods: This cohort study complied children less than 15 years old with favorable Wilms tumor pathology report, who referred to MAHAK's Pediatric Cancer Treatment and Research Center since Jan 2007 to Jan 2010. The standard checklist contained additional information filled for each individual.
Results: The enrolled patients were 33 cases (18 female, 54.5%) with the mean age of 5 ± 4.4 years old. at the time of diagnosis, the stages of patients were as III (11, 31.3%), IV (8, 25%), I

(7, 21.9%), II (6, 18.8%), V (1, 4%) respectively. Tumor involvement were 18 (54.5%) in right and 15 (45.5%) in left kidney. The most common symptoms were as 22 (66.7%) patients with mass of abdomen and 3 (9.1%) with hematuria. All of the patients had nephrectomy surgery at the early diagnosis. Twelve cases (36.4%) had relapsed during or after their treatment that the mean of relapse time was 21 ± 36.5 months. Out of enrolled patients, there were 24 (72.7%) off treatment, six (18.2%) dead and 3 (9.1%) lost to follow-up. The five years survival was the same as three years survival rate in this study ($94\% \pm 0.04$).
Conclusions: Literature and reviews determine that most children with Wilms tumor are cured and very few of them will have long-term renal problems. Multimodality therapy with surgery and radiotherapy can result in excellent tumor control rate. For achieving the highest survival rate all children with Wilms tumor should be monitor in long-term surveillance programs for the early detection and management of therapy related toxicities.

EP-556

MALIGNANT RENAL TUMOURS IN CHILDREN STUDY AT HOSPICE AFRICA UGANDA

S. Nandaula[1], S. Nandaula[1], S. Nakimbugwe[2]

[1]Palliative Care, Hospice Africa Uganda, Kampala, Uganda; [2]Research Assistant, Hospice Africa Uganda, Kampala, Uganda

Objectives: To review the frequency, mode of presentation and histological pattern of children with malignant renal tumours
Methods: A 7 year retrospective review of all our renal tumour folders in the institution
Results: 19 children qualified for the study with a male/female ratio of 1:2.8 and a mean age of 52.6 +/- 15.8 years. The peak age was in fifth birth day. Most patients present late (78.9%). Renal cell cancer was the commonest tumour type with the commonest mode of presentation being abdominal mass and pain
Conclusions: Malignant renal tumours present very late in our environment and patients hesitate in accepting available treatment option which is surgery. There is a need for increased patient awareness and high index of suspicion by the clinician, particularly during imaging procedures, as this would significantly enhance the early detection of these patients.

EP-557

WILMS TUMOR: EXPERIENCE OF 56 CASES TREATED IN A SINGLE CENTRE

A. Okur[1], F. Pinarli[1], C. Karadeniz[1], A. Oguz[1], A. Poyraz[2], H. Bora[3]

[1]Pediatric Oncology, Gazi University Medical School, Ankara, Turkey; [2]Pathology, Gazi University Medical School, Ankara, Turkey; [3]Radiation Oncology, Gazi University Medical School, Ankara, Turkey

Objectives: To illustrate our clinical experience in the long-term follow-up of children with Wilms tumor.
Methods: Medical records of 56 children with Wilms tumor diagnosed in the Department of Pediatric Oncology, Gazi University Medical School during 1991-2014 were reviewed. Clinical, radiological, pathological on a survival data were collected. The analysis was performed using SPSS version 15.0.
Results: The female/male ratio was 1.3:1. The mean age at diagnosis was 50.7 ± 40.3 (8-204) months. Clinical manifestations included abdominal mass (58.9%), abdominal pain (32.1%) and hematuria (8.9%). One of our patients had Beckwith Wiedemann syndrome and another patient had hemihypertrophy. Thirty-five patients were stage 3 or more at diagnosis. Four cases were bilateral (7.1%) and two patients had extrarenal Wilms tumor. All patients received chemotherapy; 35 patients also received radiation therapy. Blastemal predominant histology was elicited in 31 (55.4%) of our cases, focal or diffuse anaplasia were found in 13 (23.2%) of the cases. Late complications were observed in 12 patients; including proteinuria (5 patients), bronchiectasis (3 patients), secondary malignancy (2 patients), pulmonary alveolar proteinosis (1 patient) and chronic renal failure (1 patient). Mean follow-up time was 100.5 ± 84.9 (1-274) months. Thirty- one patients were alive in remission without disease. Fifteen patients experienced recurrence or progressive disease; nine of these patients died under treatment. Five-year event free survival and overall survival was 78%, 82%, respectively. Ten-year event free survival and overall survival was 66%, 73%, respectively. One patient had chronic kidney disease and the patient died due to electrolyte disturbance. Two patients had secondary malignancy: one of these had rhabdomyosarcoma, and the other patient had acute myeloid leukemia.
Conclusions: Wilms tumor is a well treatable disease. However significant number of our patients presented in advanced staged. Advance stage at presentation and presence anaplasia require more aggressive management resulting in more complications and higher mortality rate.

EP-558

A TEN YEAR RETROSPECTIVE AUDIT OF THE CLINIC-PATHOLOGICAL MANAGEMENT AND TREATMENT OUTCOMES OF CHILDREN WITH WILMS TUMOR AT A TERTIARY CENTER

P. Maturi[1], E. Rogena[1], G. Kitonyi[1]

[1]Hematology and Blood Transfusion/Pediatric oncology, University of Nairobi, Nairobi, Kenya

Objectives: The objectives of this study were to review the clinical presentation and management of children with Wilms tumor and the factors influencing the outcome at Kenyatta National Referral and Teaching Hospital (KNH). The findings of the study will form a basis for revision of treatment design for patients diagnosed with Nephroblastoma at KNH.
Methods: The records of 140 WT patients, aged less than 16 years, who were treated in Kenyatta National Hospital, Kenya, during the period from January 1997 to December 2008 were reviewed. The management protocol followed the scheme of the US National Wilms Tumor Study Group (NSWTG).
Results: Thirteen cases (38.2%) were diagnosed as stage I, 4 (11.8%) as stage II, 13 (38.2%) as stage III and 2 (5.9%) as stage IV. Two cases with bilateral disease (stage V) had stage I tumors in both kidneys. Four-year overall survival (OS) and event free survival (EFS) rates were 65.2% and 52.7%, respectively. Univariate analysis by Log-rank test revealed statistically significant associations between OS and nodal status (p-value < 0.01), manifestation of gross hematuria (p-value 0.02), and tumor size of 10 centimeters or more (p-value 0.02). Multivariate analysis found only the nodal status to be independently associated with OS at a Hazard Ratio of 16.6 (p-value < 0.01). Eight of 13 stage I cases and 6/13 stage III cases had relapsed, with two-year post-relapse survival of 42.8%. Significantly poorer outcome was found in cases with early relapse within 200 days after enrollment (p-value 0.02).
Conclusions: Childhood Wilms' tumor presents late in our setting with its consequent management challenges. The need to educate the populace and the primary healthcare providers on the benefits of early diagnosis and treatment of this condition cannot be overemphasized. Large tumor size and gross hematuria were associated with risk of a poorer outcome.

EP-559

MANAGEMENT OF BILATERAL WILMS TUMOR: OUR EXPERIENCE

B.V. Raghunath[1], B.C. Gowrishankar[1], M. Narendra babu[1], S. Ramesh[1], J. Vinay[1], J. Deepak[1], S. Jayalakshmi[1], K.L. Aravind[1], S. Ravindra[1]

[1]Pediatric surgery, Indira Gandhi Institute of Child Health, Bangalore, India

Objectives: Management of bilateral Wilms tumor is particularly challenging, considering the chances of recurrence and long term renal function for affected patients. Aggressive surgical resection to prevent recurrence must be balanced with the desire to preserve renal function. We evaluated our experience in the management of bilateral Wilms tumor stressing the challenges encountered in decision making and the role of Nephron sparing surgery (NSS) in a limited resource setting.
Methods: Four children presenting with bilateral Wilms tumor were evaluated. All of them were appropriately staged and given standard chemotherapy as per NWTS 5 guidelines. Tumors were considered to have 'good' response to chemotherapy if sufficient tumor shrinkage was observed so that renal hilum was seen free of tumor and vice-versa. NSS was considered in all and was performed when feasible; followed by completion adjuvant chemotherapy. All patients were followed up with serial ultrasound scans (3-6 monthly) and CECT abdomen (yearly once). Blood urea and serum creatinine, hypertension and proteinuria were assessed during follow up visits.
Results: All 4 children received neo-adjuvant chemotherapy as per NWTS-5 guidelines. The results are summarized in the following table

	Treatment planned based on Pre-operative imaging	Treatment executed on table
I child	Left radical and right partial nephrectomy	No treatment offered as the parents refused treatment.
2nd child	Left partial and right radical nephrectomy	Bilateral partial nephrectomy
3rd child	Bilateral nephrectomy with subsequent transplantation	Right partial and left radical nephrectomy
4th child	Right partial and left radical nephrectomy	Left radical nephrectomy with right tumor biopsy

The 4th child is presently awaiting right partial nephrectomy following 2nd line chemotherapy. The second child is on follow up for 1.5 yrs, doing well.
Conclusions: Management of bilateral Wilms tumor is challenging and NSS should be considered in all patients having bilateral Wilm's tumor with favourable histology, even if preoperative imaging studies suggest that the lesions are unresectable.

EP-560

TREATMENT-RELATED PULMONARY HYPERTENSION IN A PATIENT WITH WILMS TUMOR

M. Rayar[1], H. Tilman[2], G. Taylor[3], L. Abbott[1], R. Grant[1]

[1]Hematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Critical Care Medicine, The Hospital for Sick Children, Toronto, Canada; [3]Paediatric Laboratory Medicine, The Hospital for Sick Children, Toronto, Canada

Objectives: Patients with metastatic Wilms tumor (WT) require multimodality treatment with surgery, chemotherapy and radiation to achieve optimal outcome. Such therapy may result in toxicities; a recent clinical trial of high risk renal tumors encountered lung toxicity including pulmonary arterial hypertension (PH). We describe the development and successful treatment of PH in a patient with stage IV WT.
Methods: A 5 year-old female presented with stage IV, favourable histology WT involving the left kidney with extension into the proximal inferior vena cava, and liver and lung metastases. Treatment included surgical resection of the primary tumor, chemotherapy (doxorubicin, dactinomycin and vincristine) and irradiation to the lung and liver with boost to a poorly responding lesion in the upper left lung field. Four months into treatment, she developed persistent tachycardia, respiratory distress and subsequently decreased cardiac function without evidence of hypoxia. Spiral CT revealed no evidence of pulmonary embolism. Although her initial presentation was thought to be cardiac or pulmonary in nature, echocardiogram and subsequent cardiac catheterization were consistent with PH. A lung biopsy showed preserved lung parenchyma with patchy eccentric and mostly non-laminar concentric fibrointimal hyperplasia and medial hypertrophy noted in the small pulmonary arteries, while the pulmonary veins were unremarkable; again findings consistent with PH.
Results: She was treated with supplemental oxygen therapy, pulse intravenous doses of steroid and oral sildenafil for 10 months to maximize pulmonary vascular dilation. With normalization of ECHO and cardiac function she underwent a gradual withdrawal of PH directed therapy; she remains asymptomatic at 5 months off PH therapy.
Conclusions: Cardiac and pulmonary toxicities have been described in metastatic WT patients attributed to radiation and anthracycline administration. Our patient presented with isolated PH that was reversed with treatment. PH must be considered early in symptomatic WT patients in order to implemented appropriate therapy.

EP-561

WILMS TUMOR TREATMENT RESULTS IN PEDIATRIC POPULATION

M. Russo[1], N. Isa[1], M. Reyes[1]

[1]Pediatric Radiotherapy, National Cancer Institute, Santiago, Chile

Objectives: Introduction: Wilms tumor (WT) is the most common form of malignant kidney tumor in childhood. Ac-cording to PINDA protocols, its treatment includes, depending on stage and presentation, early surgery, ra-diotherapy (RT) and chemotherapy (CT). The objective of this work is to review the results of all patients of the National Cancer Institute (NCI) with this condition.
Methods: Patients and Method: A retrospective review of all patients diagnosed with WT at the NCI was conducted. Patient population, RT treatment received and ove-rall survival results were described and prognostic factors were searched.
Results: From September 1993 to December 2010, 110 children were treated with RT. The median age at diagnosis was 3.6 years old. Median follow-up was 148 months after RT. In March 2014, out of a total of 107 patients with follow up, 24 had died, 21 due to disease progression. All deaths occurred within three years of treatment. Overall survival at 2, 4 and 12 years old was 83%, 78%, 78% respectively. A multivariate analysis showed that each day after surgery and without starting RT, the chances of survival decreased ($p = .04$).
Conclusions: WT treatment has an excellent prognosis. Survival after 3 years stabilizes without presenting complications, regardless of the group to which the patient belongs. Among the prognostic factors for patients with RT prescription, this radiation should be started early, as close to the surgery as possible.

EP-562

URETERAL THROMBUS IN WILMS TUMOUR-THE PGIMER CHANDIGARH EXPERIENCE

R. Samujh[1], N. Peter[1], P. Menon[1], M. Bawa[1], A. Chhabra[1]

[1]Pediatric Surgery, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Objectives: Ureteral thrombus in Wilms' tumour is a rare occurrence, about 2% of all Wilms' tumour. We present our experience of these patients, being managed with a modified SIOP protocol.
Methods: Records of children with ureteral extension of tumor were reviewed over a period of two years. Presenting symptoms, diagnostic and Histopathological studies, operation performed and outcomes were recorded.
Results: Of the 67 patients operated for Wilms' tumor over a period of two years (2012-2103). There were 4 patients (~5.9%) with ureteral thrombus. All patients had received standard preoperative chemotherapy. There were 2 females and 2 males. Mean age was 3.2 years. Left sided tumour was commoner with L:R ratio 3:1. One patient presented with hematuria and the rest with asymptomatic abdominal mass. One patient was a follow up of WAGR syndrome. Preoperative ultrasound and CT scan showed ureteral involvement in 2 patients. All patients showed some degree of hydronephrosis. All patients successfully underwent nephrour-etectomy. In 3 cases we could get below the tumor thrombus and divide the ureter more than a centimetre below the thickened ureter. In the last patient the entire ureter was thickened, right down to the uretrovesical junction. All patients received adjuvant chemotherapy and are event free at mean 21.2 months post operatively.
Conclusions: The incidenceof ureteral thrombus is commoner than previously reported. There should be preoperative suspicion in patients with gross hematuria and hydronephrosis. Accurate imaging will help in preoperative planning.

RETINOBLASTOMA

EP-565

PROFILE AND OUTCOME OF RETINOBLASTOMA PATIENTS AT A PHILIPPINE NATIONAL REFERRAL CENTER

A. Alcasabas[1], G.V. Mercado[2], M.Y. Medina[1], P. Fajardo[1], R. Hernandes[1], E. Domingo[2], E.M. Melendres[1], A. Dy[1], A. Dy[1]

[1]Paediatrics, Philippine General Hospital, Manila, Philippines; [2]Ophthalmology, Philippine General Hospital, Manila, Philippines

Objectives: Retinoblastoma (RB) has a high incidence in the Philippines (17.4 per million children 0-4 years) and the expected number of new cases each year is 180. Many of these children are referred to the national referral center, Philippine General Hospital. We reviewed the cases seen at the ophthalmology and pediatric oncology charity service.
Methods: Records of newly-diagnosed retinoblastoma patients from January 2008 to December 2012 were reviewed.
Results: There were 112 cases (88 unilateral; 24 bilateral) from Jan 2008 to Dec 2012. Mean ages were 32.5 months for unilateral RB and 19 months bilateral. Initial presentation were leukocoria in 70% ($n = 79$), mass 21% ($n = 24$), strabismus 4% ($n = 4$), eye redness in 3% ($n = 3$), blindness 1% ($n = 1$) and dilated pupil 1% ($n = 1$). Staging was based on pathology report: Intra-ocular 44% ($n = 49$), extra-ocular 52% ($n = 59$) and missing data 4% ($n = 4$). Records of metastatic work-up were lacking. 109 (97%) patients were treated with upfront enucleation. Two refused treatment; one transferred care. Adjuvant chemotherapy included Vincristine, Carboplatin and Etoposide. Only two patients received radiation. For outcome, 29 patients (26%) were alive; with 19 children treated with enucleation alone. Fifty-six (50%) abandoned therapy, 17 died (15%) and 8 (7%) were lost to follow up. Of those who abandoned therapy, 52% ($n = 29$) stopped before adjuvant chemotherapy; 30% ($n = 17$) during chemotherapy; 14% ($n = 8$) before radiation; and 4% ($n = 2$) during radiation. The cause of death was intracranial extension in 65% ($n = 11$) and not recorded in 35% ($n = 6$).
Conclusions: Advanced disease and abandonment are major causes of poor outcome. Early detection campaigns and establishment of a referral system will facilitate timely diagnosis and treatment. Prospective studies are needed to identify specific barriers to care and monitor impact of interventions.

EP-566

IMPACT OF IMPLEMENTING A RETINOBLASTOMA PROGRAM IN A PUBLIC TERTIARY HOSPITAL IN A RESOURCE LIMITED SETTING

A.P. Alcasabas[1], K. Caranto[2], C. Rodriguez-Galindo[3], M.W. Wilson[4], C.G. Lam[5], G. Sundar[6], T.C. Quah[7], M.C. Dolendo[2]

[1]Section of Hematology/Oncology Department of Pediatrics, Philippine General Hospital, Manila, Philippines; [2]Department of Pediatrics Children's Cancer and Blood Diseases Unit, Southern Philippines Medical Center, Davao, Philippines; [3]Pediatric Oncology, Dana Farber Cancer Institute, Boston, USA; [4]Department of Surgery Division of Ophthalmology and Pathology, St. Jude Children's Research Hospital, Memphis, USA; [5]Department of Hematology-Oncology and International Outreach Program, St. Jude Children's Research Hospital, Memphis, USA; [6]Department of Ophthalmology, National University Singapore, Singapore, Singapore; [7]Section of Pediatric Hematology-Oncology, Khoo Teck Puat-National University Children's Medical Institute, Singapore, Singapore

Objectives: Retinoblastoma has a high incidence in the Philippines (17.8 per million children 0-4 years), and majority of the patients present late with extra-ocular extension. Reasons for delayed diagnosis include financial constraints, inaccessibility to care and misdiagnosis. For Mindanao, Philippines, 35-40 new cases are expected yearly, yet fewer than 10 were seen in the government referral center. To address this, a multifaceted program was established in May 2011 at Southern Philippines Medical Center, involving education of healthcare providers from local health centers and government hospitals on early warning signs of retinoblastoma; establishment of a referral system; development of stage-based treatment regimens; and multi-disciplinary team formation. Capacity building included a dedicated retinoblastoma patient coordinator, specialist clinic, and interdisciplinary case discussions.
Methods: Data on all retinoblastoma patients were prospectively collected as part of routine clinical care from May 2011, and compared with retrospective data prior to program implementation. Treatment included enucleation, radiation and chemotherapy with Vincristine, Carboplatin and Etoposide.

Results: From May 2011 to February 2014, 40 newly-diagnosed patients were seen (33 unilateral, 7 bilateral). Mean age was 2.6 years. Lag time to diagnosis was 16 months (median 11, range 0.5–96) IRSS staging were: Stage 0 (n = 3); Stage 1 (n = 9); Stage 2 (n = 1); Stage 3 (n = 10); and Stage 4 (n = 13). Four patients refused staging work-up. Overall and event-free survival rates were 40% and 27% at 1 year and 30% and 25% at 2 years, respectively. Nine patients (23%) abandoned treatment. Compared to baseline estimates (2005-2010), the mean annual referrals increased from 7 to 14, and extra-ocular presentation dropped by 19%.
Conclusions: The development of effective public health education and referral system for retinoblastoma and the establishment of centers of excellence through local and international collaborations increased patient referrals and decreased extra-ocular presentation rates. The sustainability of this model is needed to impact outcomes.

EP-567

ONCOGENIC HUMAN PAPILLOMA VIRUS 16 ISOLATED IN ONE-FOURTH EYES WITH NON-FAMILIAL RETINOBLASTOMA: A PROSPECTIVE CASE-CONTROL STUDY IN NORTH INDIAN CHILDREN

R. Aggarwal[1], J. Naru[1], U. Singh[2], N.K. Mangat[1], N. Kakkar[3], R.K. Marwaha[4], D. Bansal[4]

[1]Immunopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [2]Ophthalmology. Advanced Eye Center, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [3]Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [4]Pediatric Hematology-Oncology unit Dept. of Pediatrics Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objectives: The risk factors for non-familial retinoblastoma are poorly understood. The incidence of retinoblastoma is higher in developing countries. A few reports have described human papilloma virus (HPV) in retinoblastoma tumor tissue. The aim was to investigate the prevalence of HPV in retinoblastoma tumor tissue and compare with controls.
Methods: The study was prospective. The cases included eyes enucleated for retinoblastoma. Controls were donor eyes obtained from the eye-bank. DNA was isolated from normal retinal tissue from donor-eyes and tumor tissue from eyes with retinoblastoma. PCR for HPV was performed by HPV Genotyping Array kit (Hybribio Ltd., Hong Kong). It utilizes L1 consensus primers to simultaneously amplify 21-HPV genotypes followed by hybridization with respective probes embedded on membrane fibers. High-risk HPV types: 16,18,31,33,35,39,45,51,52,56,58,59 and 68; probable high-risk types: 53 and 66; low-risk types: 6,11,42,43,44 and 81.
Results: The study enrolled 42 retinoblastoma and 42 normal retinal tissues. Disease was bilateral in 14 (33%). Three (7%) patients had a family history of retinoblastoma. 10 (23.8%) tumor tissues were infected with HPV. HPV-16 was the only subtype isolated. None of the control eyes or familial cases were HPV positive.

	HPV positive n = 10	HPV negative n = 32	P-value
Mean age (months)	36.3	44.5	0.40
Males	7 (70%)	15 (47%)	0.56
Low socio-economic status	**8 (80%)**	**12 (37.5%)**	0.24
Rural background	6 (60%)	14 (44%)	0.76
Extra-ocular disease	3 (30%)	5 (15.6%)	0.41
Vaginal delivery	**10 (100%)**	**24 (75%)**	0.18

Conclusions: HPV-16 was isolated from 10 (25.6%) of the 39 eyes with non-familial retinoblastoma. None of the control or familial cases were HPV positive. A greater number (though not significant) of HPV positive cases, had a vaginal delivery and belonged to a low socio-economic background. The link of HPV with retinoblastoma can be explored for preventive strategies in developing countries.
Funding: research-grant from parent institution.

EP-568

THE IMPACT OF OPTIC NERVE RESECTION LENGTH ON SURVIVAL IN RETINOBLASTOMA

M. Bhagat[1], S. Qureshi[1], M. Ramadwar[1], N. Shetty[1], G. Chinnaswamy[1], T. Vora[1], P. Kurkure[1]

[1]Pediatric Surgery Oncology, Tata Memorial Hospital, Mumbai, India

Objectives: Enucleation cures most patients with uniocular retinoblastoma, however, some patients present with extraocular relapse after enucleation. There are many high risk factors such as scleral involvement, choroidal invasion, post laminar optic nerve involvement and disease free optic nerve length which impact survival. However due to overall good survival rate impact of tumor free optic nerve length on survival has not been studied exhaustively. This study was done to determine if the resection length of the optic nerve had an impact on the survival so as to guide surgeons to do optimum surgery and thereby improve outcomes.
Methods: This was a retrospective analysis of prospectively maintained data at our database. All patients who had undergone surgery for Retinoblastoma between September 2004 and September 2013, were included. Data was analysed using SPSS to assess the impact of optic nerve tumor free resection margin on survival and to delineate other various prognostic factors that affect survival in Retinoblastoma.
Results: A total of 115 cases were included in the study. The median length of optic nerve obtained was 1 cm (range 0.2-2.5 cm). Of the 18 cases wherein there was involvement of the optic nerve, (post-laminar: n = 11, pre-laminar: n = 3 and laminar involvement: n = 4) the cut margin was found to be positive in only one case. Histological factors were unfavorable in 44 patients, no residual tumor in two and favorable rest. The event free survival was better in patients with optic nerve length >1 cm than in patients with optic nerve length <1 cm ($p < 0.03$).
Conclusions: Better event free survival is seen with 1 cm or more of resected optic nerve length. Thus optimal surgery should include at least 1 cm of tumor free length of optic nerve to improve outcomes.

EP-569

DIENCEPHALIC TUMOR IN RETINOBLASTOMA PATIENTS: A RARE COINCIDENCE?

M.A. De Ioris[1], S.G. Colafati[2], F. Randisi[2], A. Carai[3], P. Valente[4], R. Cozza[1], A. Romanzo[4], M.G. Cefalo[1], B. Bernardi[1], A. Mastronuzzi[1]

[1]Hematology/Oncology, Pediatric Hospital Bambino Gesu', Roma, Italy; [2]Neuroradiology, Pediatric Hospital Bambino Gesu', Roma, Italy; [3]Neurosurgery, Pediatric Hospital Bambino Gesu', Roma, Italy; [4]Ophtalmology, Pediatric Hospital Bambino Gesu', Roma, Italy

Objectives: Retinoblastoma (RB) patients present an high risk to develop second malignant neoplasm (SMN), epecially children with an hereditary RB. Diencephalic tumors are rare in paediatric age. We report on three cases of diencephalic tumors occurring in RB patients
Methods: Clinical and imaging finding of the three patients were reviewed. The RB database was checked in order to identify patients with similar diencephalic lesions diagnosed from January 1999 since December 2012.
Results: 107 RB patients were diagnosed over 14 years. Three patients (2,8%) presented a diencephalic tumour during the follow-up period: none of them presented a family RB history while a RB1 alteration was identified in two patients with bilateral RB. The diencephalic lesion occurred 15, 43, and 53 months from RB diagnosis without any symptoms. Biopsy was performed in one patient and histology showed a low grade glioma. After a period of stable disease, the lesions progressed in the first two patients; the first patient received radiotherapy (54 Gy) while the later one chemotherapy based on bevacizumab plus irinotecan. Three patients are alive at 20 months, 10 months and 8 years from CNS tumour diagnosis.
Conclusions: Diencephalic tumour in previously treated RB patients seems a peculiar SMNs. Considering the site, the short time interval between tumours and the absence of risk factors clearly associated with SMNs, an alternative pathogenetic mechanism should be supposed. Further analyses of large series are needed to clarify this entity.

EP-570

ANGIOGENESIS IN RETINOBLATOMA: REVISED ASSESSMENT AND THERAPEUTIC SUGGESTION

M. De Ioris[1], R. De Vito[2], P. Valente[3], A. Spagnoli[1], S. Tomaselli[1], R. Rota[1], A. Gallo[1], R. Cozza[1], A. Mastronuzzi[1], F. Locatelli[1]

[1]Hematology/Oncology, Pediatric Hospital Bambino Gesu', Roma, Italy; [2]Pathology, Pediatric Hospital Bambino Gesu', Roma, Italy; [3]Ophtalmology, Pediatric Hospital Bambino Gesu', Roma, Italy

Objectives: Retinoblastoma (RTB) is a well-known vascularized tumor. We assessed the expression of angiogenic markers in RTB patients to explore possible associations with clinical and pathological parameters. Therapeutic considerations were addressed according to our results.
Methods: Seventy-four primary RTB paraffin-embedded samples were analyzed by immunohistochemistry. Cell proliferation potential was determined by Ki67 staining. The expression of CD31, CD105, Smooth Muscle Actin, VEGF and VEGFR2 was evaluated as indicative of the angiogenic tumor features. The tumour necrosis was also measured. The clinical and histological data such as age, laterality, clinical stage according to International Retinoblastoma Staging System (IRSS) and Classificaton System Intraocular Retinoblastoma were reviewed. Coroid, scleral and nerve involvement evaluated according to IRSS and anterior chamber involvement were correlated with markers expression.
Results: CD31, CD105 and Smooth Muscle Actin were expressed at different levels in all RTB specimens while VEGF and VEGFR2 in 70% and 58%, respectively. Ki67 was positive in 90% and tumor necrosis > 50% present in 35% of samples. CD31, CD105 and Smooth Muscle Actin were more expressed in bilateral cases and in samples from patients with anterior chamber involvement. VEGFR2 was expressed in 50% of samples from RTB patients with primary enucleation and in 71% after chemotherapy treatment ($P < 0.02$), whereas no difference was seen for the expression of VEGF.
Conclusions: Our data show that VEGFR2 is expressed in the majority of resistant RTBs. This result suggests that an anti VEGFR2 treatment could be proposed and theoretically effective.

Probably, bilateral cases and patients resistant to standard antiblastic drugs could benefit of an anti-angiogenesis approach.

EP-571

DEVELOPING CLINICAL CANCER GENETICS SERVICES IN RESOURCE LIMITED COUNTRIES: THE CASE OF RETINOBLASTOMA IN KENYA

H. Dimaras[1], L. He[2], L. Njambi[3], J.M. Nyamori[3], E. Nyenze[3], K. Kimani[3], I. Matende[4], H. Rono[5], V. Njom[6],. Retinoblastoma Genetics Task Force[7]

[1]Ophthalmology & Vision Sciences, University of Toronto, Toronto, Canada; [2]Human Biology, University of Toronto, Toronto, Canada; [3]Ophthalmology, University of Nairobi, Nairobi, Kenya; [4]Pediatrics, Lighthouse Eye Centre, Mombasa, Kenya; [5], Kitale Eye Centre, Kitale, Kenya; [6]Ophthalmology, Coast Provincial Hospital, Mombasa, Kenya; [7], Kenyan National Retinoblastoma Strategy Group, Nairobi, Kenya

Objectives: Clinical cancer genetics is an integral part of cancer control and management, yet its development as an essential medical service has been hindered in many Low-and-Middle-Income Countries. We report our experiences in developing a clinical cancer genetics service for retinoblastoma in Kenya.
Methods: A genetics task force was created within the membership of the existing Kenyan National Retinoblastoma Strategy group. The task force engaged in multiple in-person and telephone discussions, offering experiences, opinions and suggestions for an evidence-based, culturally-sensitive retinoblastoma genetic service. Discussions were recorded and thematically categorized to develop a strategy for design and implementation of a national retinoblastoma clinical genetic service.
Results: Discussion among the retinoblastoma genetics task force supported the development of a comprehensive genetic service that rests on three pillars: 1) Patient and Family Counseling, 2) Community Involvement, and 3) Medical Education.
Conclusions: A coordinated national retinoblastoma genetics task force led to the creation of a unique and relevant approach to delivering comprehensive and accurate genetic care to Kenyan retinoblastoma patients. The task force aims to stimulate innovative approaches in cancer genetics research, education and knowledge translation, taking advantage of unique opportunities offered in the African context.

EP-572

IDENTICAL TRIPLETS WITH RETINOBLASTOMA ILLUSTRATE THE SPECTRUM OF THERAPY FOR OPTIMAL OUTCOMES

B. Gallie[1], C. Ngo[1], Z. Noubari[1], M. Tennant[2], F. Shaikh[3], H. Chan[3], E. Héon[4]

[1]Ophthalmology and Vision Science, The Hospital for Sick Children, Toronto, Canada; [2]Ophthalmology, University of Alberta, Edmonton, Canada; [3]Department of Pediatrics: Hematology and Oncology, Hospital for Sick Children, Toronto, Canada; [4]Ophthalmology and Vision Science, Hospital for Sick Children, Toronto, Canada

Objectives: To describe treatment choices to optimize outcomes for identical triplets affected by retinoblastoma.
Methods: A digital image of the tear-drop shaped pupil in one eye of 2 month-old triplet males revealed leukocoria. Examination under anaesthesia revealed that five of the six eyes had retinoblastoma tumors. All eyes had varying degrees of minor iris coloboma.
Results: Treatment for each child and eye depended on size and location of tumors, and degree of involvement of the other eye. Triplet 1 had on eye International Intraocular Retinoblastoma Classification Group 0 (no tumor on visual and RetCam imaging). The other eye was Group C (macular tumor with adjacent vitreous seeds, one peripheral tumor), treated with 532 nm laser (peripheral tumor) and subtenon's Topotecan and intravitreal melphalan. Triplet 2 had Group A and B eyes, with no threat to vision. Five of ten tumors were invisible, detected by optical coherence tomography (OCT). Eight tumors were treated with laser, confirmed correct by OCT for the invisible tumors; peripheral tumors were treated with cryotherapy. Triplet 3 had Group A and D eyes. The Group D eye had macular large tumor overhanging the optic nerve, inferior retinal detachment and subretinal seeding. Extensive discussion with parents and family evaluated the child's interests: salvage of the right eye would require invasive treatments, repeated and monitored for at least 3 years under anaesthetic, with ongoing risks; simple enucleation of the Group D eye would avoid invasive extended interventions. Enucleation was performed with immediate placement of a temporary prosthetic eye.
Conclusions: All three children avoided initial systemic therapy. All children have excellent visual prognosis. Until one year of age OCT will be regularly used to detect and treat early, tiny visually threatening tumors.

EP-573

PATHOLOGYC RISK FACTORS AND ESTIMATE OF RISK OF RELAPSE IN RETINOBLASTOMA AT INSTITUTO NACIONAL DE CÂNCER- BRAZIL

N. Grigorovski A. Kuyven[1], L. Portela[1], P.S.P. Almeida[1], M.M. Garabal[1], M.M.S. Brochado[1], P.A. Faria[2], A. Soares[2], C.C.S. Mattosinho[3], E. Lucena[3], S.E. Ferman[3]

[1]Pediatric Oncology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [2]Pathology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil; [3]Ophathalmology, Instituto Nacional de Câncer, Rio de Janeiro, Brazil

Objectives: Unilateral retinoblastoma accounts for 60%of cases with advanced intraocular disease at diagnosis requiring enucleation. Adjuvant chemotherapy to avoid the risk of relapse should be based on pathologic evaluation. We describe histopathological study of intraocular unilateral RB (RE groupV/IRCE) primarily enucleated with or without adjuvant therapy according to pathologic risk factors and its correlation to outcome.
Methods: Retrospective study of primarily enucleated advanced RB between 2006 and 2013:103 patients with RB were admitted,65unilateral (63%);45/65enucleated (69%);16/45received previous treatment and one enucleated before admission at hospital were excluded from analysis. All eyes were reviewed by experienced pathologists to access choroidal and/or optic nerve involvement according to pathology guidelines from the International Retinoblastoma Staging Working Group. They were classificated as low-risk group (minimal or no choroid invasion and/or prelaminar or absence of optic nerve involvement), intermediate-risk (massive choroidal invasion and/or intraor retrolaminar involvement) and high-risk groups (scleral invasion and/or tumor at the cut end of optic nerve). Outcome was assessed in all cases.
Results: Twenty outof 28 (71,4%) had low-risk pathologic findings: in13/28, no choroidal invasion, optic nerve involvement or optic nerve involvement up to the lamina cribrosa were observed and no further treatment was given. They are alive without evidence of disease;Seven isolated choroid invasion: focal (n = 3) and massive (n = 4) and received no adjuvant chemotherapy. Of these,6/7 alive without evidence of disease and one with massive invasion, developed bone and bone marrow relapse, treated with intensive chemotherapy and is alive with evidence of disease;Eight (28.6%) had intermediate-risk and high-risk features:In 3/28cases with invasion of the optic nerve beyond the lamina cribosa and received chemotherapy. Two of them are alive disease-free and one developed CNS relapse dying from progressive disease (PD);Two or more risk factors observed in 5 cases received chemotherapy:2 alive/disease-free and 3relapsed. In our series,90% (n = 25) are alive.
Conclusions: An accurate histopathologic assessment after enucleation is crucial to indicate adjuvant therapy and graduation intensity approach. Survival was excellent and low-risk group. Intermediate-and high-risk groups indicate the need of chemotherapy intensification.

EP-574

BILATERAL RETINOBLASTOMA, CONSERVATION MODALITIES CASE REPORT

i. Chabchoub[1], M. HAJ MANSOUR[1], I. Aerts[2], H. Zaghouani[3], N. Cassoux[2], D. Levy[2], H. Bouguila[4], S. Ben Ahmed[1], J. Michon[2]

[1]Medical Oncology, Farhat Hached, Sousse, Tunisia; [2]pediatric oncology, Curie, paris, France; [3]radiological, Farhat Hached, sousse, Tunisia; [4]ophtalmology, Hedi Raies Ophtalmology institute, Tunis, Tunisia

Objectives: To report a case of a one year old bilateral retinoblastoma who was treated successfully with preoperative chemotherapy and locoregional treatment.
Methods: Case report of a one year old bilateral retinoblastoma
Results: A one year old female - with no family past history - presented a right leukocoria. Clinical examination and MRI concluded to retinoblastoma Reise V right and Reise III left with no cerebral or other second location. She received 3 courses of chemotherapy CEV (Carboplatin, Etoposide, Vincristin) well tolerated, which reduced much more the left tumor volume than the right one.A collaboration with Curie Institute was considered to offer the chance to preserve the right eye. To avoid the tumor spread during the delay, the child received 3 other CEV courses.A favorable response were noticed with only persistant calcified formations of 5-6 mm in both eyes (3 in the right eye and one in the left eye). The patient had 3 laser sessions and cryotherapy on the right eye and laser combined to plaque radiotherapy on the left eye. After 6 months, no relapse neither sequelae are noticed.
Conclusions: Combination modalities of first line chemotherapy, eye laser, cryotherapy and plaque radiotherapy are a good strategy to avoid enucleation especially in bilateral retinoblastoma.

EP-575

THE CLINICAL ANALYSIS OF 42 CASES WITH BILATERAL INTRAOCULAR RETINOBLASTOMA

M. Jin[1], J. Zhao[2], D. Zhang[1], G. Yu[3], Q. Wu[3], Y. Cui[3], X. Ma[1]

[1]Hematology/Oncology Center, Beijing Children's Hospital Capital Medical University, Beijing, China; [2]Beijing Tongren Eye Centre, Beijing Tong Ren Hospital Capital Medical University, Beijing, China; [3]Department of Ophthalmology, Beijing Children's Hospital Capital Medical University, Beijing, China

Objectives: Retinoblastoma (RB) is the most common primary malignant intraocular tumor in children. This study was to analyze the clinical characteristics of diagnosis and treatments for patients with bilateral intraocular retinoblastoma.

Methods: The clinical document of 42 cases with bilateral intraocular retinoblastoma confirmed in our hospital from December 2009 to February 2011 were retrospectively analyzed.
Results: The median age of primary diagnosis was 13 months, that was younger than unilateral Rb patients at same time. In all patients, leucocoria was the most common manifestation with the primary diagnosis rate 69% based on this symptom (29 cases). Of 84 intraocular retinoblastomas, 3 (3.6%) in Group A;9 (10.7%) in Group B; 10 (11.9%) in Group C; 40 (47.6%) in Group D;22 (26.2%) in Group E. 21 patients had enucleation. In Group D and E, Enucleation rate before chemoreduction or not had significant difference (P = 0.016). Among 42 patients 5 were dead (12%), only 1 patient for complication caused by chemoreducton. Only 3 patients occured transient hearing losses, hear losses recovered during fellow up. In sum, 67.8 percent of the sick eyes are preserved. The preserving eyes percentage of group E was 50%, that of group D was 62.5%; that of group C was 90%; Group C and group B and group A have no enucleation case.
Conclusions: Chemoreduction combined with local ophthalmic therapy is effective for treatment of intraocular retinoblastoma. Systemic chemotherapy can reduce enucleation without significant systemic toxicity.

EP-576

RB1 MUTATIONS IN SOUTH AFRICAN CHILDREN WITH RETINOBLASTOMA

M. Kruger[1], R.D. Wainwright[2], M. de la Rey[3], E.J. Van Rensburg[3]

[1]Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa; [2]Paediatrics and Child Health, University of the Witwatersrand, Johannesburg, South Africa; [3]Genetics, University of Pretoria, Pretoria, South Africa

Objectives: Retinoblastoma, the most common intraocular tumour in children, is caused by mutations in the *RB1* tumour suppressor gene. The aim of this study was to screen children with retinoblastoma, treated at two treatment centers in South Africa for *RB1* mutations.
Methods: A total of 99 blood samples and 75 FFPE tumour samples from 106 RB families; (8 familial with 17 affected individuals; 53 sporadic bilateral; 45 sporadic unilateral cases) were screened for large re-arrangements of the *RB1*-gene by MLPA analysis and for small sequence changes by SSCP and direct sequencing.
Results: A total of 94 mutations, consisting of 8 large genomic deletions/insertions, 22 frame-shift, 43 nonsense, 14 splice-site, 5 missense, one in-frame deletion and one promotor mutation, were detected. The small mutations were the most frequent (91%), and large deletions/insertions less common. Two of the large genomic deletions were somatic mutations (2 sporadic unilateral cases), whereas the other six were all germ-line changes in one familial (duplication of exon 3) and five bilateral sporadic cases (deletions of varying sizes). Frame-shift and nonsense mutations were the most frequent small mutations (75%). The R320X mutation in exon 10 was the most common recurrent (n = 8) nonsense mutation. Heritable cases (47/53 sporadic bilateral and 8/8 familial cases) had a germ-line mutation detection rate of ∼ 87% (55/61) and ∼ 18% (8/45) of the sporadic unilateral cases also had a germ-line mutation. Somatic mutations were detected in 64% (29/45) of the sporadic unilateral cases. Unidentified mutations in the bilateral probands may be due to the presence of low-level mosaicism, not detected with our screening methods. Eight unilateral sporadic cases that did not appear to have *RB1* mutations may be due to epigenetic changes.
Conclusions: This is the first report of *RB1* mutations in South African children which is important for genetic counseling.

EP-577

LIFE STYLE PARAMETERS AND PATERNAL SPERM DNA HEALTH - ROLE IN SPORADIC RETINOBLASTOMA

S.B. Kumar[1], B. Chawla[2], R. Dada[1]

[1]Dept. of Anatomy, All India Institute of Medical Sciences, New Delhi, India; [2]Retinoblastoma Clinic RPC, All India Institute of Medical Sciences, New Delhi, India

Objectives: As compared to somatic cells and oocyte sperms are most vulnerable to oxidtive stress due to minimal cytosolic anti-oxidants. Oxidative stress damage both sperm's nuclear and mitochondrial DNA. Therefore we planned to analyzed sperm DNA integrity, free radical level, oxidized DNA bases in father of children with sporadic Retinoblastoma and correlated these parameters with life style habits of the father.
Methods: A total of 115 cases of sporadic retinoblastoma and 50 control men were recruited at a tertiary referral centre in India. Semen samples were collected from the father of Rb patients and analyzed for semen parameters as per WHO (1999) guideline. Biological markers for sperm DNA damage such as DNA Fragmentation Assay (DFI) by SCSA, 8-Oxo-2'-deoxyguanosine (8-OHdG) by ELISA and Reactive Oxygen Species (ROS) levels by Chemiluminiscence assay were measured. By mutation analysis (qPCR sequencing) of Rb gene, inheritance was ruled out in blood DNA of parents. Logistic binary regression was used to compute the odds ratios (OR) for Rb.
Results: Among the cases and controls, significant difference in all experimental parameters such as ROS ($p < 0.001$), DFI (P = 0.01) and 8-OHdG ($p < 0.001$) were observed. ORs for smokers [10.0 (2.9-34.45; $p < 0.001$); 95%CI] while for pesticides exposed and alcoholics the [95% CI] was [3.5 (95%CI;1.01-12.16); $p = 0.037$)] and [7.292 (95%CI;2.13-24.92); $p < 0.001$]respectively.
Conclusions: Majority of sperm DNA damage is repaired by oocyte but there is a threshold beyond which sperm DNA damage may not be repaired, and accumulation of ethenonucleosides (type of DNA lesion) in sperm may inhibit nucleotide excision repair mechanism. The mutational load thus carried by the embryo after fertilization has a high level of DNA damage and is influenced by DNA repair capacity of oocyte. Thus accumulation of sperm DNA damage may results in sporadic Rb. Smoking, pesticides exposure and alcohol intake adversely affects DNA quality and thus life style interventions can significantly improve DNA health.

EP-578

PLASMA MIR-320, MIR-LET-7E AND MIR-21 AS NOVEL POTENTIAL BIOMARKER FOR RETINOBLASTOMA DETECTION

O. Liu[1]

[1]Pediatrics, The General Hospital of Chinese People's Armed Police Forces, Beijing, China

Objectives: Our study aimed to investigate whether the expression of candidate miRNAs (miR-373, miR-503, miR-320, miR-let-7e, miR-492, miR-498 and miR-21) show some differences between the plasma of RB patients and healthy controls by real-time quantitative polymerase chain reaction (qRT-PCR). We also discuss the relationship of plasma miRNAs and the clinical characteristics of RB patients, and evaluate the value of plasma miRNAs to distinguish RB patients from healthy controls.
Methods: In our study, we collected 65 plasma samples from RB patients and another 65 samples from healthy people as control. MicroRNA levels were measured via real-time quantitative polymerase chain reaction (qRT-PCR) and its relativity to retinoblastoma was tested through statistic data analysis and receiver operating characteristic (ROC) curve.
Results: Plasma miR-320, miR-let-7e and miR-21 were down-regulated in patient samples, AUCs ranged from 0.548 to 0.660 and those of combined classifiers were no less than 0.990.
Conclusions: Plasma miRNA level shows some importance in RB diagnose and can be regarded as novel diagnose biomarker especially for miR-320.

EP-579

PRESENTATION AND OUTCOME OF RETINOBLASTOMA (RB) IN A DEVELOPING COUNTRY: EXPERIENCE AT A SINGLE INSTITUTION

F. Naz[1], S. Mir[1], S. Khan[1], H. Saeed[1]

[1]Pediatric Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

Objectives: In Pakistan, the incidence of RB is 4/100,000 children but there is limited information about their outcomes. Objective of this study is to review the presenting features and outcome for RB at a tertiary care cancer center in Pakistan.
Methods: We conducted a retrospective review of all the patients treated at SKMCH &RC for RB between January 2007-2012. Demographics, presenting features, treatment details and outcomes were collected and analyzed using SPSS 19.
Results: Out of 139 patients studied 67% (n = 87) had unilateral disease. Median age at presentation was 3 years with male to female ratio of 1.6:1. Median time to presentation was 5 months. Most common presenting symptom was leukocoria in 83%. Forty percent (n = 55) reported loss of vision at the time of presentation. Almost half of the patient underwent upfront enucleation, 48% had extraocular disease and 15% presented with distant metastases. Cut end of optic nerve was involved in 37% of patients while 16% had scleral involvement, 33% showed choroidal involvement, 32% anterior chamber involvement and 35% lamina cribrosa invasion. Twelve percent (n = 17) abandoned before initiation of therapy. Only 13% did not require chemotherapy whereas others were treated with 4-6 cycles of chemotherapy (Carboplatin/Vincristine/Etoposide). Half of the patients had intraocular disease and eye salvage was possible in only 10% of them. Overall survival was 44% at 5 years. Event free survival was significantly better ($p < 0.01$) for patients without cut end involvement (70% vs. 20%). In terms of global survival, 88% of patients with unilateral disease underwent enucleation while in case of bilateral disease, 56% lost one eye whereas 19% underwent bilateral enucleation.
Conclusions: Global and overall survival in our patient is much lower than that reported in the literature. This may be related to advanced stage and adverse histologic features due to delay in presentation.

EP-580

RETINOBLASTOMA IN INDIAN CHILDREN: CLINICAL PROFILE AND PREDICTORS FOR METASTASIS

R. Seth[1], A. Singh[1], B. Chawla[2], T. Thomas[1]

[1]Pediatrics, ALl India Institute of Medical Sciences, Delhi, India; [2]Ophthalmology, ALl India Institute of Medical Sciences, Delhi, India

Objectives: Retinoblastoma is the most common primary intraocular malignancy in children. The tumor is highly curable when it is intraocular. In developing countries rate of ocular salvage and patient survival are low since diagnosis is delayed. Objective: To determine the burden and clinical profile of retinoblastoma in a tertiary center in India and to ascertain the risk factors for metastasis. Retinoblastoma is the most common primary intraocular malignancy in children. The tumor is highly curable when it is intraocular. In developing countries rate of ocular salvage and patient survival are low since diagnosis is delayed. Objective: To determine the burden and clinical profile of retinoblastoma in a tertiary center in India and to ascertain the risk factors for metastasis.
Methods: Retrospective analysis of case records of newly diagnosed patients of retinoblastoma over a period of 18 months was done. Clinical profile was ascertained. Reasons for delayed presentation and risk factors for metastasis were identified.
Results: There were 201 patients of retinoblastoma diagnosed in the study period. 35 patients (51 eyes) had extraocular retinoblastoma (non metastatic). Majority of children with EORB were below 4 years of age. Bilateral involvement was seen in about 46% cases. M;F ratio was 1.5:1. Majority belonged to low socio economic strata. Family history was seen in only 4 cases;these cases had a bilateral involvement. leukocoria was the commonest presentation followed by squint and proptosis.
Conclusions: Extraocular involvement was seen in 35 cases. All children were below 4 years of age and majority presented with proptosis/exopytic mass. All 4 children with EORB and bilateral disease developed metastatic disease. Delayed diagnosis was a risk factor for metastasis. Ignorance on behalf of parents, delay in referral on behalf of general practitioner/ pediatrician and refusal of medical advice lead to delayed diagnosis and poor treatment outcomes.

EP-581

CORRELATION OF HIGH MOBILITY GROUP PROTEIN (HMGB1) WITH HISTOPATHOLOGICAL HIGH RISK FACTORS IN RETINOBLASTOMA

M.K. Singh[1], S. Kashyap[1], L. Singh[1], N. Pushker[2], S. Sen[1], A. Sharma[3]

[1]Ocular Pathology, All India Institute of Medical Sciences, Delhi, India; [2]Ophthalmology, All India Institute of Medical Sciences, Delhi, India; [3]Ocular Microbiology, All India Institute of Medical Sciences, Delhi, India

Objectives: Retinoblastoma is a malignant tumor composed of embryonic tumor cells from retinoblasts of neuroepithelial origin. HMGB1 is the most important chromatin proteins. This protein organizes the DNA and regulates transcription. HMGB1 are associated with cell proliferation, differentiation and neoplastic transformation. However, the role of HMGB1 is still unclear in retinoblastoma.
Methods: Prospective analyses of 69 primary enucleated retinoblastoma cases over a period of one year were included. Expression of HMGB1 was performed by immunohistochemistry (IHC) in formalin fixed retinoblastoma specimens. mRNA expression was performed by semi-quantitative Reverse Transcriptase PCR (RT-PCR).
Results: A total of 69 eyes were taken of which 12 (17.39%) eyes had bilateral involvement. Ages ranged from 7months to 8years. 53 (76.81%) cases were reported as poorly differentiated tumors whereas 38 (55.07%) and 20 (28.98%) cases had necrosis and calcification respectively. Histopathologically, 16 (23.18%) had massive choroid invasion, 16 (23.18%) had optic nerve invasion, 6 cases each had sclera and ciliary body invasion. Strong expression of HMGB1 were seen in 38/69 (55.07%) cases. RT-PCR was performed on 31 cases in which 24 cases show mRNA expression (24/31) (77.41%). Expression of HMGB1 was statistically significant with poor differentiation ($p = 0.0440$), optic nerve invasion ($p = 0.0128$) and with HRF ($p = 0.0166$).
Conclusions: Expression of HMGB1 is more frequently found in poorly differentiated tumors and those with, histopathological high risk factors. HMGB1 could serve as a poor prognostic marker in retinoblastoma. Further understanding of the molecular mechanisms underlying HMGB1 function could yield novel therapeutic approaches to anti-cancer strategies.

EP-582

EVALUATION OF THE CEREBROSPINAL FLUID IN RETINOBLASTOMA: USE OF CYTOLOGY, IMMUNOCYTOLOGY AND MOLECULAR MARKERS

M. Sobrero[1], V. Laurent[1], J. Rossi[2], A. Torbidoni[3], C. Romero[2], C. Sampor[2], S. Eandi[2], G. Chantada[2]

[1]Hemato Oncology, Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [2]Hemato Oncology, Hospital de Pediatria Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina; [3]Hemato Oncology, Conicet, Buenos Aires, Argentina

Objectives: To evaluate the role of immunocytology for the ganglioside GD2 and RT-PCR for GD2 synthase and the cone transcription factor CRX for confirmation of malignancy and minimal dissemination (MD).
Methods: From 2007 to 2012, CSF evaluation was done at diagnosis in children IRSS stages II-IV, trilateral disease, high risk stage I and in all cases where an extraocular relapse was clinically suspected. Morphological evaluation of the CSF was done and immunocytology for GD2 was done for confirmation in cases with pleocytosis or abnormal cells in the morphologic examination
Results: No positive CSF was detected in 68 children with high risk stage I (1 had MD). One CNS relapse occurred in a child that had negative MD. Nineteen children had stage II-IVa (CNS relapse occurred in 7, 2/5 of those with MD). There were 4 patients with stage IVb or trilateral disease (2 relapsed, 1/1 with minimal disease). One patient with stage 0 had a CNS relapse after delayed enucleation because of problems in compliance. Overall, 11 positive diagnostic CSF examinations were obtained at the moment of CSF relapse in symptomatic patients. Nine had a positive cytology confirmed by immunocytology, 2 had inconclusive cytology with positive immunocytology or evaluation of CRX. In 2 children, molecular detection of MD preceded CNS relapse.
Conclusions: In cases with positive or inconclusive CSF examinations, the use of immunocytology for GD2 or PCR for CRX may improve diagnostic accuracy. MD may be detected in children with advanced disease correlating with increased risk of CSF relapse.

EP-583

THE PREDICTIVE VALUE OF TNM CLASSIFICATION, THE INTERNATIONAL CLASSIFICATION, AND REESE-ELSTHWORTH STAGING OF RETINOBLASTOMA FOR THE LIKELIHOOD OF HIGH RISK PATHOLOGIC FEATURES

Y. Yousef[1], M. Al-Hussaini[2], I. Sultan[3], Y. Hijja[1], I. Jaradat[4], M. Mehyar[1], R. Deebajah[3], K. Rawashdeh[1], S. Khurma[1], I. Nawaiseh[1]

[1]Department of Surgery, King Hussein Cancer Center, Amman, Jordan; [2]Department of Pathology, King Hussein Cancer Center, Amman, Jordan; [3]Department of Pediatrics, King Hussein Cancer Center, Amman, Jordan; [4]Department of Radiotherapy, King Hussein Cancer Center, Amman, Jordan

Objectives: To evaluate the predictive value of the 7th edition American Joint Committee on Cancer/the Union for International Cancer Control (AJCC/UICC) TNM classification, the International Classification (ICRB), and Reese-Elsthworth (RE) Staging for Retinoblastoma (RB) for the likelihood of High risk pathologic features (HRF) in eyes treated by primary enucleation.
Methods: A retrospective, observational case series of 50 eyes of 49 patients who had pathologically confirmed RB after enucleation as primary therapy by reviewing medical records, pathology reports and Ret-Cam images. The main outcome measures included: demographics, laterality, TNM stage, ICRB group, RE stage, choroid invasion, optic nerve invasion, anterior chamber invasion, and scleral invasion.
Results: The median age at enucleation was 30 months. Twenty-seven (55%) patients were males, and 19 (39%) patients had bilateral RB. HRF mandating adjuvant chemotherapy were seen in 5 (22%) of T2 eyes, and in 15 (56%) of T3 eyes ($p = 0.021$), and in 1 (13%) of ICRB group C eyes, 8 (33%) of group D eyes, and 11 (61%) of group E eyes ($p = 0.035$). Stage RE-Va tumors had higher incidence of HRF than the upstaged RE-Vb eyes. Twenty (40%) patients received adjuvant chemotherapy for HRF, and at median follow up of 40 months, no single case had metastasis or was dead.
Conclusions: The higher AJCC/UICC T stage of the disease and the more advanced IIRC group at presentation are associated with a higher incidence of HRF, while that was not the case for RE staging system. Very large tumors (occupying >50% globe) should be considered ICRB group E rather than group B since they have a higher incidence of HRF.

SOFT TISSUE SARCOMAS

EP-584

PACLITAXEL IN RELAPSED OR REFRACTORY PEDIATRIC BONE AND SOFT TISSUE SARCOMAS

B. Aydin[1], C. Akyuz[1], T. Kutluk[1], A. Varan[1], B. Yalcin[1]

[1]Pediatric Oncology, Hacettepe University- Institute of Oncology, Ankara, Turkey

Objectives: Given the poor outcomes of relapsed/refractory soft tissue and bone sarcomas we retrospectively review our results with paclitaxel, cyclophosphamide and carboplatin (PCC) regimen to evaluate the effectiveness and outcome.
Methods: The files of 12 children diagnosed as rhabdomyosarcoma ($n = 9$), Ewing sarcoma ($n = 2$) and malignant mesenchymal tumor ($n = 1$) treated with PCC regimen on relapsed/ refractory disease were retrospectively.
Results: The median age of 7 males and 5 females was 11,6 years (ranged 0,7-17). Median EFS until the first event was 7,2 months (3,4-63,5). PCC regimen was used as 2nd-line in 2 patients, 3rd-line in 9 patients and 4th-line regimen in 1 patient. Patients received median 4 courses (1-10) either as the only PCC 4-weekly in 6 patients or alternated with reduced dose VAC regimen (vincristine, dactinomycin and cyclophosphamide) in 6 patients. Objective response rate was% 58 (2 CR + 3 VGPR + 2 SD). Five patients had progressive disease. Median EFS and OS after PCC were 7,8 months (1-68 months) and 13,5 months (2,5-82 months). Two-year EFS and OS rates were%33 and%81 for 12 patients. Median EFS of PCC and alternated PCC-VAC regimens were 12 and 19 months ($p = 0,5$).
Conclusions: Relapsed or refractory soft tissue and bone sarcomas have dismal prognosis. Paclitaxel might be an alternative for these patients. Although patient numbers are low to conclude PCC alternated with reduced dose VAC might have better response rate. Further studies should be warranted.

EP-585

TREATMENT OUTCOME OF GENITOURINARY RHABDOMYOSARCOMA -10 YEARS EXPERIENCE

S. Fadel[1], A. Kamal[2], M. Yousef[2], A. Hanoo[2]

[1]Pediatric Oncology, Faculty of Medicine, Alexandria, Egypt; [2]Pediatric Urology, Faculty of Medicine, Alexandria, Egypt

Objectives: Genitourinary rhabdomyosarcoma is a special entity that needs complex treatment algorithm with chemotherapy, surgery and radiotherapy, which impacts the disease control and long term outcome. We aim to retrospectively review genitourinary rhabdomyosarcoma outcome in our limited resources country
Methods: A retrospective review was made of the clinical records of all patients younger than the age of 18 years diagnosed with Genitourinary RMS and treated at Alexandria University Hospital, over a period of 10 years (2002 – 2012). The primary outcome examined was Overall survival. A secondary outcome, local recurrence, and progression free survival rates were calculated. Toxicities and adverse effects following treatment were evaluated by the National Cancer Institute–Common Toxicity Criteria version 4.0.
Results: Twenty patients histologically confirmed GU – RMS. The age at presentation varied between 9 months to 18 years with a median of 9 years. There were 11 males (55%) and 9 females (45%). Median follow up for the entire group was approximately 2.6 years (range 0.8 to 8.3) from initiation of therapy. The most common primary tumor site was the Bladder / Prostate 9 patients (45%), paratesticular in 4 (20%), retroperotineum in 2 (10%), uterus in 3 (15%), cervix in 1 (5%) and vagina in 1 (5%). All patients presented with IRS group III disease. 16 patients were treated according to SIOP MMT protocol, while the remaining 4 patients were treated according to IRSG protocol IV. At the end of our study, 15 patients (75%) showed no evidence of disease. 4 cases showed recurrence (22%). Grade 3/4 toxicities were 20% diarrhea and 19% febrile neutropenia.2 cases died, one case died due to severe febrile neutropenia, the other died from advanced disease.
Conclusions: Our results in a limited resource country, is close to published data, when multimodal treatment was applied.

EP-586

SURVIVAL AND FACTORS AFFECTING THE OUTCOME OF SYNOVIAL SARCOMA IN CHILDREN AND ADOLESCENTS

H. Hafiz[1], E. Elnadi[1], H. Taha[2], A. Younes[3], M.S. Zaghloul[4], M. Elwakeel[5], S. Ahmed[4], G. Taha[3], R. M Labib[6]

[1]Pediatric Oncology, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt; [2]Surgical Pathology, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt; [3]Surgery, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt; [4]Radiotherapy, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt; [5]Radiodiagnosis, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt; [6]Research, Children's Cancer Hospital-Egypt-57357, Cairo, Egypt

Objectives: To evaluate the impact of the clinicopathologic features at diagnosis and treatment given, on the outcome of synovial sarcoma in children and adolescents.
Methods: Retrospective analysis of patients below 19 years old diagnosed by synovial sarcoma and treated at Children Cancer Hospital Egypt 57357 (CCHE) between July 2007 and May 2013. Clinical characteristics, pathological information, treatment modalities and survival data were reviewed.
Results: Seventeen patients were included with median age at diagnosis was 14.8 years, the most common affected primary site were the extremities (n = 8, 47.1%), tumor size was less than or equal 5 cm in only 4 cases (23.5%). Initial surgical excision was feasible in 10 patients (58.8%) while 5 (29.4%) patients underwent surgical excision after response to preoperative chemotherapy. Two patients had unresectable tumor, showed no response to chemotherapy and received radiotherapy as the only local control therapy. Adjuvant radiotherapy only was given in 2 patients and 5 patients received chemotherapy without local radiotherapy and 8 patients received both modalities. The estimated 3 –year overall survival and failure free survival rates for the entire group were $86.5 \pm 8.9\%$ and $48.8 \pm 14.8\%$ respectively, the 3-year FFS was better in patients who underwent complete surgical excision either initial or post chemotherapy as it was 66.7% versus 55.6% for those with gross or microscopic residual (p-value = 0.38). Also, the 3-year failure free survival was 75% versus 56.3% for those smaller than or equal 5 cm and those larger than 5 cm respectively (p-value = 0.3).
Conclusions: Tumor size and complete surgical excision are important prognostic factors though they were statistically insignificant. Preoperative chemotherapy can help for delayed excision in patients presented initially with unresectable tumors.

EP-587

LOCALIZED RHABDOMYOSARCOMA OF HEAD AND NECK: A RETROSPECTIVE ANALYSIS OF 80 PATIENTS TREATED AT A TERTIARY CARE CENTRE IN INDIA

N. Iqbal[1], A. Thakar[2], S. Agarwala[3], D.N. Sharma[4], M.C. Sharma[5], S. Bakhshi[1]

[1]Medical Oncology, All India Institute of Medical Science, Delhi, India; [2]ENT, All India Institute of Medical Science, Delhi, India; [3]Pediatric Surgery, All India Institute of Medical Science, Delhi, India; [4]Radiation Oncology, All India Institute of Medical Science, Delhi, India; [5]Pathology, All India Institute of Medical Science, Delhi, India

Objectives: Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children, however, it is rare in adults. The head and neck site accounts for 35% of all RMS. The study aim was to retrospectively review the clinic-pathologic factors, treatment outcome and prognostic factors in patients of localized RMS of head and neck treated at our centre.
Methods: Data pertaining to 80 patients reported in the database as having localized RMS of head and neck, diagnosed from May 2003- Dec 2012, was retrieved. Factors evaluated were age, histology, site, tumor size, stage, risk and Intergroup Rhabdomyosarcoma study (IRS) group. Survival estimate were determined using survival time with the end point being event or death from any cause.
Results: Median age was 10.8 years and median symptom duration was 3 months. Males constituted 68.7% and females 31.2% with a male:female ratio of 2.2:1. The primary site of tumor was orbit in 23.7%, parameningeal in 56% and non-orbit non-parameningeal in 20%. Median tumor size was 6 cm (range 2-12 cm). The most common histology was embryonal in 76% cases. Forty-four percent patients were stage III, 51% were intermediate risk and 75% were IRS group III. Seventy-three percent (73%) patients received chemo-radiotherapy. Five-years EFS and OS were 36.4% and 57% respectively. Univariate survival analysis found that intermediate risk group patients had worse EFS as compared to low-risk (27.3% vs 44.6%, p = 0.02). Stage III tumors and tumor size >5 cm had a trend towards poor EFS with a p value of 0.06 and 0.06 respectively. None of the factors affected overall survival.
Conclusions: This is a single center experience of unselected patients. The survival in our cohort is less as compared to published data from West. Intermediate risk was significantly associated with poor EFS. Perhaps relatively large tumors contributed to higher failure rates.

EP-588

MALIGNANT RHABDOID TUMORS OF SOFT TISSUE. SINGLE CENTER EXPERIENCE IN RUSSIA

D. Kachanov[1], M. Teleshova[1], A. Usychkina[1], R. Moiseenko[1], G. Muftahova[1], A. Mitrofanova[2], T. Shamanskaya[1], S. Varfolomeeva[1]

[1]Clinical Oncology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia; [2]Pathology, Federal Research Center of Pediatric Hematology Oncology Immunology, Moscow, Russia

Objectives: The aim of the study was to analyze clinical data and therapy results in a cohort of patients with malignant rhabdoid tumor of the soft tissue (MRT) treated in federal cancer center in Russian Federation.
Methods: Eight patients included in this analysis were treated in Federal Research Center of Pediatric Hematology, Oncology and Immunology during the period of 01.2012 - 01.2014. We analyzed age at diagnosis, primary tumor location, stage of the disease (according to Intergroup Rhabdomyosarcoma Study criteria). All diagnosis were established by histopathologic examination and confirmed by lack of nuclear expression of INI1. Patients were treated according to European Rhabdoid Tumor Registry recommendations.
Results: Median age at diagnosis was 8.3 months (0.3-126 months). Diagnosis was verified on the 1st year of life in 5 (62.5%) patients (in 1 case on the 8 day of life). M:F ratio was 1:1. Topography of primary tumor included liver - 3 (37.5%) cases, deep soft tissues of a neck – 2 (25%) cases, abdominal cavity – 2 (25%) cases, orbit – 1 (12.5%) case. In 1 (14.3%) tested case germ-line mutation in INI1 gene (c.362G – T) was identified. 4 (50%) patients had localized disease, 4 (50%) patients had distant metastases. Clinical group distribution according to IRS: III – 2 (25%) patients, IV – 6 (75%, in 1 case - because of initial tumor rupture, in 2nd case - because of intraoperative tumor rupture) patients. Outcomes: 3 (37.5%) patients alive (2 - completed therapy, 1 – is undergoing therapy). 5 (62.5%) patients died (4 - due to early progression, 1 - due to refractory disease).
Conclusions: Our data confirmed presentation of disease in most cases on the first year of life and demonstrate unfavorable prognosis due to advanced stage of the disease and poor response to therapy.

SOFT TISSUE SARCOMAS

EP-589

CLINICAL ANALYSIS OF THREE CASES OF RHABDOMYOSARCOMA WITH BONE MARROW METASTASIS

X. Li[1]

[1]Hemotology Center, Bei Jing Children's Hopspital, Beijing, China

Objectives: To investigate violations of children rhabdomyosarcoma with bone marrow metastasis, clinical characteristics, treatment and outcomes.
Methods: Retrospectively analyzed three cases of children rhabdomyosarcoma with bone marrow metastasis from January 2008 to December 2012.
Results: Three patients were males, mean age 5 years (1 year 8 months to 11 years old in November). According to U.S. Rhabdomyosarcoma Study Group (IRS) staging criteria, 3

patients were stage IV stages, clinical grouped is high-risk group. Primary in the head and neck, the other two cases were primary in the pelvic cavity, retroperitoneal area, buttock mass, partially occupying oppression cause oliguria, anuria, all patients were confirmed by biopsy and immunohistochemical staining confirmed, histological type, including 2 cases of alveolar type, one case of embryonal. The clinical manifestations, mainly for tumor tissue mass, oppression caused by the invasion. Carried out strictly in accordance with the treatment of children with IRS installment. U.S. Oncology Research Center using the group (COG) rhabdomyosarcoma chemotherapy. one case's tumor progression in the treatment after 4 months, one case in the treatment of more than one year, through chemotherapy, surgery, radiotherapy and autologous stem cell transplantation relapse, and the other one case in accepting chemotherapy and surgery,1 year later recurrence. Currently, survived only one case.
Conclusions: Children with bone marrow involvement rhabdomyosarcoma, early diagnosis is difficult, generally poor, no specific clinical features, often misdiagnosed as other hematologic malignancies, complications and more often associated with renal failure, various serious infections, poor long-term prognosis, survival rate is low, chemotherapy combined with surgery, radiotherapy, stem cell transplantation combined therapy is an effective treatment to control the disease, but the treatment scheme requires further discussion.

EP-590

SUCCESSFUL TREATMENT OF SCLEROSING RHABDOMYOSARCOMA IN A PATIENT WITH DUCHENNE MUSCULAR DYSTROPHY

R. Mehrotra[1], S. Smith[1], F. Perez-Marques[1], J. Panicker[1]

[1]Pediatrics, University Of Kansas Medical Center, Kansas City, USA

Objectives: A 22 year old male with Duchenne Muscular Dystrophy (DMD) and Clinical Stage III sclerosing Rhabdomyosarcoma (sRMS) was successfully treated with surgery, chemotherapy and radiation.
Methods: The patient presented with a one month history of a painful thigh mass; staging studies showed a heterogeneous mass (8 × 8 cms) within the left rectus femoris muscle with localized and regional node involvement. Tumor biopsy and sentinel node dissection showed sclerosing rhabdomyosarcoma. Treatment consisted of 12 weeks of Vincristine, Cyclophosphamide and Actinomycin (with cardiac monitoring in the PICU), then tumor resection, followed by radiation to the tumor bed and nodal sites and additional chemotherapy (for a total of 39 weeks). Anthracyclines were avoided due to underlying cardiac dysfunction.
Results: After 12 weeks of chemotherapy, the tumor mass showed no metabolic activity on PET scan compared to an SUV of 11 at presentation. The resected tumor (6 × 6 cms) showed an excellent pathological response to chemotherapy with less that 5% viable tumor cells. The patient tolerated therapy well but did have episodes of fever and neutropenia and needed parenteral nutrition and blood product support. He did not experience any significant deterioration in his neuromuscular or cardiac function during treatment.
Conclusions: There have been only a few patients with DMD who have developed RMS. Successful treatment can be accomplished by a coordinated treatment plan between the oncologist, oncology surgeon, PICU, and radiation therapy.

EP-591

OCCIDENT OF MEXICO RHABDOMYOSARCOMA (RMS) EXPERIENCE: SLIGHT IMPROVEMENT WITH A LOT OF WORK TO DO

X.A. Ramirez-Urenda[1], J. Paniagua-Padilla[1], F.A. Sanchez-Zubieta[1]

[1]Servicio de Oncologia y Hematologia Pediatrica, Hospital Civil de Guadalajara, Guadalajara, Mexico

Objectives: Identify the clinical characteristics, event free survival and global survival of the patients of the Occident of Mexico with RMS from 1998 to 2012
Methods: This study reviewed 60 children's electronic charts with RMS from 1998 to 2012 from the institution. They were treated with Intergroup Rhabdomyosarcoma Study Group (IRSG) III or IV regimens.
Results: Median age of diagnosis was 5.3 years range (0.2 to 14 years); geographical characteristic of the patients 47% where from Jalisco, Mexico. According to IRSG classification, 4 (7%) were staged as low-risk (LR); 29 (48%) Intermediate-Risk (IR), 15 (25%) were high-risk (HR), and it was unknown in 12 patients (20%). The primary sites of tumor were: trunk and retroperitoneum (n = 16); head and neck (n = 11), parameningeal (n = 9), orbit (n = 9), genitourinary (n = 7), paratesticular (n = 2), extremity (n = 6), Histopathology (n = 41) embrionary, alveolar (n = 8), bothroyd (n = 3), anaplastic (n = 4), unknown (n = 4). IRSG group I Localized disease 3%, microscopic residual disease group II 12%, group III incomplete resection or biopsy with macroscopic residual 60%, group IV distant metastases 25%, received radiotherapy (n = 36), no radiotherapy (n = 24), at the time of the study 3% was alive with activity, alive without activity 43%, 25% died of the disease, 10% died from a different cause, abandonment 13%, transferred to another unit 3%. By disease risk group the 5 and 10 year event free survival (EFS) for LR group disease was survival 75% at 17 months, 64% for IR, 46% HR. global survival (GS) for LR 75% at 79 months, 62% IR, HR 51%.
Conclusions: In the comparison between EFS that we had in 2007 and 2012 with slight improvement. The outcome of patients with RMS in the Occident of Mexico can be further improved by coming together as a cooperative group to provide the best of care. Improved communication, multidisciplinary team collaboration.

EP-592

WILMS TUMOR TREATMENT AND OUTCOME AT A MULTIDISCIPLINARY PEDIATRIC CANCER CENTER IN LEBANON

W. Rabeh[1], S. Akel[2], S. Muwakkit[1], M. Abboud[1], H. El Solh[1], R. Saab[1]

[1]Children's Cancer Institute, American University of Beirut, Beirut, Lebanon; [2]Department of Surgery, American University of Beirut, Beirut, Lebanon

Objective: The approach to treatment of Wilms Tumor (WT) differs between the European school, which advocates for neoadjuvant chemotherapy, and the North Americans school, which favors upfront tumor resection. At the Children's Cancer Institute in Lebanon, the approach to WT has followed the North American protocols since 2002, using a multidisciplinary approach to diagnosis and treatment planning. We here review the clinical outcomes of patients with WT and identify prognostic determinants of outcome.
Methods: After IRB approval, we retrospectively reviewed the clinical records of patients with WT treated at our hospital between April 2002 and June 2013.
Results: Our study included 35 children. Male: female ratio was 1:2.5, with a mean age of 3.9 years. Eight patients (23%) had stage I disease, 4 (11%) stage II disease, 9 (26%) stage III disease, 9 (26%) stage IV disease and 4 (11%) stage V tumors. Treatment was as per the North American NWTS protocols. Upfront resection was done in 24 cases; while biopsies were performed for Stage V tumors (n = 5), tumors associated with IVC thrombus (n = 3), locally extensive tumors that were deemed unresectable (n = 1), and patients that had been subtotally resected prior to referral (n = 2). At the time of the analysis, 30 (88.1%) of patients were free of disease, at a median follow-up of 57 months from diagnosis (range 5-124 months). Four patients had relapse, at a median time of 8.75 months (range 7- 12 months); all four had initial metastatic disease. One patient developed chronic renal failure during treatment.
Conclusion: NWTS protocols resulted in favorable outcome in children with non-metastatic Wilms tumor, in the setting of multidisciplinary approach to therapy. We observed a relatively high incidence of patients with bilateral tumors- a finding which suggests the need for further studies at genetic and molecular levels in this group of patients.

EP-593

LYMPHOCYTE RECONSTITUTION AS A PROGNOSTIC FACTOR IN SARCOMAS

A. Sobrino Baladrón[1], C. Mata Fernández[1], E. González Ruiz de Leon[1], J. Cayrol[1], R. Herrainz Cristobal[1], C. Gonzalez Sansegundo[1], J. Huerta Aragonés[1], E. Cela de julián[1], C. Garrido Colino[1], C. Beléndez Bielez[1]

[1]Pediatric Onco-hematology Deparment, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Objectives: The lymphocyte reconstitution has been identified as a prognostic factor in malignancies. We try to determine if early lymphocyte recovery is a predictor of survival in our cohort of paediatric patients with any type of sarcoma receiving chemotherapy.
Methods: All children diagnosed of a sarcoma and treated with chemotherapy in our institution from 2000 to 2012 were retrospectively evaluated. Chemotherapy was applied according to international protocols then current. Demographic, hematologic and related to treatment data were collected.
Results: Data of 33 pediatric sarcoma patients were analyzed (median age 12.2 [0.5-16.8]; male:female 18:15). Diagnosis were: 9 Ewing sarcoma/PNET, 6 Osteosarcoma, 10 rhabdomyosarcoma and 8 non rhabdo-soft tissue sarcomas. Six (18.2%) were metastatic at diagnosis and 27 (81.8%) non-metastatic. Twenty-six (78,8%) had a surgery done and 21 (63.6%) received any type of radiotherapy (including intraoperative radiotherapy). Five year overall survival [OS-5] was 63.3% (19 alive and 11 deceased). Good histological response at time of resection (>90%) was founded in 6/14 patients with an OS-5 of 100% and poor histological response in 8/14 patients with an OS-5 of 23%. Classifying patients into two groups according to a threshold absolute lymphocyte count 15 days after starting chemotherapy [ALC+15]. OS-5 in patients with ALC+15 ≥800 cells/(L was 86% while OS-5 with ALC+15 <800cells/(L was 58% although difference was not statistically significant (p = 0.136). Analyzing it separately in each tumor, data of 7 rhabdomyosarcomas: 3 with ALC+15 ≥800cells/(L are alive more than 10 years after diagnosis while 4/7 with ALC+15 <800cells/(L died of disease (p = 0.007).
Conclusions: Despite the limitations of such a small study, it supports the role of lymphocyte recovery in paediatric sarcomas and it potential usefulness on risk stratification after initiation of therapy in addition to the need of inmune reconstitution as a treatment strategy.

EP-594

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS (NRSTS): A SINGLE-CENTRE STUDY IN SINGAPORE

E. Tan[1], P. Iyer[1], S.Y. Soh[1]

[1]Paediatric Haematology/Oncology, KKH, Singapore, Singapore

Objectives: Non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) represent 4% of childhood cancers. Though useful, adult data cannot be directly translated to children, as paediatric entities have been shown to be different in biology, treatment response and outcomes. We report our experience with NRSTS in the largest public paediatric hospital in Singapore.
Methods: Retrospective analysis of 22 children with NRSTS diagnosed between 1997 to 2011 was conducted. Data on patient demographics, tumour characteristics, treatment and survival status was obtained from Singapore Children's Cancer Registry and reviews of case records. The study was approved by the Institutional Review Board.
Results: Median age of diagnosis was 10.8 years (range: 0.2 – 17.8 years). Male: female ratio was 1:2.7. The different types of tumours seen were: infantile fibrosarcomas (n = 4), malignant peripheral nerve sheath tumours (MPNST) (n = 4), fibrous histiocytomas (n = 2), leiomyosarcomas (n = 2), alveolar soft part sarcoma (ASPS) (n = 1), hemangioblastomas (n = 2), spindle cell sarcomas (n = 2), myofibroblastic sarcoma (n = 1), rhabdoid tumours (n = 2), embryonal sarcoma (n = 1), angiosarcoma (n = 1). Staging was done according to IRSG in all except one where it was not described – seven (32%) were stage 1, four (18%) were stage 2, seven (32%) were stage 3, three (14%) were stage 4. All patients underwent tumour resection, nine had chemotherapy (out of which three patients received neoadjuvant chemotherapy) and five received radiotherapy. Median follow-up was 2.3 years. Three patients relapsed, all within the first year. At time of analysis, sixteen patients survived – seven had stage 1, four had stage 2, three had stage 3 and two had stage 4 disease. The six non-survivors were patients with MPNST, myofibroblastic sarcoma, malignant rhabdoid tumour, hemangioblastoma and spindle cell sarcoma.
Conclusions: The spectrum of NRSTS seen showed great heterogeneity in histology. Survival outcome was good. Multidisciplinary treatment with uniformity of approach is vital in treating this heterogeneous group of tumours.

EP-595

EPITHELIOID ANGIOSARCOMA OF COLON: A RARE CASE REPORT IN AN INFANT

R.A.P. Teixeira[1], J.Q.S. Leão[2], R.H. Baroni[3], R.Z. Filippi[4], J. Oba[5]

[1]Pediatria, Instituto da Criança/Instituto do Tratamento do Câncer Infantil - HC -FMUSP, Sao Paulo, Brazil; [2]Cirurgia Pediátrica, Hospital Albert Einstein, Sao Paulo, Brazil; [3]Radiologia, Hospital Albert Einstein, Sao Paulo, Brazil; [4]Laboratório de Patologia Cirúrgica, Hospital Albert Einstein, Sao Paulo, Brazil; [5]Gastroenterologia Pediátrica, Hospital Albert Einstein, Sao Paulo, Brazil

Objectives: Epithelioid angiosarcoma (EA) is a rare tumor affecting children and usually occurs in liver and extremities. Mesenteric angiosarcoma that occurs in infants has only rarely been reported. We report a case of colon EA affecting a female child, emphasizing the clinical features, its difficult management and a brief review of literature.
Methods: A four-month-old female presented with three-week history of intestinal bleeding associated with paleness, inadequate weight gain and perineal dermatitis. Initially dairy allergy was considered, however, as the intestinal bleeding persisted, the infant was hospitalized for investigation.
Results: The imaging findings on US and CT showed a heterogeneous-vascularized mass in the cecum extending into the mesentery. Small liver and lung nodules were also found. Surgery was performed with complete resection of the tumor. Anatomopathological result showed a 4.5 x 3.5 x 2.0 cm hemorrhagic tumor involving the colon with 60% necrosis and classified as a high grade sarcoma. Surgical margin was tumor-free. EA was confirmed by immunohistochemistry, with strong reactivity for endothelium markers (CD31, CD34) with negative markers for other tumors. The infant has undergone four chemotherapy cycles with Ifosfamide and Adriamycin, with disappearance of the pulmonary nodes. No signs of tumor were found on second-look surgery and also in the liver node biopsy. She did two more equal chemotherapy cycles and now is 4 months off therapy with an excellent recovery and normal CT images without any signs of relapse.
Conclusions: Angiosarcomas are rare tumors of vascular endothelium cell origin that may occur anywhere in the body. The occurrence in the gastrointestinal tract is quite uncommon with a few cases reported in the medical literature and with unfavorable outcomes. To our best knowledge, this is the first reported case in a child bellow one year of age and with a very good response.

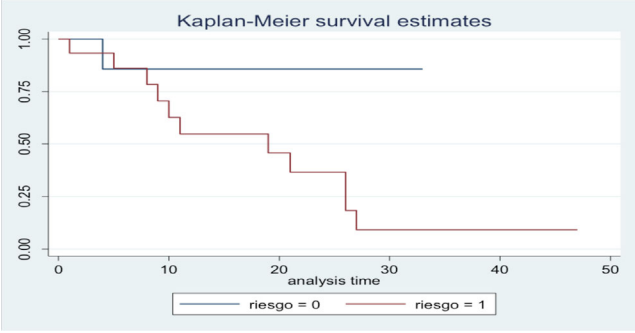
EP-596

NATIONAL TREATMENT PROTOCOL FOR PEDIATRIC PATIENTS WITH NON-RHABDOMYOSARCOMA SOFT TISUE SARCOMAS: THE NATIONAL INSTITUTE OF PEDIATRICS (MEXICO) EXPERIENCE

R. Cardenas[1], L. Velasco[1], J. Shalkow[2], M. Zapata[1], Y. Melchor[3], A. Gonzalez[3], R. Rivera-Luna[4]

[1]Oncology, National Institute of Pediatrics, Mexico City, Mexico; [2]Federal Director Pediatric Cancer Program, National Center for Pediatric and Adolescent Health, Mexico City, Mexico; [3]Research, National Institute of Pediatrics, Mexico City, Mexico; [4]Head Division of Oncology, National Institute of Pediatrics, Mexico City, Mexico

Objectives: Non-Rhabdomyosarcoma soft tisue sarcomas (NRMSSTS) are infrequent malignant tumors in children. Treatment depends on histology, biologic behaviour and staging. Mexico implemented a national treatment protocol for this entity seven years ago. We present herein the results obtained at the National Institute of Pediatrics.
Methods: We studied a cohort of patients with NRMSSTS between january 2007 and january 2014. Patients were categorized as high or low risk according to clinical and histological features. Depending on risk stratification, treatment included surgery and radiotherapy, with or without 6 cycles of ifosfamide and doxorrubicine.
Results: There were 22 patients with a median age of 9 years. 55% were males with a ratio of 1.2:1. Median time between first symptoms and arrival to our department was 3.3 months. Most frequent histologic types were peripheral nerve sheath tumor (PNST) and sinovial sarcoma (SS). Every patient underwent surgical resection of the primary tumor. 95% received radiotherapy. Sixteen patients were categorized as high-risk, thus reciveing chemotherapy. Overall survival was 50%. However, for the low-risk group, survival was 85%, compared with a 45% survival rate for the high-risk group (p = 0.05). (Table 1)



Conclusions: NRMSSTS are an heterogenous group of neoplasms. Prognosis depends on histology and staging. In low-risk patients, surgery and radiotherapy alone offer a good chance for survival. However, in high-risk patients, prognosis remains dismall in spite of multimodal therapy. New treatment strategies are required for this group of patients.

EP-597

MALIGNANT RHABDOID TUMOR OF THE POSTERIOR BLADDER WITH SEVERAL LOCAL RELAPSES

M.O. Candir[1], C. Bozkurt[1], S. Yesil[1], G. Tanyildiz[1], S. Tekgündüz[1], S. Toprak[1], G. Sahin[1]

[1]Pediatric Oncology, Dr. Sami Ulus Pediatric Research and Training Hospital, Ankara, Turkey

Objectives: Malignant rhabdoid tumors are generally characterised aggresively and overall survival is approximately%20-25 if not sugically resected. One of the supressor genes, INI-1 exone mutation or deletion could be found in these kind of tumoral tissue. Central nervous and urinary systems are frequently involved. Extra-renal and extra-cranial involvements could be seen in thorax, liver, cervical region and axilla. Multimodal therapies combined with surgical resection are the best treatment option.
Methods: Here we present a case diagnosed malignant rhabdoid tumor of the posterior bladder represented with renal failure when 12 years old. He is now 18 years old and had local relapses for five times and exprienced several surgical interventions.
Results: Rhabdomyosarcoma protocol firstly initiated but after that vincristine, adriamicyn, topotecan protocol; after that vinorelbine, cytarabine protocol; than oral etoposide protocols have been used until the last relapse and surgery. Total 5600 cGy dosage radiotherapy was applied following the end of firstly used rhabdomyosarcoma protocol. Pathological immunhistochemical examination of tumoral tissue from the resection material revealed INI-1 mutation.
Conclusions: Our case is now in remission with repeating eight cures of gemcitabin combined with docetaxel therapy after surgery.

EP-598

COMPARATIVE STUDY ON 184 PEDIATRIC AND ADULT PATIENTS WITH RHABDOMYOSARCOMA

Q. Zhao[1], J.f. Wang[1], Z.y. Li[1]

[1]Department of Pediatric Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

Objectives: To compare the prognostic factors and clinical differences between pediatric and adult rhabdomyosarcoma.

Methods: We reviewed the clinical data of 184 patients who were diagnosed to have RMS by pathology and had complete follow-up data between January 1993 and June2009 in our Hospital. There were 93 pediatric patients and 91 adult patients.
Results: The 1,3and 5-year survival rates in the pediatric group were 90.3%, 62.0%, 43. 1%, respectively, while these were 86.8%,35.1%, 20. 0%, Significant statistical differences were showed between the pediatric group and adult group in the factors of histological subtypes, primary site and distant metastasis by Chi-square Test.
Conclusions: The prognosis of adult with rhabdomyosarcoma is significantly worse than pediatric tumor, and the differences of the histological subtypes, primary site and distant metastases between the two groups should be responsible for it.

SUPPORTIVE CARE/PALLIATIVE CARE

EP-599

OUTCOME OF PATIENTS WITH SOLID TUMORS AFTER FIRST EVENT

A. Al- Nassan[1], A. Al-Nassan[1], S. Awadi[1], I. Sultan[1]

[1]*Pediatric, King Hussien Cancer Center, Amman, Jordan*

Objectives: Limited publications are available regarding the outcome of pediatric patients with solid tumors after first event. Recognizing the outcome of this group of patients can help in selecting patients who may benefit from further treatment and improve utilization of palliative care.
Methods: A retrospective chart review of patients registered in POND database in King Hussein Cancer Center from Jun2006 till Dec2013. Events were defined as relapse, progression or refractory disease. Patients who had death as their first event were excluded.
Results: Among 615 patients with solid tumors, 131 (46% females) experienced an event after a median of 9.6 months (range, 0 to 47) after diagnosis. Median age at relapse was 7.2 years (range 0.1 to 19.4). The most common disease categories were bone tumors (31%), neuroblastoma (26%), soft tissue sarcomas (13%) and renal tumors (11%). The 4-year overall survival of the whole group was $12\% \pm 3.8\%$. The 4-year overall survival for different disease categories were as follows: bone tumors ($4 \pm 4\%$), neuroblastoma ($11 \pm 7\%$), soft tissue sarcomas ($8.3 \pm 7.9\%$) and renal tumors ($16 \pm 13\%$). We did not find significant differences between patients who received and did not receive multiagent chemotherapy in terms of survival andthe last reported pain score. Patients who did not receive chemotherapy were more likely to spend less time in hospital and to have earlier placement of DNR orders.
Conclusions: The findings of our study are important in highlighting the importance of early palliative care for this group of patients. The burden of treatment on the family and the unit are not justified in most cases where open clinical trials are not available.

EP-600

PEDIATRIC PALLIATIVE PROGRAM IMPLEMENTING HOME CARE IN JORDAN

A. Al- Nassan[1], S.H. Awadi[1], I.H. Mezher[1], S. Jmean[1], M. Wawi[1], A. Hmood[1], I. Sultan[1]

[1]*Pediatric, King Hussien Cancer Center, Amman, Jordan*

Objectives: Pediatric palliative care decreases pain and suffering of children with cancer and their families. It also decreases the burden on busy units allowing them to treat more patients. Home care is an essential extension of this important service.
Methods: We started a home care service attached to our pediatric palliative care program. A driver, 2 nurses and a social worker made daily visits to a prepared list of patients. Vists vary in duration from 0.5 to 3 hours based on patients' needs. The frequency to individual patient varied according to specific needs. After 6 months of starting home care visits, data was collected by visiting nurses using a data collection sheet. Data collected included demographics, disease -related data, home care issues, and family social issues.
Results: There were 30 patients included in this analysis (10 females). Patients with CNS tumors (14) and solid tumors (12) were the majority of referred patients. After referral, the majority of patients had pain well controlled (N = 27,90%) using one or more medications. Emergency room visits (median = 2 per patient) and hospital admission days (median = 3) were minimal and reflected satisfaction with home care. Six patients (20%) needed enteral feeding by nasogastric or PEG tubes. Two patients needed intensive wound care for deep ulceration. Three patients were referred back to the center for palliative procedures (Tracheostomy, VP shunt placement). Of note, families represented typical social status in Jordan with a median income of 300 JD (420 US$ per month) and a median family size of 5.
Conclusions: Home care is essential even in low-income countries to enhance the services of palliative care. With limited resources, we were able to demonstrate the successful implementation of the service and had impact on the quality of life of patients at home with minimal utilization of services at the center.

EP-601

COMPOSITE ADVERSE EVENT OUTCOME IN PROLONGED FEBRILE NEUTROPENIC PEDIATRIC CANCER PATIENTS

M.M. Alam[1], A. Naqvi[2], A. Belgumi[3], Z. Fadoo[4]

[1]*Pediatric & Child Health, Aga Khan University Hospital, Karachi, Pakistan;* [2]*Pediatric Hematology/Oncology, Sick Kid, Toronto, Canada;* [3]*Pediatric Hematology/Oncology, KFSH&RC, Riyadh, Saudi Arabia;* [4]*Pediatric Hematology/Oncology, Aga Khan University Hospital, Karachi, Pakistan*

Objectives: Pediatric cancer patients (PCP) with prolonged neutropenia have increased risk for severe, recurrent or new bacterial and fungal infection and adverse outcome. The aim of this study was to identify the risk factors associated with adverse outcomes in this group.
Methods: This study was a retrospective analysis of clinical data on PCP with prolonged febrile neutropenia (PFN) from a tertiary health care center of Pakistan.
Results: We analyzed 135 hospitalizations of PCP with PFN. The mean age was 7.3 ± 4.1 years. There was 98 (72.6%) male. The mean duration was 10.3 ± 5.2 days (range:1–25 days). Acute leukemia 88 (65.2%) were the most common diagnosis followed by lymphomas 19 (14.1%) and solid tumors. Cause of neutropenia were identified in only 58 (43%) patients, out of BSI 22 (16.3%), pneumonia 15 (11.1%), fungal infection 13 (9.6%), infectious diarrheas 5 (3.7%) and UTI 3 (2.2%). More than 50% of the patients had severe myelosuppression. The composite adverse event outcome were observed in 28 (20.7%) of patients, with in-hospital mortality occurring in 7 (5.2%), PICU admission occurring in 12 (8.9%) and inotropic support was required in 9 (6.7%). On logistic regression analysis cancer type AML (AOR, 7.63 [95% confidence interval, 1.12-91.35]; $P < 50$/ cm (AOR, 10.83 [95% CI, 1.37-65.74]; $p < 0.001$), Platelets count < 50,000/ cm (AOR, 5.17 [95% CI, 1.17-23.78]; $p < 0.001$), BSI (AOR, 2.33 [95% CI, 0.84-15.79]; p 0.05) and fungal infection (AOR, 4.26 [95% CI, 1.34-86.57]; $p < 0.001$) were found as independent risk factors associated with development of composite AE outcome in PCP with PFN.
Conclusions: AML, severe myelosuppression, blood stream infection and fungal infection were identifiable risk factors associated with development of adverse event outcome in PCP with PFN. Prospective studies in large cooperative trials may be beneficial in evaluating these risk factors further.

EP-602

FEBRILE NEUTROPENIA IN PEDIATRIC CANCER PATIENTS: EXPERIENCE FROM A TERTIARY HEALTH CARE FACILITY OF PAKISTAN

M.M. Alam[1], S. Qureshi[1], R. Matloob[1], Y. Channa[1], N. Mushtaq[1], Z. Fadoo[1]

[1]*Pediatric & Child Health, Aga Khan University Hospital, Karachi, Pakistan*

Objectives: Febrile neutropenia (FN) is a common complication of therapy among children with cancer. The aim of this study was to describe the demographic, clinical feature, laboratory data and management outcomes of FN in pediatric cancer patients.
Methods: This study was a retrospective analysis of clinical data on pediatric cancer patients with febrile neutropenia from a tertiary health care facility of Pakistan.
Results: We analyzed 872 hospitalizations of pediatric cancer patients with FN. The mean age of the study population was 5.32 ± 4.07 years. There was 559 (64.1%) male and 313 (35.9%) female. ALL (n = 590; 67.7%) was the most common diagnosis followed by AML (n = 105; 12.2%), lymphoma (n = 86; 9.9%) and sarcomas (n = 51; 5.8%). Cause of neutropenia were identified in only 58 (43%) patients, out of URTI (n = 192; 22%), BSI (n = 58; 6.6%), pneumonia (n = 31; 3.5%), infectious diarrheas (n = 16; 1.8%) and UTI (n = 11; 1.3%). Age less than 5 year (OR = 1.5; p = 0.043), AML (OR = 1.8; p = 0.019), patients who received chemotherapy within 2 week of FN (OR = 1.9; p = 0.007), severe neutropenia ANC < 50/ cm (OR = 1.5; $p < 0.041$), platelets count < 50,000/ cm (OR = 1.5; $p < 0.027$), Fungal infection (OR = 15.6; p 5 days) in pediatric cancer patients. A total of 25 (2.9%) patients were required PICU admission and overall 12 (1.4%) patients were expired. Both outcome variables were statistically significant regarding PICU admission (9% Vs 2%; OR = 5.4; $p < 0.001$) and mortality rate (5.2% Vs 0.8%; OR = 8.1; $p < 0.001$) in patients with prolonged FN versus FN respectively.
Conclusions: Younger age, AML, severe myelosuppression, fungal infection and pneumonia were identifiable risk factors associated with prolonged FN. Outcomes regarding PICU admission and mortality was worse in patients who had prolonged FN.

EP-603

PROLONGED FEBRILE NEUTROPENIA: RISK FACTORS AND OUTCOME IN PEDIATRIC ONCOLOGY PATIENTS

M.M. Alam[1], S. Qureshi[1], R. Matloob[1], Z. Fadoo[1]

[1]*Pediatric & Child Health, Aga Khan University Hospital, Karachi, Pakistan*

Objectives: Pediatric cancer patients with febrile neutropenia (FN) have increased risk for severe, recurrent or new bacterial and fungal infection. Although prompt initiation of empirical antibacterial antibiotics has leads to substantial improvement in morbidity and mortality, infectious complications still persist. The aim of this study was to describe the demographic, clinical feature, laboratory data, risk factors and outcomes of FN in pediatric cancer patients.
Methods: This study was a retrospective analysis of clinical data on pediatric cancer patients with FN from a tertiary health care center of Pakistan.

Results: We analyzed 872 hospitalizations of pediatric cancer patients with FN. The mean age of the study population was 5.32 ± 4.07 years. There was 559 (64.1%) male and 313 (35.9%) female. ALL (67.7%) was the most common diagnosis followed by AML (12.2%), lymphoma (9.9%) and sarcomas (5.8%). Cause of neutropenia was identified in only 58 (43%) patients, out of URTI (22%), BSI (6.6%), pneumonia (3.5%), infectious diarrheas (1.8%) and UTI (1.3%). Additionally, the median neutrophil count and platelet count revealed profound myelosuppression in more than 50% cases. Age less than 5 year ($p = 0.043$), AML ($p = 0.019$), patients who received chemotherapy within 2 week of FN ($p = 0.007$), severe neutropenia ANC $< 50/$ cm ($p < 0.041$), platelets count $< 50{,}000/$ cm ($p < 0.027$), Fungal infection (p 5 days) in pediatric cancer patients. A total of 25 (2.9%) patients were required PICU admission and overall 12 (1.4%) patients were expired. Both outcome variables were statistically significant regarding PICU admission and mortality rate in patients with prolonged FN versus FN respectively.
Conclusions: Younger age, AML, severe myelosuppression, fungal infection and pneumonia were identifiable risk factors associated with development prolonged FN. Outcomes regarding PICU admission and mortality were worse in patients who had prolonged FN.

EP-604

ADRENAL INSUFFICIENCY IN CHILDREN WITH CANCER PRESENTING WITH FEVER IN NEUTROPENIA

S. Bank[1], C.E. Flück[1], O. Teuffel[1], P. Agyeman[2], G. Hofer[1], K. Leibundgut[1], R.A. Ammann[1]

[1]Department of Pediatrics, University of Bern, Bern, Switzerland; [2]Department of Pediatrics and Institute for Infectious Diseases, University of Bern, Bern, Switzerland

Objectives: To detect whether children with cancer have a sufficient adrenal function at presentation with fever in neutropenia (FN).
Methods: In the setting of a a prospective observational single-center study, serum was sampled in pediatric patients with cancer presenting with FN, and stored at -20˚C. Cortisol concentration was measured by a commercially available ELISA. It was correlated to different clinical characteristics, including cumulative doses of past corticosteroid therapy. Cortisol concentrations < 500 nMol/L were considered insufficient in the stressful FN situation. This study was approved by the Institutional Review Board. Patients, if able to judge, and their legal guardians gave written informed consent prior to study entry.
Results: Serum samples were available in 21 (49%) of 43 FN episodes, from 14 patients aged 1.2 to 16.5 years. Patient characteristics and outcome were comparable in patients with and without serum samples. Freezing time was not significantly associated with cortisol. Median cortisol was 435 nMol/L (IQR, 262 to 653; range, <28 to 1301), with 11 concentrations <500 nMol/L (52%; exact 95% CI, 30% to 72%). Cumulative doses of corticosteroid therapy within one month preceding FN were tendentially associated with cortisol (Spearman's rho, -0.39; 95% CI, -0.85 to 0.07, $p = 0.080$), while earlier doses were not. Cortisol was not significantly associated with patient characteristics, temperature at presentation, or outcomes (adverse events, duration of hospitalization and of intravenous antimicrobial therapy).
Conclusions: At presentation with FN, about one half of pediatric patients with cancer had an insufficient adrenal stress response, which was associated with past corticosteroid therapy. Larger prospective studies of adrenal response in FN are warranted.

EP-605

THE INFLUENCE OF DIFFERENT FEVER DEFINITIONS ON THE RATE OF FEVER IN NEUTROPENIA DIAGNOSED IN CHILDREN WITH CANCER

R.A. Ammann[1], O. Teuffel[1], P. Agyeman[2], N. Amport[1], K. Leibundgut[1]

[1]Department of Pediatrics, University of Bern, Bern, Switzerland; [2]Department of Pediatrics and Institute for Infectious Diseases, University of Bern, Bern, Switzerland

Objectives: The temperature limit defining fever (TLDF) is based on scarce evidence. This study aimed to determine the rate of fever in neutropenia (FN) episodes additionally diagnosed by lower versus standard TLDF.
Methods: In a single center using a high TLDF (39.0˚C tympanic temperature, $\text{Limit}_{\text{Standard}}$), pediatric patients treated with chemotherapy for cancer were observed prospectively. Results of all temperature measurements and CBCs were recorded. The application of lower TLDFs ($\text{Limit}_{\text{Low}}$; range, 37.5˚C to 38.9˚C) versus $\text{Limit}_{\text{Standard}}$ was simulated *in silicon*.
This study was approved by the Institutional Review Board. Patients, if able to judge, and their legal guardians gave written informed consent prior to study entry.
Results: In 39 patients, 8896 temperature measurements and 1873 CBCs were recorded during 289 months of chemotherapy. Virtually applying $\text{Limit}_{\text{Standard}}$ resulted in 34 FN diagnoses. At $\text{Limit}_{\text{Low}}$ 38.4˚C 10 additional FN were recorded (Poisson rate $\text{ratio}_{\text{Additional/Standard}}$, 0.29; 95% lower confidence bound, 0.16). Further lowering $\text{Limit}_{\text{Low}}$ to 37.5˚C led to earlier diagnosis in the majority of FN (median, 4.5 hours; 95% CI, 1.0 to 20.8), and to 53 additional FN diagnosed. In 51 (96%) of them, spontaneous defervescence without specific therapy was observed in reality.
Conclusions: Lower TLDFs led to many additional FN diagnoses, implying overtreatment because spontaneous defervescence was observed in their vast majority. The question if the high TLDF is not only efficacious but as well safe remains open.

EP-606

POSACONAZOLE SALVAGE THERAPY IN IMMUNOCOMPROMISED CHILDREN WITH MALIGNANCIES OR IMMUNE DEFICIENCIES: A PRELIMINARY REPORT

S. Anak[1], A. Somer[2], M. Sutcu[2], E. Uysalol[3], M. Bulut[4], S. Hancerli Torun[2], S. Karaman[3], N. Salman[2], A. Unuvar[3], Z. Karakas[3]

[1]Pediatric Hematology & Oncology, Medipol University Medical Faculty, Istanbul, Turkey; [2]Pediatric Infectious Diseases, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey; [3]Pediatric Hematology & Oncology, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey; [4]Pediatrics, Istanbul University Istanbul Medical Faculty, Istanbul, Turkey

Objectives: Posaconazole is an extended spectrum triazole with invivo and invitro activity against Aspergillus and mainly used for prophylaxis in immunocompromised children with malignancies. We present five cases with refractory and/or relapsing invasive pulmonary Aspergillosis (IPA) treated with Posaconazole as salvage therapy.
Methods: All five patients with either relapsed leukemia (n:3) or chronic granulomatous disease (CGD) (n:2), of age $\geq$13 years (median: 14, range: 13-17) were treated with Posaconazole (200mg tid, po) for IPA resistant to Voriconazole or combination therapies for 15 days to 4 months till radiologic regression and/or resolving Galactomannan. Their initial diagnosis was based on clinical symptoms, weekly Galactomannan survey and/or radiologic findings while they were severely immunocompromised due to their diseases and or agressive treatments including BMT.
Results: Two of the three relapsed leukemia patients expired in 15 days to 3 months after the initiation of Posaconazole mainly because of the progression of their underlying disease. One patient was responsive and currently under treatment for IPA since 4 months. Two patients with CGD were responsive and still under treatment for 3 and 4 months. The drug is well tolerated without ant majör side-effects.
Conclusions: An azole-based, mould-active antifungal, Posaconazole might be an efficient alternative salvage therapy for pediatric patients with resistant IPAs. Although it is a safe drug in children, its efectiveness is dependant on factors like the state of underlying disease, drug absorbtion and metabolism, but iv formulation might solve this problem in the near future.

EP-607

SUPPORTIVE CARE AFTER CHEMOTHERAPY AND RADIATION WITH A SWISH & SWALLOW GLUTAMINE + DISACCHARIDE NUTRITIONAL SUPPLEMENT TO REDUCE MUCOSITIS AND IMPROVE ENTERAL NUTRITION

P. Anderson[1]

[1]Pediatrics, Levine Cancer Institute, Charlotte, USA

Objectives: Two of the of the most common supportive care questions parents and patients ask are: 1) What foods and diet can help fight cancer, and 2) do you recommend nutrition supplements? Prior evidence has shown that glutamine + disaccharide suspensions can reduce mucosal toxicity; glutamine supplementation of diet may also be associated with less cancer growth by facilitating improved lymphocyte proliferation and immune function. However, because of time to write prescriptions for glutamine + disaccharide suspensions, pharmacy to compound, taste of sucrose vehicle, and caking during refrigeration, a more convenient product was needed. Therefore, a powder that contains glutamine, sucrose + trehalose, suspending agents, and orange or grape flavoring (Healios) was developed.
Methods: Glutamine powder (from Healiosproducts.com) as 1 scoop containing 4 gm glutamine + disaccharides is added to 50mL water, swished 10 seconds, and swallowed twice/day during and after chemotherapy or radiation involving mouth, throat or esophagus.
Results: Rapid facilitated uptake of glutamine by disaccharide reached peak uptake within 10 seconds. Glutamine suspended in water had poor cellular uptake. Glutamine+ disaccharide suspensions were successful in in reducing mucosal toxicity of cancer therapy in 1 pilot and 4 different randomized, placebo double-blind trials, 3 of which included children. Glutamine suspensions were needed not only during, but also after completion of radiation for at least an additional 7 days - probably to facilitate healing of residual damage.
Conclusions: A glutamine + disaccharide supplement has been developed that has high patient acceptance; it is useful when chemotherapy and/or radiation have high likelihood of causing stomatitis, pharyngitis, and/or esophagitis. If there are enteral nutritional concerns, care providers can consider recommending this safe and inexpensive nutritional supplement as a rational supportive care measure to reduce and ameliorate mucosal toxicity of cancer therapy and to promote better enteral nutrition during chemotherapy and/or radiation.

EP-608

ESTABLISHING A PAEDIATRIC PALLIATIVE CARE UNIT WHERE NON/INADEQUATE FACILITIES EXIST – CHALLENGES AND OPPORTUNITIES

P. Bagai[1], L. Crack[1], S. Ahuja[1], H. Anis[1], R. Arora[2]

[1]Quality Care Research and Impact, Cankids…Kidscan, New Delhi, India; [2]Medical Oncology, Max Super-Specialty Hospital, New Delhi, India

Objectives: Can kids support children and their families from the time of diagnosis of cancer through treatment and on to survival, reintegration or into bereavement in 34 centres across India. Few children have access to palliative care within cancer centres in India and in order to address this need Cankids has set up a dedicated palliative care service for children in Delhi with the vision to develop a model of cost effective paediatric palliative care support pan India.
Methods: An inpatient facility was opened in New Delhi in August 2012 close to the major cancer centres, with easy access to public transport which can accommodate and care for up to 14 children plus attending parents. Creating a child friendly, hygienic environment was essential in order to nurse children undergoing chemotherapy with increased risk of infection. Educational support and an activities programme, together with counselling, psychological support and physical therapy were considered core components of the service which are provided free of charge.
Results: In the first year of operation there were 197 admissions and a bed occupancy ranging from 50 to 130%. Around 75% of admissions were for less than 14 days with only 9% of children needing to stay longer than 2 months. More males (71%) than females (29%) were admitted supporting the sad reality that females are neglected even at the end of life.
Conclusions: The Cankids palliative care centre fills gaps at cancer centers with no or inadequate palliative care facilities. The need to provide 24 hour access to suitably trained medical and nursing staff to comply with nursing home regulations and palliative care standards proved a major challenge and is likely to limit the development of inpatient services in favour of a nurse led, doctor supported outpatient/day care model to disseminate pan India.

EP-609

A SURVEY OF IMMUNISATION PRACTICES IN CHILDREN WITH CANCER IN INDIA

S. Prabha[1], P. Bagai[1], R. Arora[2]

[1]Quality Care Research and Impact, Cankids...Kidscan, New Delhi, India; [2]Medical Oncology, Max Super-Speciality Hospital, New Delhi, India

Objectives: Children with cancer, when on treatment and immunosuppressed, are at risk of infection from live vaccines and do not mount an adequate protective response to inactivated vaccines. Hence, immunizing them during and after treatment requires special considerations. We wanted to identify the immunization practices for these children in India.
Methods: Clinicians attending the Indian Pediatric Oncology Initiative meeting, the Indian Pediatric Oncology Group meeting, and the Pediatric section of the Indian Cancer Congress in 2013 were invited to complete a questionnaire.
Results: Respondents were from 37 institutions in 21 cities (49% public sector; 46% annual caseload >100 new patients). 46% advised inactivated but not live vaccines and 40% advised no vaccine during cancer treatment to the child. 67% recommend Hepatitis B vaccine (83% public hospitals, 53% private hospitals, $p = 0.08$) and 34% annual Influenza vaccine (25% public hospitals, 42% private hospitals, $p = 0.48$) to the child undergoing treatment. 76% recommenced vaccination 6 months after completion of treatment. Revaccination was in the form of booster + continue normal schedule 32%, continue normal schedule 30%, repeat entire immunization schedule 16% and measure antibody levels and then decide 11%.
Conclusions: There is heterogeneity in the immunization practices of children with cancer. Development and dissemination of immunisation guidelines specific to India in children who are undergoing or have completed cancer treatment would be useful in standardizing practice.

EP-610

QUALITY OF LIFE OF CHILDREN WITH CANCER TREATED WITH PALLIATIVE CARE: A QUALITATIVE STUDY ON PROFESSIONALS' PERCEPTIONS

J. Avoine-Blondin[1], M. Lahaye[2], V. Parent[3], M. Duval[4], N. Humbert[5], S. Sultan[4]

[1]Hemato Oncology, CHU Sainte-Justine, Montreal, Canada; [2]Hemato Oncology, Université Catholique de Louvain, Louvain-la-Neuve, Belgium; [3]Psychology, Université de Sherbrooke, Longueuil, Canada; [4]Hemato Oncology, CHU Sainte-Justine Université de Montréal, Montreal, Canada; [5]Palliative care, CHU Sainte-Justine Université de Montréal, Montreal, Canada

Objectives: The Steering Commitee of the Canadian Cancer Society (2011) estimated that in 2011, 1,310 people aged between 0 and 19-year-old have been diagnosed with cancer. Close to 1 in 7 will die from it. Partly due to the deteriorated health status of these children, clinical and ethical literature has raised the question of the valid definition of quality of life (QoL) of children in palliative care. The ability of professionals to define and evaluate QoL is key to make appropriate decisions in the trajectory of children and end-of-life issues. Although the concept behind adult QoL in palliative care has been clarified and is now subjected to measure, this is not the case in pediatric palliative care. Our objective is to describe the main dimensions of QoL in the context of pediatric palliative care in hematology-oncology, based on professionals' views.
Methods: Semi-structured interviews were conducted with 20medical and non-medical professionals of CHU Sainte-Justine Hematology-Oncology department. The interview guide was inspired by questions used by Hinds & al. (2004) in their qualitative study to assess how children with cancer perceived their QoL. During interviews, professionals were asked about their representations of QoL of children with cancer receiving palliative care, based on their past experiences. Interview data were analyzed using thematic analysis and coded using QDAMineur.
Results: The analysis identified dimensions of QoL in this context with the following elements being prominent aspects: social relationships, physical and psychological health status, autonomy, unmet needs and pain. Verbal descriptions of professionals insisted on preserved abilities and positive behaviors and emotions such as smiling, playing, etc.
Conclusions: The representation of professionals on QoL in this context is marked by maintained abilities including social ones likely to be changing over time. It makes it possible to develop appropriate measures to evaluate QoL in very ill children.

EP-611

ONE-THIRD PATIENTS WITH FEBRILE NEUTROPENIA AND UPPER RESPIRATORY TRACT INFECTION HAVE AN IDENTIFIABLE VIRAL ISOLATE IN NASOPHARYNGEAL ASPIRATE: A PROSPECTIVE OBSERVATIONAL STUDY FROM NORTH INDIA

K. Ananta Rao[1], S. Sarkar[2], D. Bansal[1], R.K. Ratho[2], A. Trehan[1], R.K. Marwaha[1]

[1]Pediatric Hematology-Oncology unit Dept. of Pediatrics Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India; [2]Virology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Objectives: The aim was to identify viruses in nasopharyngeal aspirate in children with hematological malignancy with febrile neutropenia and upper respiratory tract infection.
Methods: Hospitalized children, on treatment for hematological malignancies, with febrile neutropenia and clinical evidence of upper respiratory tract infection (rhinorrhea and/or cough) were enrolled. Patients with lower respiratory tract infection were excluded. Nasopharyngeal aspirate was obtained in each patient for qualitative polymerase chain reaction for 5 viruses: Respiratory syncytial virus, Influenza A, B, Human parainfluenza virus-3 and Human Metapneumovirus.
Results: The study included 57 children; all were receiving broad-spectrum antibiotics. The mean age was 6 years (range: 0.5-14). The majority (89.5%) had ALL. At admission, the duration of fever ranged from 1-10 days (mean: 2.3 ± 1.3). The absolute-neutrophil-count was $<200/mm^3$ in 51 (89.5%), and $200\text{-}500/mm^3$ in 6 (10.5%). Platelet count was $<20 \times 10^9/L$ in 23 (41%) patients. The mean duration of hospitalization was 5.7 days (range: 3-16). Viruses were isolated in 19 (33%) patients. The most common identified virus was Influenza (A and B) (62% of positive cases), followed by RSV and HPIV-3 (14% each), and hMPV (10%). Two had coinfection. Age ($p = 0.35$), ANC ($p = 0.68$), phase of chemotherapy ($p = 0.36$) or duration of hospitalization ($p = 0.73$), did not influence viral positivity. Patients with a positive viral isolate were more in winter/spring (57%), as compared to the rest of year (15%) ($p = 0.036$). None of the Influenza viruses were isolated in summer/autumn. The procedure of nasopharyngeal aspirate was well tolerated with transient epistaxis in 44%. No bacterial organism was isolated from blood culture in any patient. There were no complications/deaths.
Conclusions: One-third children with febrile neutropenia and upper respiratory tract infection had an identifiable viral isolate in nasopharyngeal aspirate along with a sterile blood culture. Trials need to be conducted which would explore the option of early cessation of antibiotics in this select group.

EP-612

PATIENT REPORTED OUTCOMES IN CLINICAL TRIALS AND RANDOMISED CLINICAL TRIALS IN CHILDREN RECEIVING PALLIATIVE OR END OF LIFE CARE

C. Barton[1], L. Brook[2]

[1]Paediatric Oncology, Alder Hey Children's Hospital, Liverpool, United Kingdom; [2]Paediatric Palliative Care, Alder Hey Children's Hospital, Liverpool, United Kingdom

Objectives: The purpose of this study was to identify published research describing the use of patient reported outcomes (PRO) in clinical and randomised clinical trials in children receiving end-of-life/palliative care, and explore the medical conditions, health care domains and clinical trends that they describe.
Methods: A literature search was conducted using the NHS-Evidence (MEDLINE, CINAHL, EMBASE, PsychINFO). All search terms were cross referenced to the thesaurus of each database. Results were limited to < 18 years-of-age, English language and clinical-trials/randomised clinical-trials.
Results: A total of 18 articles were identified (PsychINFO 4, EMBASE 4, CINAHL 10, MEDLINE 0) Defining a PRO as any report of the status of the child's health condition that came directly from the patient, without interpretation by a clinician or other, no articles were included as none described a PRO, or relevant measure or tool. A manual literature and internet search further identified no relevant articles.
No database included PRO as a search term within their Thesaurus. Further to this, there was low consistency between the definition (i.e. scope) and indexing of basic search terms (e.g. end of life) as referenced in the Thesaurus of each database.
Conclusions: Despite increasing interest in the use and development of patient reported outcomes in the development of health care services, their use as primary and even secondary outcomes in clinical trials within paediatric palliative care research remains limited at best.

Perhaps the greatest barrier is the lack of developed, fit for purpose and validated outcome measures. A significant amount of research needs to be done before PRO can be used to measure and evaluate the benefit of potential treatments at the end of life in children.

EP-613

PREVALENCE AND OUTCOME OF MULTIDRUG RESISTANT BACTERIAL SEPSIS IN CHILDREN ON CHEMOTHERAPY

A. Bhattacharyya[1], S. Krishnan[1], S. Dalvi Mitra[1], R. Tiwari[1], D. Ghosh[1], S. Ferdousi[1], V. Saha[1], S. Bhattacharya[2]

[1]Paediatric Oncology, Tata Medical Center, Kolkata, India; [2]Microbiology, Tata Medical Center, Kolkata, India

Objectives: Multidrug resistance (MDR) gram negative sepsis is associated with high mortality in children undergoing chemotherapy. We report on the prevalence and outcome of MDR bacterial sepsis in children at a tertiary cancer centre in India.
Methods: Positive blood cultures obtained from all in-patients from Jan 2012 -Dec 2013 were reviewed. MDR in gram negative bacteria were defined as those producing carbapenemase, extended spectrum beta lactamase (ESBL) or those resistant to multiple broad spectrum antibiotics. All patients admitted with febrile neutropenia initially received Cefepime empirically and changed to Meropenem if ESBL organisms were isolated. Patients with carbapenemase producing organisms received Colistin in addition.
Results: Of the 335 blood cultures sent during the study period, 105 positive blood cultures were obtained in 65 patients with a mean age of 6.6 years (range 0.9-16.1 years). Forty seven patients (72%) had hematological malignancies and 18 (28%) had solid tumors. 28/105 (26.6%) blood cultures were identified as probable non-significant isolates. Of the remaining 77, MDR gram-negative organisms were identified in 24 (31%) [ESBL 8, carbapenemase producer 15, other MDR 1], and obtained from 20 patients. Thus 17/47 (36%) and 3/18 (17%) of patients with hematological and non-hematological malignancies respectively had MDR organisms isolated from blood cultures. Three (15%) patients, all with hematological malignancies and carbapenemase producing organisms, succumbed to their infections; while prolonged intravenous antibiotic successfully cleared the MDR in the others.
Conclusions: In our experience, MDR organisms are isolated in a third of positive blood cultures obtained from children with cancer undergoing therapy. Over half of these were carbapenemase producing MDR's. MDR's were also more likely to be isolated from patients with hematological malignancies. Early identification and prompt intervention can decrease mortality associated with MDR organisms. Nevertheless, more effective antibiotics against carbapenemase resistant organisms are required especially with the emergence of Colistin resistance.

EP-614

ASSESSMENT OF NUTRITIONAL STATUS IN NEWLY DIAGNOSED PEDIATRIC PATIENTS: MAYO CLINIC EXPERIENCE

B. Bidadi[1], A. Al Nofal[1], P. Marri[1], M. Lamprecht[1], C. Arndt[1]

[1]Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, USA

Objectives: Children newly diagnosed with cancer are at high risk for developing weight loss. Causes include treatment related adverse effects and disease related reasons. Despite the high prevalence of malnutrition, there is a paucity of data on appropriate management. We reviewed the nutritional status of pediatric cancer patients receiving chemotherapy and/or radiation who were diagnosed and treated at our institution from 2011 to 2012.
Methods: Retrospective chart analysis. Patients older than 21 years or younger than 2 years were excluded.
Results: Our cohort included 55 patients (31 male, 24 female) with mean age at diagnosis of 11.1 +/-5.6 years. All patients received chemotherapy and thirty received radiation therapy. Diagnoses included leukemia (n = 11), lymphoma (n = 13), central nervous system tumors (n = 10), sarcomas (n = 12), wilms tumor (n = 5) and other tumors (n = 4). 29% of patients had 5-10% weight loss (n = 16), 29% had between 10 to 20% weight loss (n = 16), and 11% had >20% weight loss (n = 6). Median time to nadir weight loss was 2.1 (0.9 to 3.7) months. Patients with metastases (n = 9) had a higher median percent weight loss (12.5%, range of 4.4 to 20.8%) than other patients (8.2%, range of 3.3 to 13.6%). Patients with osteosarcoma had the greatest median weight loss after eight weeks (7.9%, range of 1.8 to 10.9%). Eighteen patients received either nasogastric (n = 15, 27%) or gastrostomy tube feeds (n = 3, 5%). Patients receiving nasogastric or gastrostomy feeds had a median percent weight loss of 9.5% (6 to 15%) at the time feeds were started. Median time to tube insertion was 2.8 months (1.2 to 4.9).
Conclusions: Our cohort had a high prevalence of weight loss especially in patients with osteosarcoma and metastatic disease. Patients tended to have the most weight loss within about eight weeks from initiation of therapy. Our results highlight the need for early nutrition intervention in newly diagnosed cancer patients.

EP-615

SYMPTOMS AND SUFFERING PERCEPTION AT THE END OF LIFE OF CANCER CHILDREN AND THE IMPACTS ON THE CAREGIVERS

E. Boldrini[1]

[1]Pediatric, Barretos Cancer Hospital, Barretos, Brazil

Objectives: Little is known about the symptoms and suffering at the end of life in children with cancer. Facing this, we assessed the perception that parents have of the symptoms and suffering that the children underwent at the end of life, and the presence of mood disorders and grief reactions in the parents and their correlations.
Methods: The casuistics comprised parents whose children were admitted to Barretos Cancer Hospital with a cancer diagnosis and died between 2000 and 2010. The patients were all under 21 years old. Self- Administered questionnaires were sent by mail. A Brazil Economic Classification Criteria, a symptom scale, the Hospital Anxiety Depression Scale (HADS) and the Texas Revised Inventory of Grief (TRIG) were used.
Results: The caregivers reported an average of 10 symptoms for leukemia/lymphoma and central nervous system tumour patients and an average of 12 symptoms for solid tumour patients. There was considerable disagreement when the questionnaires were compared to the doctors' reports, even regarding the presence of pain (Kappa 0.236). With regard to caregivers, 73.7% presented symptoms of anxiety and 81.0% presented symptoms of depression. Regarding their grief, 8 of them (16.0%) presented accute grief, 19 (38.0%) presented moderate grief, 6 (12.0%) presented delayed grief, and 17 (34.0%) presented prolonged grief. There was statistical significance among education (p 0.052), economic status (p 0.021) and delayed/prolonged grief, as well as association with HADS anxiety (p 0.001) and depression (p <0.001) with delayed/prolonged grief.
Conclusions: The presence of a symptom during the last week of life of the child showed no association with complicated grief (TRIG). There was statistical significance among education (p 0,052), economic status (p 0,021) and delayed/prolonged grief, as well as association with HADS anxiety (p 0,001) and depression (p <0,001).

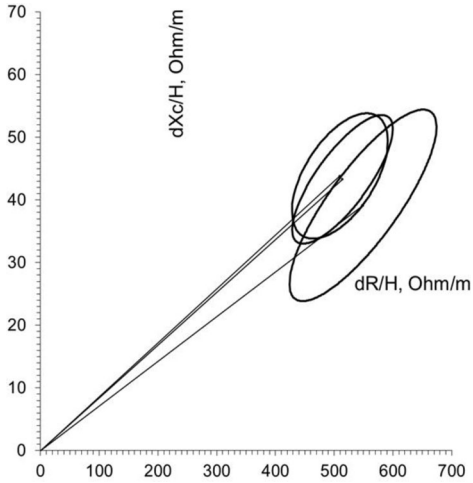
EP-616

BIOELECTRICAL IMPEDANCE VECTOR ANALYSIS (BIVA) IN CHILDREN AND ADOLESCENTS WITH CANCER UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SAO PAULO, BRAZIL

G. Bouchabki[1], K. Viani[1], J.M. Nabarrete[1], A.C.L. Silva[1], V. Oliveira[1]

[1]Nutrition, Instituto de Tratamento do Câncer Infantil Instituto da Criança do Hospital das Clínicas Faculty of Medicine University of Sao Paulo, Sao Paulo, Brazil

Objectives: The Hematopoietic Stem Cell Transplantation (HSCT) represents increased nutritional risk to pediatric oncology patients. Considering that nutritional status is a prognostic factor in HSCT, the nutritional assessment during this procedure is essential. Bioelectrial Impedance Vector Analysis (BIVA) is used for screening and monitoring of nutrition and hydration status, and the Phase Angle (PA) has been considered a prognostic and nutritional status indicator as it estimates body cell mass. The aim of this study is to investigate whether the confidence ellipses of mean vectors and PA, assessed through Bioimpedance Analysis (BIA) techniques, differed from a group of children and adolescents with cancer in three different moments of HSCT.
Methods: A prospective study was carried out with pediatric oncology patients undergoing HSCT. Resistance, reactance and PA were assessed before, 15 and 30 days after HSCT. BIVA Software 2002 was used to construct confidence ellipses of mean vectors and SPSS 22.0 to conduct the related samples Wilcoxon signed rank test with PAs.
Results: At the beginning of this study there were 12 patients (n = 12) aged from 4 to 14 years old, 50% were female. Due to clinical conditions, 2 patients were excluded in the second analysis (n = 10) and 2 more in the third analysis (n = 8). The confidence ellipses of mean vectors graph showed similarity between the three HSCT moments, as did the phase angle statistical analysis, with p = 0.513, p = 0.235 and p = 0.204 at before and 15 days, before and 30 days and 15 and 30 days after HSCT, respectively.



Conclusions: Although no statistical difference between BIVA and PA in the three analyzed moments was found in this study, a trend of decrease in both parameters was observed. However, further studies with larger samples should take place in order to better understand the behavior of those variables during HSCT.

EP-617

AN EVALUATION OF PHYSICIAN KNOWLEDGE AND ATTITUDES TO PAEDIATRIC PALLIATIVE CARE (PPC)

M.Y. Chan[1], R.T. Chin[2], D.F. Chuang[2], P.L. Koh[3]
[1]Paediatric Subspecialties, KK Women's and Children's Hospital, Singapore, Singapore; [2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; [3]Paediatrics, National University Hospital, Singapore, Singapore

Objectives: Many children with life-limiting illnesses are referred late to PPC or not at all, particularly those with non-oncological illnesses. Paediatricians' knowledge and attitudes are important because they are the primary gatekeepers. We aim to evaluate physician knowledge and attitudes to PPC, specifically when to refer and barriers faced.
Methods: This is a multi-centre, cross-sectional anonymised self-administered questionnaire study.
Results: Seventy paediatricians were recruited, majority from KK Women's and Children's Hospital or National University Hospital, with equal proportion of generalists and subspecialists and even spread of seniority. Although > 90% is aware of PPC availability, majority (63%) feel they have inadequate knowledge and skills. The roles of PPC are clear but there is no consensus on when or who to refer. Most (65%) believe that parents should decide whether to involve the sick child in decision-making. The barriers to referral identified include difficulty in matching appropriate services to patient's needs, lack of resources and parental factors, like denial, communication difficulties and fear of 'giving up'. Physician factors (like lack of knowledge, 'prognostic paralysis') are rarely a barrier. Interestingly 58% feel that burnout is common and that grieving of health care professionals remains hidden while 54% feel there is inadequate grief support. Most (61%) agree that PPC needs to be integrated into mainstream practice and that all paediatricians equipped with basic palliative skills.
Conclusions: The identified barriers can be used to set direction in PPC education and service provision so that integration into mainstream practice is possible; and all children are given the option of palliative care, regardless of stage of disease.

EP-618

EFFECTS OF STRONG OPIOIDS ON INFLAMMATORY COMPLICATIONS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

Y. Cho[1], A. Iguchi[1], T. Sato[1], J. Ohshima[1], Y. Terashita[1], M. Sugiyama[1], T. Ariga[1]

[1]Pediatrics, Hokkaido University Hospital, Sapporo, Japan

Objectives: Use of the strong opioids is increasing in the pediatric field through education about supportive care. Preconditioning for hematopoietic stem cell transplantation (HSCT) often brings patients severe mucositis, resulting in need of strong opioids. However, strong opioids can raise the risk of intestinal bacterial translocation and systemic inflammation, because of the suppression of intestinal motility, especially in strongly immunocompromised patients. Furthermore, systemic inflammation sometimes induce other complications. The purpose of this research is to estimate the association between use of strong opioids and inflammatory complications with HSCT in children.
Methods: Consecutive HSCTs for patients younger than 20 years old from October, 2003 were analyzed retrospectively. Strong opioids were used within the periods from the starting of preconditioning to the engraftment. Sedative use was excluded. The analytical factors included HSCT modality, opioid and dosage, stool frequency, fever duration, CRP, and blood culture.
Results: One hundred and nineteen HSCTs for 105 pediatric patients were done for these 10 years. Strong opioids were used in 26 HSCTs (10 autologous PBSCT, 4 related allogeneic BMT, 1 related allogeneic PBSCT, 4 unrelated allogeneic BMT, 7 unrelated allogeneic CBSCT) for severe pains that were not controlled by NSAIDs and weak opioid. Continuous intravenous Fentanyl (5.32 - 42.61mcg/kg/day, 7 - 24days) was given in 16 cases and Morphine (0.28 - 1.27mg/kg/day, 5 - 58days) in 10. Both opioids provided enough pain-killing effects. A decrease in stool frequency was observed after starting of strong opioids in most of patients. However, there was not statistical significance between use of strong opioids, kinds of opioids and duration of fever, maximum CRP.
Conclusions: These data suggest that strong opioids can be used safely in pain control during HSCT in children.

EP-619

THE EFFECTS OF USING GLUTAMINE AND HYDROXYMETHYL BUTYRATE ON THE GASTROINTESTINAL MUCOSITIS DUE TO THE USE OF METHOTREXATE IN RATS

C. Citak[1], M. Alakaya[2], S. Kaya[2], S.N. Yilmaz[3], G.D. Kulekci[3], A.A. Ozcimen[4], M.Y.B. Cimen[5]

[1]Pediatric Oncology, Mersin University Faculty of Medicine, mersin, Turkey; [2]Pediatric Oncology, Mersin University Faculty of Medicine, Mersin, Turkey; [3]Histology and Embriology, Mersin University Faculty of Medicine, Mersin, Turkey; [4]Biology, Mersin University Faculty of Science and Letters, Mersin, Turkey; [5]Medical Biochemistry, Mersin University Faculty of Medicine, Mersin, Turkey

Objectives: In this study, glutamine (Gln) and β-hydroxy β-methylbutyrate (HMB) were used combined or one by one, for the prevention of intestinal mucositis, and there was made the comparison of the efficacy of either methods.
Methods: Fifty Wistar albino rats were divided to 5 groups. All of the study groups got 20 mg/kg MTX intraperitoneally at the third day. At the third day of the experiment, 6 ml/kg distilled water was given by nasogastric route for 5 days to the first 2 groups as placebo. The third group was "MTX and Gln" group and they were given 1 g/kg Gln for 5 days. "MTX and HMB" group was 4th group and was given 200 mg/kg HMB for 5 days. "MTX, Gln ve HMB" combination was used to the fifth group and they had been given 1g/kg Gln with 200 mg/kg HMB for 5 days. On the fifth day of the experiment, blood and intestinal tissue samples were obtained form all of the groups.
Results: When compared, the degree of the intestinal cripts were deepest in the MTX group ($p < 0.05$), despite that MTX-Gln and MTX-HMB groups were shown better scores ($p < 0.05$). When park scoring system and "erythrocyte reproduction index" were applied, the MTX-Gln-HMB group had higher scores among five study groups. When the tissue was inspected by caspase-3 coating, apopitosis was highest in MTX group. The percentage of apopitosis was lowest in MTX-Gln-HMB group. Expression of caspase-3, -8, and -9 genes were highest in the MTX group ($p < 0.05$) where lowest in the MTX-Gln-HMB group but there was no significant difference ($p>0.05$).
Conclusions: This research showed that the combination Gln and HMB use is more effective then the seperate use of both chemicals.

EP-620

HOW TO EVALUATE ANTI-EMETIC PROPHYLAXIS IN CHEMOTHERAPY-INDUCED VOMITING IN CHILDREN?

F. Puglisi[1], A. D'Ambra[1], M. La Spina[1], L. Lo Nigro[1], P. Samperi[1], S. D'Amico[1], F. Bellia[1], M. Meli[1], A. Di Cataldo[1], G. Russo[1]

[1]Pediatric Hematology and Oncology, University of Catania, Catania, Italy

Objectives: Lack of specific schemes for chemotherapy-induced nausea and vomit in children may lead to inadequate management of emesis. In our unit we chose to adapt to our pediatric population the same guidelines designed for adult patients, including combinations of ondansetron, dexamethasone and aprepitant. These schemes were applied to all patients according to administered chemotherapy and to age and weight of the child, and their effectiveness was assessed through medical record data and the opinions of parents and patients.
Methods: Data collection was performed on patients aged between 3-17 years, who received chemotherapy for malignancy through October-December 2013. We considered data of nausea and vomiting reported in the nursing records and carried out, after informed consent, a structured interview to the parents, asking their opinion on the effectiveness of antiemetics. Finally, it was requested the child's opinion by a visual-analog method (BRAF scale).
Results: We evaluated 186 courses of chemotherapy with different degree of emetic risk: high, 23%, moderate, 34%, low, 33%, and very low 10%. Medical records showed a total control of nausea and vomiting in 72% of cases and absence of vomiting, with occasional episodes of nausea in 21%. Among parents, 87.6% rated the treatment as effective, while 11.8% considered it as not effective. Data collection concerning the BRAF scale showed that 80% of children selected the cartoons equivalent to a state of little or no nausea, without vomit.
Conclusions: Our data indicate that nurses, parents and children expressed a concordant evaluation of effectiveness of the anti-emetic prophylaxis and, therefore, our method of assessment appears sufficiently reliable. The schedule used was efficacious for 80% of patients; therefore efforts need to be pursued in order to improve stratification of patients according to emetic risk and subsequent selective intensification of anti emetic strategy.

EP-621

PEDIATRIC PALLIATIVE CARE AT A TERTIARY ONCOLOGY DEPARTMENT IN BANGLADESH

M. Doherty[1], A. Islam[1]

[1]Pediatric Hematology/Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Objectives: Pediatric palliative care services are unavailable for the majority of children in Bangladesh. The Pediatric Hematology/Oncology Department at Bangabangu Sheikh Mujib Medical University is the only cancer treatment facility which provides pediatric palliative care consultations for children with cancer. Our objective was to describe the palliative care services provided to children at this tertiary care hospital in Dhaka, Bangladesh.
Methods: A retrospective chart review of pediatric palliative care records for children treated in our department from January to March 2014 was performed. All palliative care encounters are documented electronically in our online patient database using a standardized data collection tool.

Results: There were 163 patient palliative care encounters with 70 unique patients during the specified time period. The median number of encounters per patient was 2. Twenty patients were treated for physical symptoms, 80% of these children had pain and 20% had gastrointestinal symptoms. In children with physical symptoms, medications prescribed included paracetamol (56%), morphine (50%), laxatives (50%), and other medications (19%). Emotional interventions, including play therapy, art therapy and supportive counseling, were provided on 155 occasions. On eight occasions the palliative care team was asked to assist in discussing the child's incurable disease status with family members. In all of these meetings, families were also taught how to provide basic end of life care at home.
Conclusions: The majority of children with cancer in Bangladesh have significant palliative care needs. A previous study in our department found that 43% of families will refuse or discontinue treatment after their child's diagnosis. Training of oncology care providers (physicians and nurses) to address the physical, psychological, social and emotional needs of children with cancer will improve palliative care for children in Bangladesh.

EP-622

INDICATORS FOR ASSESSING THE QUALITY OF PALLIATIVE AND END-OF-LIFE CARE FOR CHILDREN WITH CANCER

J.K. Duc[1], K.A. Widger[2], E. Bouffet[3], S. Friedrichsdorf[4], M. Greenberg[3], A. Husain[5], S. Liben[6], J.D. Pole[7], H. Siden[8], J. Whitlock[3], J. Wolfe[9], A. Rapoport[1]

[1]Department of Paediatrics, The Hospital for Sick Children, Toronto, Canada; [2]Faculty of Nursing, University of Toronto, Toronto, Canada; [3]Department of Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [4]Department of Pain Medicine Palliative Care and Integrative Medicine, Children's Hospitals and Clinics of Minnesota, Minnesota, USA; [5]Temmy Latner Centre for Palliative Care, Mount Sinai Hospital, Toronto, Canada; [6]Palliative Care Program, Montreal Children's Hospital, Montreal, Canada; [7]Department of Research, Pediatric Oncology Group of Ontario, Toronto, Canada; [8]Faculty of Medicine, University of British Columbia, Vancouver, Canada; [9]Pediatric Advanced Care Team, Boston Children's Hospital, Boston, USA

Objectives: The purpose of our systematic literature review was to 1) identify potential structure, process, and outcome indicators of quality palliative and end-of-life care (PEOLC) for children with cancer and their families and 2) identify reliable and valid methods of measurement for these indicators.
Methods: We conducted our search using 3 electronic databases (CINAHL, MEDLINE, EMBASE) and a combination of the following key terms: neoplasms, palliative care, terminal/hospice care, advance care planning, outcome assessment, and quality of life. Results were limited to studies in children, published in English since 2003. Book chapters and theses were excluded. An iterative process was used to screen article titles and abstracts for relevance and then review the selected full articles. Two reviewers were involved at each level of review.
Results: After removal of duplicates, 5191 titles and abstracts were screened for relevance and 626 full articles obtained for further review. Many articles were excluded as children (0-18 years) constituted less than 5% of the sample. More than 100 articles were retained in the final review. The most common indicator identified was health-related quality of life for the child, siblings, or parents, with a number of potential tools for measurement available. Other indicators included a reduction in pain, fatigue, or other symptoms. Nevertheless, the majority of indicators identified were related to structures and processes of care, rather than outcomes.
Conclusions: There are a number of indicators and associated measures for assessing the quality of PEOLC in children with cancer; however, further work is required to identify additional outcomes indicative of high-quality PEOLC. A comprehensive summary of key quality indicators and associated measures will provide a basis for assessing the impact of interventions designed to improve the quality of PEOLC for children with cancer.

EP-623

BLOOD TRANSFUSION IN PAEDIATRIC ONCOLOGY PATIENTS: A REPORT OF THE AUDIT IN A TERTIARY CARE HOSPITAL FROM INDIA

T. Durugappa[1], P. Malhotra[1], D. Thakkar[1], N.I.T.A. Radhakrishnan[1], M. Kalra[1], A. Sachdeva[1], S. Aggarwal[1]

[1]Pediatric Hematology Oncology, Sir Gangaram Hospital, New Delhi, India

Objectives: Transfusion therapy is key to successful management of children with cancer or hematologic diseases and recepients of HSCT. We observed the pattern of blood product requirement in patients diagnosed at our center.
Methods: All paediatric oncology patients who received blood products during the period from 2010 to 2013 were analysed for age, gender, primary diagnosis, treatment protocol, phase of therapy and blood products received. Patients were given blood transfusion as per BCSH guidelines.
Results: A total of 210 patients received 655 episodes of transfusion during the study period. Among which majority were males (n = 143) and mean age was 5.4 years (6 months to 15 years). Mean hemoglobin of 7 gm/dl (4.2gm/dl to 8.6gm/dl) and platelet of 27,000/ul (2000/micL to 60,000/micL) was observed. Patients with Acute lymphoblastic leukemia (ALL) received transfusion most often (504 episodes, 76.9%) among which majority had B-cell ALL (404, 61.6%), followed by neuroblastoma stage IV (53, 8%). Among patients of ALL, Patients on UKALL-XI protocol received maximum number of transfusion (262, 40%) followed by patients on BFM-95 protocol (227, 34.6%). Majority of patients required transfusion during reconsolidation phase (190, 29%). Platelets transfucion (514,78.4%) were required more often than PRBC (371, 56.6%) and 230 episodes required both. 124 episodes required prophylactic PRBC transfusion and 243 prophylactic Platelet transfusions.
Conclusions: Red cells and platelet concentrates are frequently used in Paediatric oncology patients during chemotherapy. Patients with acute lymphoblastic leukemia during reconsolidation phase require more episodes of transfusion.

EP-624

ONCOLOGIC EMERGENCIES THAT NEED INTENSIVE CARE AT DIAGNOSIS IN CHILDREN WITH CANCER

I. Astigarraga[1], A. Echebarria[1], R. Adan[1], M. Garcia-Ariza[1], R. Lopez-Almaraz[1], J. Gil-Anton[2], J. Lopez-Bayon[2], Y. Lopez-Fernandez[2], J. Pilar-Orive[2], A. Navajas[1]

[1]Pediatric Oncohematology Unit. Department of Pediatrics, Hospital Universitario Cruces, Barakaldo, Spain; [2]Pediatric Intensive Care Unit, Hospital Universitario Cruces. Department of Pediatrics, Barakaldo, Spain

Objectives: The onset of some oncologic processes is a life-threatening condition that needs to be managed at Intensive Care Units (ICU). The aim of this study is to analyse our experience in the management of severe complications observed before confirming the malignancy diagnosis.
Methods: Retrospective study of children who need critical care at diagnosis, from January 2004 to December 2013. Epidemiological data, tumour characteristics, site, type of complication, treatment and mortality, were reviewed. The statistical analysis was performed by SPSS 22.0.
Results: Emergencies as presenting symptoms were observed in 60 out of 391 new cancer patients and 47 required admissions in ICU at diagnosis. 63% were males and the median age at diagnoses was 6 year-old (range 0.25-14). These complications were intracranial hypertension-67%, haemorrhage-13%, airway obstruction-6% and 2% each (hyperleukocytosis, tumor lysis syndrome, arterial hypertension, cardiac tamponade, hypercalcemia, superior vena cava syndrome and urinary obstruction). Most frequent diagnoses were brain tumours-72%, lymphoma-6%, acute leukemia-6%, rhabdomyosarcoma-4% and rhabdoid tumour-4%. Most malignancies were located in brain-78%, bone marrow-6%, mediastinum-6% and abdomen-4%. Therapy included ventriculoperitoneal shunt 55%, surgery 10%, ventilatory support 10%, external ventricular drainage 6%, ventriculostomy 2%. The death rate was 8%, before reaching cancer diagnosis.
Conclusions: Early identification of symptoms before life-threatening situations at onset in suspected malignancies and the admission at ICU are crucial for improving the prognosis of severe cases. Innovative ways to educate the communities and health professionals in recognising the warning signs and symptoms for cancer are essential to improve early detection and ensure prompt referral to specialist medical care. Collaboration among physicians of ICU and Oncology Units is very important for the management of children with cancer and it supports the need of therapy in specialized tertiary hospitals.

EP-625

TUMOUR LYSIS SYNDROME IN CHILDHOOD MALIGNANCIES IN A TERTIARY HOSPITAL IN NIGERIA: A CALL FOR INCREASED VISIBLITY OF SUPPORTIVE/PALLIATIVE CARE

G.K. Eke[1], N.A. Akani[1], I.E. Yarhere[1]

[1]Department of Paediatrics, University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria

Introduction: Tumour lysis syndrome is a life-threatening emergency due to metabolic derangements secondary to tumour cell necrosis. Early detection of the metabolic disturbances is imperative to avert this complication, promptly initiate treatment and thus improve management outcome of the primary disease.
Objectives: To determine the prevalence of tumour lysis syndrome among children treated for malignancy at the University of Port Harcourt Teaching Hospital (UPTH), evaluate its impact on the primary disease management.
Materials and Methods: This retrospective study reviewed all cases of childhood malignancies admitted into the Paediatric Oncology unit of the UPTH over a two year period, January 2011 to December 2012. Clinical profile of patients, uric acid levels, serum calcium, phosphate, potassium and bicarbonate, and outcome of treatment were reviewed. Also retrieved were the duration of disease before presentation, diagnosis and mode of therapy. Data was analysed using SPSS version 20.0 and p value was significant if less than 0.05.
Results: Out of 58 children treated for malignancy, 16 (27.5%) had laboratory parameters suggestive of TLS. Half of them (8 children) were identified prior to chemotherapy whilst the other half had commenced chemotherapy before developing TLS.
Five (31.25%) of those who had TLS presented within 4 weeks of onset of illness and 11 (68.75%) of them presented with metastatic disease. ALL and nephroblastoma topped the list in terms of diagnosis with 5 cases each, followed by hepatoblastoma (2). They all had hyperuricaemia, 8 (50%) had hyperkalemia while 5 had low serum calcium. Mortality was recorded in 10 (62.5%) of these cases. Performance status was also correlated with outcome.

Conclusion: Prevalence of TLS in more than 25% of the patients is quite high. Since the presence of TLS can delay specific therapy of the primary disease creating opportunity for further spread worsening outcome, there is need to advocate for intensification of supportive management and palliative care as many care givers may give up too early on their patients because of the poor clinical picture that patients with TLS may present with.
Acknowledgements: All residents of the paediatric oncology unit and staff nurses on children medical ward 2.

EP-626

INCIDENCE AND OUTCOME OF INFECTIOUS COMPLICATIONS AMONG PEDIATRIC CANCER PATIENTS RELATED TO PERMANENT CENTRAL VENOUS CATHETERS

A. Elhemaly[1], A. Hamoda[1]

[1]Pediatric Oncology, National Cancer Institute, Cairo, Egypt

Objectives: To asses the incidence of permanent catheter –related morbidities including blood stream infections and catheter related septicemia, systemic infection as toxic endocarditis, toxic myocarditis among immunocompromised pediatric patients, finally outcome of portcath infection (regarding salvalgibilty of the line and mortality related to central line infection
Methods: A study done on 78 out of 151 pediatric cancer patient below age of 18 years who inserted portcath with microbiological documented permentant central line infection in the period between 1st of October 2010 till the end of March 2012. Each episode was analyzed regarding causative organism, morbidities related as septicemia, toxic myocarditis and endocarditis, cause of removal of central line and mortality related to central line infection
Results: There is total number of 107 episodes of portcath infection, gram + ve organisms 60/107 (56%), gram – ve organisms 45/107 (42%) and finally candida 2/107 (2%). The most common organisms was coagulase – ve staph (28.03%). Among patients with gram + ve organisms (40 patients) 34patients (34/40) (85%) had normal echo, four patients 4/40 (10%) had septic myocarditis, two patients 2/40 (5%) with impaired contractility &valvular affection with vegetations& valvular regurge. Regarding patients with gram – ve organisms episodes (38 patients (33/38) (86.8%) had normal echo, three patients (7.89%) had septic myocarditis and finally two patients (5.2%) with impaired contractility &valvular affection with vegetations. Porta- cath were removed in 53 patients (67.9%) due to failure of sterilization (45.3%) and sepsis (54.7%) while in 25 patients (32.1%) portcath were salvaged.
7 patient died from central line infection (9%), gram + ve were isolated in 5 patients who died while gram – ve were isolated in 2 patients
Conclusions: gram + ve pathogens are most common cause of permenant central line (portacath) infection which required better infection control, high mortality rate related to portcath systemic infection enforce us to select patients who are in urgent need for portcath insetion.

EP-627

DELAYED PRESENTATION AND EARLY DEATHS IN A PEDIATRIC ONCOLOGY UNIT: A SINGLE CENTER EXPERIENCE IN A DEVELOPING COUNTRY

A. Farrag[1], M.H. Ghzally[2]

[1]Pediatric Oncology Department, South Egypt Cancer Institute Assiut University, Assiut, Egypt; [2]Department of Pediatrics, faculty of Medicine, Assiut University, Egypt

Objectives: To evaluate patients who died early after first admission to a Pediatric oncology unit, in a center located in a developing country.
Methods: The following data were collected by a retrospective review of reports of all newly admitted patients in the pediatric oncology unit, South Egypt Cancer Institute (SECI), Assiut University, Egypt, between 2006 and 2010 who died very early after admission and before reaching a final diagnosis: sex, symptoms, time interval between initial symptoms and first time admission to the pediatric oncology department and after admission until death, and cause of death.
Results: For all available data of 712 patients who were admitted in SECI, 21 patients (3%) (13 males and 8 females) died early after presentation to the unit with a mean of 1.2 day after admission, and a mean duration since initial symptoms till first visit to the pediatric oncology unit of 64.5 days. Initial symptoms were: abdominal swelling (n = 7, 33.3%), fever (n = 6, 28.6%), head and neck swellings (n = 3, 14.3%), hemorrhage (n = 3, 14.3%), pallor (n = 2, 9.5%). Main causes of death were due to a pulmonary complication (n = 8, 38.1%), tumor lysis syndrome and acute renal failure (n = 5, 23.8%), septicemia (n = 3, 14.3%), mediastinal syndrome (n = 2, 9.5%), anemic heart failure (n = 2, 9.5%), and hemorrhage (n = 1, 4.8%).
Conclusions: There are special problems of childhood tumor management in developing countries; one of them is the initial very late presentation of these patients with advanced disease which leads to early death before appropriate management.

EP-628

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN CHILDREN RECEIVING HIGH DOSE METHOTREXATE WITH OR WITHOUT VINCRISTINE

J. Flank[1], S.R. Lavoratore[1], H. Vol[1], T. Taylor[1], E. Zelunka[1], P.C. Nathan[2], A.M. Maloney[3], L.L. Dupuis[1]

[1]Pharmacy, The Hospital for Sick Children, Toronto, Canada; [2]Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [3]Nursing, The Hospital for Sick Children, Toronto, Canada

Objectives: Chemotherapy-induced nausea and vomiting (CINV) negatively influences the quality of life of children receiving chemotherapy. Little is known about the severity of CINV experienced by children receiving IV methotrexate $\geq$ 1g/m^2/dose (HD-MTX). The purpose of this study was to describe the prevalence of acute and delayed phase CINV in children receiving HD-MTX $\pm$ vincristine.
Methods: Children aged 4-18 years about to receive HD-MTX participated in this prospective, observational study. Nausea severity, time of emetic episodes, and administration of antiemetics were recorded in a diary beginning immediately before HD-MTX administration, for 24 hours after achievement of the protocol-specific threshold MTX concentration (acute phase), and for an additional 7 days (delayed phase). Nausea severity was assessed by children using a validated tool (PeNAT). Children received antiemetics as ordered by their primary care team. Complete CINV control was defined as no vomiting, no retching and a maximum nausea assessment score of 1 (out of 4).
Results: Thirty children (mean age $\pm$ SD: 11.8 $\pm$ 4.0 years; 19 males) who received HD-MTX plus vincristine (19) or HD-MTX alone (11) participated. Antiemetic prophylaxis consisted of ondansetron (21) or granisetron (9) with (13) or without (17) dexamethasone. Eleven patients received CINV prophylaxis consistent with institution-specific antiemetic guidelines. Two (7%) and 10 (33%) patients experienced complete CINV control during the acute and delayed phases, respectively. More patients experienced complete vomiting control during the acute (57%) and delayed (60%) phases than experienced complete nausea control (7% vs 33%). Of the 11 children who received guideline-consistent acute CINV prophylaxis, none experienced complete and six experienced partial acute CINV control.
Conclusions: Acute and delayed phase CINV control following HD-MTX administration is sub-optimal. The emetogenicity ranking of HD-MTX should be reconsidered in light of these findings. Attention should also be focused on provision of guideline-consistent CINV prophylaxis.

EP-629

OPTIMIZING MUCOSITIS PREVENTION PROTOCOL DECREASES LOCAL INFECTION IN CHILDREN AND ADOLESCENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

S. Gallego Zapata[1], O. O. Ramirez[2], C. Portilla[3], M. Quintero de Charry[2], A. Martinez.[4]

[1]Odontologia General y especializada, Centro Medico Imbanaco, Cali, Colombia; [2]Bone Marrow Transplant Unit, Centro Medico Imbanaco, Cali, Colombia; [3]Bone Marrow Transplant Unit, Universidad del Valle, Cali, Colombia; [4]Direct. Medic Research Centro Medico Imbanaco., Universidad del Valle, Cali, Colombia

Objectives: Mucositis is a frequent adverse event of conditioning regimens in HSCT in children. It is a painful complication that predisposes to local and systemic infections due to the disruption of the mucosal barrier. In our BMT unit, we have established a specific protocol for the prevention of this complication. Our aim was to compare the frequency of local infections among groups with good and poor adherence.
Methods: The mucositis prevention protocol was as follows; 1. Panorex radiography, 2. Ondontogram (to identify deteriorated amalgams), 3. Bacterial plaque index, 4. Soft tissue status, 5. Use of antibacterial disinfectants (Clorhexidine), 6. Family education, and 7. Frequent use of sugar free gum. The BMT unit dentist had daily active surveillance in the application and adherence to the protocol, and also, in the classification of mucositis severity. We estimated the OR of local infection by adherence group. We used multivariate logistic regression to adjust the OR by age, type of conditioning regimen, and graft source.
Results: We included in the protocol 46 patients from March/2011 to January/2014. Mean age was 9 years old; 63% males and 59% showed an optimal adherence to the protocol. The overall frequency of mucositis and local infection was 28%, and in patients with mucositis GII to III was 11%. Adjusted OR for local infection by adherence group was 5.2 (95% CI: 1.4, 23.0).
Conclusions: We found that achieving optimal oral hygiene, before and during HSCT, strongly reduces the risk of local mucosal infections. This is relevant, not only to decrease the risk of systemic infections but also to improve the quality of life during pre-engraftment phase of the transplant. Moreover, this could have an effect in decreasing the occurrence of acute GvHD, an issue that merits further studies.

EP-630

PALLIATIVE CARE IN PEDIATRIC ONCOLOGY: MATERNAL PERSPECTIVES

D.A. Geronutti[1], R.C. Popim[2], V.L.P. Tonete[2]

[1]Palliative Care, Hospital de Câncer Infanto Juvenil - Presidente Luiz Inácio Lula da Silva, Barretos, Brazil; [2]Nursing, Universidade Estadual Paulista, Botucatu, Brazil

Objectives: The overall goal of this research was to understand the concepts and experiences about palliative care from mothers whose children had been hospitalized in a national cancer hospital, located in the state of São Paulo.
Methods: This is a qualitative study, descriptive in nature. For data analysis, the method of content analysis of Bardin was used, thematic approach.
Results: The maternal testimonies collected were organized into five themes: Conceptions about palliative care; Maternal care after the announcement of impossibility of healing; Professional care after the announcement of impossibility of healing; Maternal feelings about the stage of palliative care; Maternal perspectives on children's feelings when under palliative care. Maternal conceptions about palliative care proved to be vague, distorted or even nonexistent, showing a need for institutional investments to change this situation. As to the experiences reported by these women, those were permeated by feelings of different types and intensities, especially those of helplessness and nonconformity. The religious conviction proved to be an important resource for the acceptance and the overcoming of problems. The perceptions about maternal and professionalcare during the palliative phase pointed to the importance of comprehensive care to children and their families, the team's qualification for such care and inclusion, guidance and active participation of family in decisions to be taken to get the best quality of life for these children during this same phase.
Conclusions: By the end of this study, in addition to what was proposed, it could be confirmed the necessity of establishing a line for comprehensive care to children with cancer, from its municipalities, as well as the importance of continuity of care for the service, to families who have lost their children.

EP-631

CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN NON-CNS CANCERS: COMPARISON BETWEEN DIAGNOSTIC GROUPS

L. Gilchrist[1], L. Tanner[2]

[1]Hematology and Oncology, Children's Hospitals and Clinics of Minnesota, Minneapolis, USA; [2]Rehabilitation Services, Children's Hospitals and Clinics of Minnesota, Minneapolis, USA

Objectives: Chemotherapy-induced peripheral neuropathy (CIPN) is a common side-effect of cancer treatment in children that can have lasting, negative consequences. CIPN is commonly recognized in patients with acute lymphoblastic leukemia (ALL), but is not well documented in other populations. The purpose of the study was to identify severity and clinical characteristics of CIPN that occurs in children/adolescents treated across a variety of cancers.
Methods: The pediatric modified Total Neuropathy Score (ped-mTNS) as well as standardized measures of balance and manual dexterity were administered to all subjects ($n = 85$). Patients treated for ALL ($n = 31$) were tested near the end of delayed intensification (approximately 6 months into treatment) whereas subjects treated for lymphoma ($n = 32$) or other non-CNS solid tumors ($n = 22$) were tested approximately 3 months into treatment. Treatment information was extracted from the medical record. Total and item ped-mTNS scores, as well as balance and manual dexterity scores, were compared between diagnostic groups using ANOVA.
Results: Although subjects treated for ALL received longer duration of treatment and were exposed to higher cumulative doses of vincristine (22.1 mg/m^2 ALL, 8.86 lymphoma, 11.34 other solid tumors), they had lower overall ped-mTNS scores (7.7 ± 3.1) than patients with lymphoma (10.8 ± 5.5, $p = 0.003$) and other solid tumors (10.4 ± 4.5, $p = 0.035$). Subjects with lymphoma had increased sensory symptoms, vibratory impairment, and deep tendon reflex decrements while subjects with ALL had worse strength deficits. All groups had mean balance and manual dexterity scores that were not significantly different from one another but were below normative values with the exception of manual dexterity in subjects with ALL which was in the normal range.
Conclusions: Patients with lymphoma and other solid tumors experience on-treatment CIPN that may be more significant than in patients with ALL. Increased attention to CIPN needs to occur in these groups.

EP-632

PALLIATIVE CARE AND END-OF-LIFE ISSUES IN PEDIATRIC ONCOLOGY: REPORT FROM A MOROCCAN PEDIATRIC ONCOLOGY UNIT

L. Hessissen[1], A. Ziani[2], M. Elkababri[1], A. Kili[1], M. Elkhorassani[1], M. Khattab[1]

[1]Mohamed V University Souissi, Hemato-oncology Pediatric Center, Rabat, Morocco; [2]University Hospital of Rabat, Hemato-oncology Pediatric Center, Rabat, Morocco

Objectives: The care of children at the end of life may be particularly complex and high-quality palliative care is now an expected standard at the end of life. To better understand the needs of the Moroccan children and their families the parents of terminally ill children were asked to answer to a questionnaire.
Methods: The study was conducted in the Pediatric Hematology and Oncology Institute of Rabat during 2013. We interviewed the parents of children who were in palliative care about physical symptom, psycho-social needs and whether or not they talk about death with their child. The questionnaire was administered in Arabic by a psychologist. Medical records were reviewed for additional informations.
Results: Among the 20 parents who participated to the study, 19 refused that announcement of the palliative phase to their children. The most frequent parent reaction was death anticipation and resignation. Most of the parents avoid discussing with the child about his imminent death or talk about indirectly discussing the death of "the others". Concerning the preferred place for the end of life 55% chose the patient's house and 40% the hospital. The main symptoms reported were pain (75%) and fatigue (75%). Finally Over 20 relatives interviewed 19 of them expressed physical needs such as a better symptoms management and more contact with the caregivers, 15 expressed a need of social support (transport fees, support for medication fees.), and all the parents reported the need of psychological support.
Conclusions: In pediatric oncology, palliative cares are the most difficult phase for the parent, the children and also for the caregiver especially in low income countries where palliative care are poorly structured. One of the most important steps to improve its management is to understand the needs of each person involved.

EP-633

NUTRITIONAL STATUS OF CHILDREN WITH MALIGNANCY

A. Islam[1], M. Doherty[2], F. Afroze[2]

[1]Pediatric Hematology & Oncology, Bsmmu, Dhaka, Bangladesh; [2]Pediatric Hematology & Oncology, Bsmmu, Dhaka, Bangladesh

Objectives: Nutritional assessment is an essential component of the initial assessment of children with cancer, and malnutrition is associated with an increased risk of morbidity and morality. This study evaluated the nutritional status of children with cancer during initial diagnosis, in a tertiary health care center in Bangladesh
Methods: A cross sectional observational study was done in the Paediatric Haematology & Oncology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) between May and October 2010. Nutritional status of one hundred children, under 15 years of age, with newly diagnosed malignancy was evaluated. Weight, height/length, and mid upper arm circumference (MUAC) were recorded at the time of diagnosis, before beginning treatment, using standard techniques. Z-scores for weight for height/length, height/length for age, and weight for age were derived using National Center for Health Statitics (NCHS) growth curves. Body mass index (BMI) was calculated using standard formula.
Results: A total of one hundred patients were included. The mean age was 6 years (range 2 months to 14 years). Sixty-four percent of patients were male and thirty-six percent were female. Hematological malignancies accounted for 87% of diagnoses, with solid tumors comprising 13% of diagnoses. The overall proportion of under nutrition, wasting & stunting were 61%, 59% and 20% respectively. The proportion of malnutrition by body mass index & mid upper arm circumference were 69% and 63% respectively.
Conclusions: In this study the proportion of malnutrition among children with cancer was high. Fifty-nine percent of Bangladeshi children are wasted at the time of presentation and sixty-one percent are underweight. Children with solid tumors are more frequently severely wasted (50% vs. 33%) and severely underweight (40% vs. 24%) than children with hematological malignancies. These results suggest that interventions to improve the nutritional status of children with cancer are needed for the majority of children presenting with cancer in Bangladesh.

EP-634

IMPACT OF CANCER FINANCIAL SUPPORT GROUPS ON CHILDHOOD CANCER TREATMENT AND ABANDONMENT IN A PRIVATE PEDIATRIC ONCOLOGY CENTRE IN A DEVELOPING COUNTRY

J. James martin[1], A. srinivasan[1], P. ramachandran[2], M. Ramakrishnan[3]

[1]Pediatric Hematology And Oncology, Kanchi Kamakoti Child Trust Hospital, Chennai, India; [2]pediatric Surgery, Kanchi Kamakoti Child Trust Hospital, Chennai, India; [3]child Trust Medical Research Foundation, Kanchi Kamakoti Child Trust Hospital, Chennai, India

Objectives: Globally, an estimated 2,50,000 children develop cancer each year, and 80% of them live in developing countries. In India, approximately 45,000 children are diagnosed with cancer every year. Treatment abandonment is a significant barrier to cancer care in the developing world. Though the reasons for abandonment are complex and multifactorial, economic issue appears to be the main factor in abandonment. We analysed the impact of financial support of two cancer support groups on the treatment and abandonment in pediatric oncology. Aims:To analyze the impact of two cancer support groups in the treatment and abandonment of childhood cancer.
Methods: Methods and Material: This is a retrospective review of children with cancer funded and non funded who were treated at Kanchi Kamakoti CHILDS Trust Hospital from 2010 to 2013
Results: A total of 100 patients funded, 57 by Ray of Light Foundation and 43 by Pediatric Lymphoma Project and 70 non-funded. The total current survival of 80%, including those who have completed treatment and those currently undergoing treatment is comparable in both the groups. Abandonment of treatment after initiating therapy was not seen in the financially supported group whereas abandonment of treatment after initiation was seen in one child in the non funded group.
Conclusions: Besides intensive treatment with good supportive care, financial support also has an important impact on compliance and abandonment in all the socioeconomic

strata of society. Financial supports from private cancer support groups also has its impact beyond the patient and family in reducing the burden on government institutions by non-governmental funding in private sector. Improvement in the delivery of pediatric oncology care in developing countries could be improved by financial support from the private sector.

EP-635

VITAMIN D DEFICIENCY IN CHILDREN WITH CANCER

V. Paramasivam[1], R. Mohan[1], J.X.S. James Martin[1]

[1]Pediatrics, Sri Ramachandra University, Chennai, India

Objectives: INTRODUCTION: Very few studies only have measured vitamin D levels in pediatric patients with malignancy. We undertook a study to assess vitamin D status in pediatric cancer patients in a developing country in our pediatric oncology centre.
AIM: This study aims to compare the vitamin D levels between a population group of childhood cancer patients and a control group in a tertiary care pediatric oncology unit in a developing country.
Methods: This is a prospective case control study conducted in Sri Ramachandra Medical College, pediatric oncology tertiary care centre. A total of 51 children were included in this study from the age group of one month to 18 years of age who has been diagnosed with cancer and on treatment for atleast six months. Controls were age and sex matched who are without cancer. The duration of sampling was from March 2012 to July 2013. 25 OH Vitamin D levels were assessed by chemiluminesence. Comparison of the two groups was done using t tests, ANOVA and Mann Whitney test as appropriate. Statistical analysis was done with the use of SPSSv17.
Results: Mean vitamin D levels among cases were found to be 22.6 ng/dl, while mean vitamin D levels among the controls were found to be 33 ng/dl. 78.43% of children with cancer were found to have insufficient levels of vitamin D as opposed to 50.98% of controls. Other factors compared included age, sex, type of malignancy and nutrition status. Mild variables were seen in each factor but were deemed to be not statistically significant.
Conclusions: Children with cancer have a lower vitamin D level than children of a control population. Since cancer survivors are at a higher risk for low bone mineral density, interventions to improve 25-OH D status in this vulnerable population are needed.

EP-636

INFECTION ASSOCIATED MORBIDITY AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT IN CHILDREN AND ADOLESCENTS: WHAT IS THE OPTIMAL PROPHYLAXIS STRATEGY?

R. Johnston[1], L. Funston[1]

[1]Paediatric Haematology and Oncology, Royal Belfast Hospital for Sick Children, Belfast, United Kingdom

Objectives: Invasive infections are a major cause of morbidity and mortality following hematopoietic stem cell transplantation (HSCT). Standardised strategies to prevent infections are established in allogeneic HSCT; however, evidence to recommend prophylactic antimicrobial drugs in autologous HSCT is limited. In addition these drugs have potentially significant side effects. Our aim was to review the practice and experience in this Regional Children's Cancer Centre over a ten year period; to undertake a review of the literature, and produce guidance to standardise the approach to infection prophylaxis and management in this patient group.
Methods: We retrospectively analysed data relating to children and adolescents undergoing autologous HSCT at our institution between January 2004 and December 2013. Additional information included source of stem cells, diagnosis, and age at transplant, diagnosis, source of stem cells, infection prophylaxis, complications and outcome.
Results: Twenty-seven children underwent autologous HSCT, totalling 30 HSCT procedures. Neuroblastoma was the most common diagnosis (11/27). 13 patients underwent autologous bone marrow transplants, 14 peripheral blood stem cell transplants. Fungal, viral or a combination antimicrobial prophylaxis was used in 18 patients. Bacterial infections occurred in 8 patients including bacteraemia in 3 patients and lower respiratory tract infection in 2. Viral infections affected 5 patients including 2 episodes of VZV reactivation and 1 HSV reactivation. Fungal infection was uncommon; only 1 case of pulmonary aspergillosis was strongly suspected clinically and on imaging but unproven on BAL. Relapse of disease accounted for all 6 deaths following HSCT.
Conclusions: To date there is no standard practice for infection prophylaxis although our review of practice did not reveal a high incidence of invasive infection. Production of an evidence based guideline will lead to patient focussed infection prophylaxis and minimise morbidity associated with infection and its management.

EP-637

ABANDONMENT OF TREATMENT AS A BANE FOR CARE GIVERS IN THE PEADIATRIC ONCOLOGY UNIT AT UNIVERSITY OF PORT HARCOURT TEACHING HOSPITAL, RIVERS STATE NIGERIA

I. Kalagbor[1], G. Eke[2]

[1]Department of Science Laboratory Technology School of Applied Sciences, Rivers State Polytechnic, Bori, Nigeria; [2]Department of Paediatrics, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

Objectives: The Peadiatric Oncology unit at University of Port Harcourt Teaching Hospital over the years has experienced a high incidence of abandonment of treatment by parents/guardians of children who have been admitted and undergoing chemotherapy. This is attributable to a number of reasons such as cost implications, ignorance, denial syndromes and granting patronage to traditional healers. Most often than not, the latter reason accounts for the late presentation of the patients in the hospital. There are few treatment centres across the state.
Methods: The study was carried out using cohorts from the patients in the ward and those coming from time to time for chemotherapy spanning a period of one year (2013 - 2014
Results: About 55% the patients presented four weeks after the onset of (symptoms) of the illness. In the course of their therapy, 40% defaulted for several reasons. Mortality recorded is 45%. Statistical evaluation using ANOVA was also carried out.
Conclusions: Late presentation due to the various reasons and high default rates are contributory factors to poor out come in the treatment of patients even for those who have good prognosis.

EP-638

ONCE A DAY CEFTRIAXONE-AMIKACIN COMBINATION AS INITIAL EMPIRIC THERAPY FOR FEBRILE NEUTROPENIA IN CHILDREN

S. Kanvinde[1], A. Deshpande[2]

[1]Pediatric Hematology and Oncology, Deenanath Mangeshkar Hospital, Pune, India; [2]Pediatrics, Deenanath Mangeshkar Hospital, Pune, India

Objectives: We present our experience regarding the use of once daily (OD) ceftriaxone (CFT) plus amikacin (AMK) as initial therapy for febrile neutropenia (FN).
Methods: Retrospective Study; Study period January2002--December2011; Inclusion Criteria: age<18 years, treatment for cancer, fever >100.4^{o}F with ANC<500/ cmm. Exclusion criteria: FN at time of diagnosis of malignancy; patients undergoing BMT. Empiric therapy for FN was IV CFT 100mg/kg and AMK 15mg/kg OD. Patients having respiratory distress, hypotension or altered sensorium were treated with Piperacillin-tazobactam (PTZ) and AMK as initial therapy. Antibiotics were upgraded if no response within 48-72 hours, or earlier if clinical deterioration. Vancomycin was added in case of skin/soft tissue infections, line-related sepsis or documented infections on culture. Amphoterecin was added if persistent fever > 4-5 days. Age<1year, AML chemotherapy, poor performance status, need for blood products, insurance, patient convenience were indications for admission. High-risk FN was defined as duration of neutropenia>7days, malignancy not in remission and poor performance status.
Results: There were 464 episodes of FN documented, of which 418 episodes were initially treated with CFT-AMK. (hemato-lymphoid malignancies in 82%). There was no focus of infection in 49% episodes. 224/418 episodes were considered high risk as per our definition. 148/418 episodes were treated initially on OPD basis, of which 19 required admission for persistent fever. There were no deaths in this group. In 270/418 episodes, patients were initially admitted for treatment, of which 66 could be discharged within 3-4 days. There were 6 deaths in the admission group. Overall, 214/418 (52%) episodes could be managed wholly/partially on OPD basis. 327/418 (78%) episodes responded to CFT-AMK, while 91/418 required switch to other antibiotics. Additionally, in 25 episodes, breakthrough fever occurred after initial response and required change in antibiotics.
Conclusions: Use of CFT-AMK combination as initial empiric therapy for FN may permit OPD management of a significant number of patients, considerably reducing the burden on indoor services.

EP-639

PAEDIATRIC PALLIATIVE CARE: A SYSTEMATIC REVIEW AND RECOMMENDATIONS FOR TREATMENT OF SYMPTOMS

R.R.G. Knops[1], L.C.M. Kremer[1], A.A.E. Verhagen[2]

[1]Paediatric oncology, Academic Medical Center, Amsterdam, Netherlands; [2]Paediatrics, Beatrix Children's Hospital/University of Groningen, Groningen, Netherlands

Objectives: Children dying of a life threatening disease suffer a great deal at the end of life. Symptom control in children dying of cancer is often unsatisfactory at this stage of disease, partly because many caregivers are simply not familiar with paediatric palliative care. Symptom control and relieve of suffering are the cornerstones of paediatric palliative care, but evidence based recommendations in paediatric palliative care are not available. The aim of this study is to improve palliative care for children by making high quality care recommendations to recognize and relieve symptoms in paediatric palliative care.
Methods: An extensive search was performed for guidelines and systematic reviews on paediatric palliative care. An expert panel combined the evidence that resulted from this

search with consensus to form recommendations on the treatment of symptoms in paediatric palliative care.
Results: We appraised 21 guidelines and identified 693 potentially eligible articles of which only four met our inclusion criteria. None gave recommendations on recognizing and treating symptoms in paediatric palliative care. Two textbooks and an adult palliative care website were eventually our main sources of evidence on recognizing and treating symptoms in paediatric palliative care.
Conclusions: Hardly any evidence is available for the treatment of symptoms in paediatric palliative care. By combining evidence for adult palliative care and the sparse evidence for paediatric palliative care with paediatric expert opinion we were able to define a unique set of high quality care recommendations to relieve symptoms and lessen the suffering of children in palliative care. The results of this study are an important tool to educate caregivers on how to relieve symptoms in children with life threatening conditions and improve quality of paediatric palliative care.

EP-640

DEVELOPMENT OF AN EDUCATIONAL BOOKLET FOR FAMILIES OF CHILDREN WITH LEUKEMIA

K. Kobayashi[1], E. Yamaguchi[2], A. Hayakawa[3], N. Maeda[4], M. Sawada[5], H. Hisakawa[6], U. Koudera[7], M. Yoshida[8], T. Imai[9], T. Rikiishi[10], H. Hori[11]

[1]School of Nursing, Jichi Medical University, Shimotsuke, Japan; [2]Department of Medical Quality and Safety Science, Osaka City University Graduate School of Medicine, Osaka, Japan; [3]Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan; [4]Department of Pediatrics, National Hospital Organization Nagoya Medical Center, Nagoya, Japan; [5]Department of Pediatrics, Takashima Municipal Hospital, Takashima, Japan; [6]Department of Pediatrics and Adolescent, Kochi Medical University, Nankoku, Japan; [7]Department of Pediatrics, Nakano Children's Hospital, Osaka, Japan; [8]Department of Pediatrics, Asahikawa Medical University, Asahikawa, Japan; [9]Department of Pediatrics, Kagawa University, Takamatsu, Japan; [10]Department of Pediatrics, Tohoku University, Sendai, Japan; [11]Department of Pediatrics, Mie University, Sendai, Japan

Objectives: Although the survival rate of childhood leukemia in Japan has exceeded 80%, being diagnosed with leukemia, a life-threatening illness, still causes great anxiety for patients and their families (i.e., parents and siblings). Families face unpredictability and uncertainty both in their present situation and future lives. Providing education to patients and families about the prospect of recovery, quality of life (QoL), and management of family life would help families to deal with hardship more easily. The purpose of this study was therefore to develop an educational booklet promoting parental involvement and providing instructions about parental management of the child's and family's life, both during and after treatment.
Methods: To compile information and select the contents of the educational tool, the members of the Committee of QoL in the Japan Association of Childhood Leukemia Study Group (JACLS) reviewed previous studies regarding the family life and QoL of families of children with leukemia. In addition to literature reviews, we referred to the results of previous longitudinal studies that had been conducted by the JACLS to clarify family life trajectory and the QoL of children with leukemia and their families.
Results: Based on the results of this research, the educational booklet contains three themes: 1) the QoL of children with leukemia and their family members, 2) family life challenges by treatment phase, and 3) support resources and hints for overcoming family life challenges. The cardinal messages of the booklet are to provide hopeful prospects to patients and their families and to encourage family management.
Conclusions: The acceptability, utility, and helpfulness of the educational booklet should be examined in future research.

EP-641

EARLY PALLIATIVE CARE CONSULTATION FOR HIGH RISK PEDIATRIC ONCOLOGY PATIENTS: A FEASIBILITY STUDY

L. Mahmood[1], A. Dozier[2], J. Dolan[2], D. Casey[3], C. Mullen[4], D. Korones[4]

[1]Pediatric Hematology Oncology, Golisano's Children Hospital at University of Rochester Strong Memorial Hospital, Rochester, USA; [2]Public Health Sciences, University of Rochester, Rochester, USA; [3]Food and Drug Administration, US Department of Health and Human Services, Maryland, USA; [4]Pediatric Hematology Oncology, Golisano's Children Hospital at University of Rochester, Rochester, USA

Objectives: As part of a larger study evaluating the impact of early palliative care in children with high risk malignancies, we assessed the feasibility of obtaining palliative care consultations within one month of diagnosis.
To assess the feasibility of obtaining early (at diagnosis) palliative care consultations for children with high risk malignancies
Methods: Children were eligible for early palliative care consultation if they had a high risk malignancy, defined as: 1) relapsed disease, 2) need for stem cell transplantation (SCT), or 3) newly diagnosed with an estimated overall survival of $< 50\%$. The pediatric hematology/oncology division identified eligible patients at a weekly patient-care conference. Medical charts were reviewed every two weeks to assess the status of the consultation and number of follow-up visits after initial consultation.
Results: Since implementation in March 2013, 20 of 25 eligible patients received an early palliative care consultation. No children or families declined the consult. Four patients did not participate in the study: two were children from an outside hospital referred to our institution for autologous SCT, two were children with recurrent disease treated primarily as outpatient, and one patient had a long post-operative course and was discharged prior to receiving a consult. The median time from diagnosis to consult was 12 days (2 - 180). Seventeen of 20 (85%) patients received consultation within 30 days of diagnosis. Eight of 20 (40%) were newly diagnosed, and 12/20 (60%) had relapsed/recurrent disease. Fifteen of 20 (75%) had follow up palliative care visits after initial consultation; 2/20 had only one follow visit. The median number of follow up visits for the group was 4 visits (1-24).
Conclusions: An early palliative care consultation program for children with high risk malignancies is feasible and is well-accepted by pediatric hematologist/oncologists, children and families.

EP-642

ATYPICAL PELLAGRA IN PEDIATRIC ONCOLOGY PATIENTS: THE MYSTERIOUS RASH

K. Kulkarni[1], T. Baker[2], D. Eisenstat[2]

[1]Pediatric hematology Oncology, IWK Health Centre and Dalhousie University, Halifax, Canada; [2]Pediatric Hematology Oncology Palliative Care and Environmental Health, Stollery Children Hospital, Edmonton, Canada

Objectives: Pellagra is a severe state of niacin deficiency. Pellagra in pediatric cancer patients is unknown in developed world. We describe two pediatric oncology patients who developed pellagra.
Methods: Case records of pediatric cancer patients managed at the Stollery Children Hospital were reviewed.
Results: Case 1: A 5 year old male diagnosed with Burkitt's lymphoma was treated using protocol ANHL01P1 (Group C). On day +29 of consolidation I chemotherapy, he developed a hyperpigmented, symmetrical rash on the neck and dorsum of his hands and wrists. This patient also had a 4 week history of diarrhea. Supplemental niacin 100 mg daily was given for 14 days, then a multivitamin with 10 mg niacin was given daily. His rash resolved within 8 days of supplementation. Preceding the rash, the patient's niacin intake was $\geq$ 8.8 mg daily (Dietary Reference Intake is 8 mg daily).
Case 2: A 13 year old male with acute myeloid leukemia was treated as per protocol AAML0531. On day +10 of induction-II, the patient developed a dark brown hyperpigmented rash on the dorsum of wrists, elbows and face without diarrhea but with fatigue 3 weeks prior to presentation. On day +22, the Dermatology service suggested pellagra. Niacin supplementation of 100 mg daily was initiated for 10 days, then a multivitamin with 15 mg niacin was provided daily. The rash resolved within 20 days of supplementation. Enteral and parenteral niacin intake prior to pellagra diagnosis was $\geq$ 17 mg daily (Dietary Reference Intake is 12 mg daily).
Conclusions: Pellagra is extremely unusual in pediatric oncology patients. These cases illustrate the potential for development of relative niacin deficiency following chemotherapy, possibly related to high-dose cytarabine. Clinical evidence of pellagra existed despite assessed adequate niacin intake, suggesting higher requirement during certain phases of treatment.

EP-643

A CROSS-SECTIONAL SURVEY EXPLORING BEHAVIORS AND PSYCHOSOCIAL DETERMINANTS OF PHYSICAL ACTIVITY AND DIET DURING AND AFTER TREATMENT FOR A PEDIATRIC MALIGNANCY

N. Arbit[1], C. Buck[1], E. Ladas[1]

[1]Pediatrics, Columbia University Medical Center, New York, USA

Objectives: Unhealthy lifestyle behaviors can promote the development of cancer-related morbidities among children and adolescents with cancer across all phases of treatment. Lifestyle interventions may reduce this risk during and after treatment. We performed a cross-sectional survey to learn about current practices and barriers to healthy lifestyle behaviors.
Methods: Information on fruits and vegetable (FV) and dietary fat intake, physical activity (PA), and their associated psychosocial variables were measured using the Patient-Centered Assessment & Counseling for Exercise survey during a routine clinical visit. Frequencies of demographics and survey responses were analyzed with SPSS (v21).
Results: Data from 61 patients (31F/30M; Mean age: 18.2y (range: 12-25y); 19% Hispanic, 11%% Asian, 10% Black) were available. Only 13% of patients reported meeting PA recommendations, though 55% intended to meet guidelines within 6 months. Eighty seven percent reported eating < 5 servings of FV per day, but 71% of them intended to increase FV consumption within 6 months. 43% reported consistently avoiding high fat foods; yet dietary analysis revealed fat intake (55g/d) in excess of guidelines (20 – 35g/day). Only 40% of subjects had consistent friend or family support for eating low fat foods, only 46% had support for PA, and only 55% had support for FV consumption.
Conclusions: Pediatric oncology patients are not following healthy lifestyle behaviors, despite the majority intending to do so. The gap between intentions and reported behavior may be partly explained by data indicating a lack of support for these behaviors. Improving support

for and access to healthy lifestyle resources may facilitate the adoption of healthy behaviors and improve the health outcomes and quality of life for these patients.

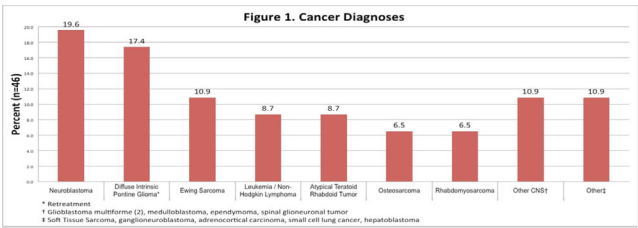
EP-644

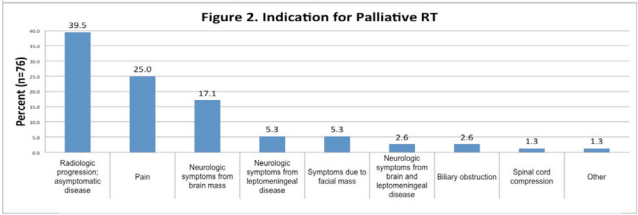
PALLIATIVE RADIOTHERAPY FOR CHILDHOOD CANCERS

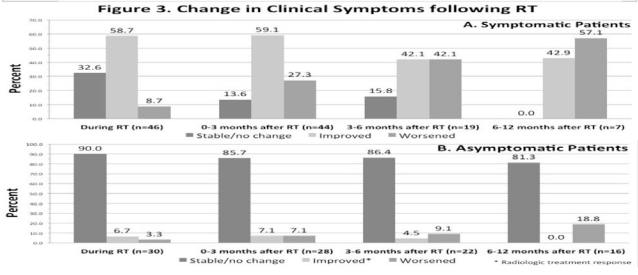
K. Mak[1], S.W. Lee[2], T.A. Balboni[3], K.J. Marcus[4]

[1]Department of Radiation Oncology, Harvard Radiation Oncology Program & Dana-Farber/Brigham and Women's Cancer Center, Boston, USA; [2]Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer Center, Boston, USA; [3]Department of Radiation Oncology & Department of Psychosocial Oncology and Palliative Care, Dana-Farber/Brigham and Women's Cancer Center & Dana-Farber Cancer Institute, Boston, USA; [4]Department of Radiation Oncology & Department of Pediatric Oncology, Dana-Farber/Brigham and Women's Cancer Center & Dana Farber/Boston Children's Cancer and Blood Disorder Center, Boston, USA

Objectives: Despite accepted and widespread application of palliative RT for children with advanced malignancies, few reports have been published on its use. The goal of this study was to describe clinical characteristics, treatment response, and survival of children receiving palliative RT.
Methods: Pediatric patients (age ≤18 years) treated with palliative RT for advanced incurable cancer from 01/01/08-02/26/14 were included. Diagnosis, indication and details of palliative RT, treatment response, toxicity, and survival were retrospectively reviewed.
Results: Forty-six patients were treated in 76 palliative treatment courses. Fifteen patients (33%) had ≥2 palliative RT courses (maximum: 6 courses). Median age at time of palliative RT was 10.3 years (range: 1.5-18.9); 54% were male. The most common diagnoses (Figure 1) were neuroblastoma (20%) and diffuse intrinsic pontine glioma (retreatment; 17%). The most common indications for RT were radiologic progression in asymptomatic patients (39%) and pain (25%; Figure 2). The most common treatment sites were brain (32%) and bone (29%). Six treatment courses were not completed (8%). Median RT dose was 30 Gy (range: 2.5-54). Median duration of RT was 16 days (range: 1-48). Sixty-five treatment courses (86%) were delivered with fraction sizes ≥250 cGy. Twenty-seven treatment courses (36%) were given under general anesthesia. Median follow-up was 3.9 months. RT-related toxicity was 24% during treatment and 8%, 5%, and 4% at 0-3, 3-6, and 6-12 months after RT, respectively. Over 80% of asymptomatic patients, and 91%, 73%, 58%, and 43% of symptomatic patients had improved or stable symptoms during RT and 0-3, 4-6, and 6-12 months afterwards, respectively (Figure 3). Median survival after palliative RT was 4.2 months. Of 21 surviving patients (46%), four (19%) were in hospice care at last follow-up.







Conclusions: Palliative RT was well-tolerated in children with incurable malignancies, and was associated with improved or stable symptoms in the majority of cases.

EP-645

THE PROFILE OF INFECTIONS IN THE RECIPIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANT- A SINGLE CENTRE EXPERIENCE FROM INDIA

P. Malhotra[1], A. Gupta[1], M. Kalra[1], N. Radhakrishnan[1], A. Sachdeva[1]

[1]Pediatric Hemato Oncology and Bmt Unit, Sir Ganga Ram Hospital, Delhi, India

Objectives: Infections are an important cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients. Knowledge about the infections patterns at a centre would facilitate early initiation of treatment. This review was done to analyze the pattern of infections in the first 100 days following HSCT.
Methods: A retrospective review of data of pediatric patients who underwent HSCT between January 2007 and December 2013 was done to find out the number and types of infection upto day +100.
Results: Of 56 HSCT patients, 28 (50%) had at least one episode of proven sepsis. Of 56 transplants, 38 (67.85%) were allogeneic and 18 (32.14%) autologous. The M:F ratio was 3.33:1 and the mean age was 6.7yr (range: 8m-18.3yrs). According to HSCT source, 27 Peripheral blood stem cell transplants (PBSCT), 11-Cord Blood Transplants (CBT), 16 Bone Marrow (BM) and 2 BM+CBT. Among allogeneic transplants 25 (65.7%) were Matched Sibling Donor (MSD), 10 (26.3%) were CBT, 1 (2.6%) was a MSD+CBT, and 2 (5.2%) were haplotransplants (donors were parents- 1 BM and 1 PBSCT). There were a total 56 episodes of infections, of which 31 (55.3%) were culture proven bacterial infections (*Kleibsella sp*-4, *Staphylococcus aureus*-2, staphylococcus hominis-2, *Acinetobacter sp*-1, *Enterococcus fecalis*-3 psuedomonas-2 others-17), 10 (17.8%) were CMV. There were 15 (26.7%) fungal infections of which probable were 8 (14.2%) and proven infections 7 (12.5%) (*Aspergillus sp*-8, *Candidasp*-6, *Trichosporon sp*-1). There were 30 (53.5%) episodes of infection in allogeneic transplant and 26 (46.4%) in auto transplant. Total episodes of infection in the PBSCT were 23 (41%), 10 (17.8%) in CBT, 18 (32.1%) in BM and 5 (8%) in BM+CBT group. There were total of 19 (33.9%) transplant related mortalities of which 6 (31.5%) were attributable to infections.
Conclusions: Infections are very common post HSCT. *Kleibsella sp*, CMV and *Aspergillus sp* were the most common infections in their respective categories.

EP-646

EFFORTS TO CONTROL INVASIVE FUNGAL INFECTION IN A DEVELOPING COUNTRY

E. Ebeid[1], A. Mansour[2]

[1]Pediatric Hematology Oncology, National Cancer Institute, Cairo, Egypt; [2]Pediatric Hematology Oncology, Nasser Institute, Cairo, Egypt

Objectives: A single institution retrospective study to analyze the outcome of pediatric cancer patients who are at risk of developing invasive fungal infection (IFI). Patients with IFI were treated with antifungal drugs according to availability and financial support. Diagnosis of IFI was only done by CT chest.
Methods: The study included 126 pediatric cancer patients (80 females, 46 males) at risk of developing IFI, with hematological malignancies and solid tumors (85 and 41 respectively) from 2012 till 2014. Patients were divided into 3 groups. Group A (58 patients): 48 patients received prophylactic Itraconazole, 10 patients received prophylactic Voriconazole. Group B (55 patients) who developed fever and neutropenia during treatment. Group C: 13 patients who presented with IFI.
Results: In group A, 48/58 (82.7%) patients received prophylactic Itraconazole, while 10/58 (17.3%) received prophylactic Voriconazole. 27/48 (56.2%) receiving Itraconazole were controlled and did not develop IFI, while 31/48 (64.5%) developed IFI and received AmphotericinB: 7/31 (22.5%) died, 11/31 (35.5%) were shifted to Caspofungin and 13/31 (42%) shifted to Voriconazole. Those receiving Voriconazole, 5/10 (50%) were controlled while 5/10 (50%) developed IFI. Group B: 8/55 (14.5%) were controlled on antibiotics, 47/55 (85.5%) were given empiric AmphotericinB, where 14/47 (30%) were controlled while 33/47 (70%) had IFI, 12/33 (36.4%) were controlled on AmphotericinB, while 21/33 (63.6%) had progressive IFI. Goup C: 10/13 (77%) received Voriconazole. 8/10 (80%) were controlled, while 2/10 (20%) had progressive IFI. 3/13 (23%) received AmphotericinB with a complete response in 2/3 (66.6%) and 1/3 (33.4%) were shifted to Voriconazole. Caspofungin was better than Voriconazole as salvage ($p = 0.632$). Voriconazole was significantly superior than Itraconazole as prophylaxis ($p = 0.002$).
Conclusions: Prophylactic Itraconazole and empirical AmphotericinB seem suitable in developing countries. Caspofungin is preferred as second line.

EP-647

THE TRANSITON FROM ACTIVE TO PALLIATIVE CARE IN CHILDREN WITH CANCER: EXPERIENCES OF PARENTS AND STAFF

R. McAndrew[1], P. Smith[2], M. Nelson[2], D. Kelly[3], W.H.B. Wallace[1], K. Kelsey[1], C. Applegath[1]

[1]Oncology, Royal Hospital for Sick Children, Edinburgh, United Kingdom; [2]Nursing Studies, University of Edinburgh, Edinburgh, United Kingdom; [3]Nursing Research, Cardiff University, Edinburgh, United Kingdom

Objectives: Exploration of personal and professional challenges associated with the period of transition between active and palliative care for paediatric oncology. This uncertain, little

researched, turning point of treatment will be described and, aspects of effective and less effective practice in managing such situations will be highlighted.
Methods: Qualitative interviews with 2 groups took place. Firstly, 10 staff members working within the Oncology/Haematology ward at a single Primary Treatment Centre, (PTC) were interviewed and a staff focus group followed to discuss the common themes arising within the interviews. Secondly, 7 sets of parents who had lost a child to cancer within the last 1-10 years. All parents had children who were treated for cancer at the same 'PTC'. Each parent was offered a second interview which explored themes arising from the first interview using the technique of emotional touch point stories.
Results: Established transition theories were supported although complex interplay between the transition for each group was present. Requirements for transition were described clearly by both groups, awareness & acknowledgement of the move from active to palliative care was particularly evident in the parent group. The importance of support systems and strong connections with others was a strong focus for both groups, particularly staff.
Use of the Emotional Touchpoint Tool aided families in finding the right words.
Conclusions: The process of the transition differs between families as different circumstances undeniably lead to individual experiences; however arising themes have met required aims allowing effective description of transition. Interviews naturally alluded to the greater transition following the death of the child and the move into bereavement. Importance of continuing support mechanisms were identified and will lead to recommendations for local practice, especially relating to introduction to the ward environment and continuity of care through palliation and beyond into bereavement care.

EP-648

KETAMINE HALVES OPIATE REQUIREMENTS AND SIMULTANEOUSLY REDUCES PAIN SCORES TO ZERO IN HIGH RISK NEUROBLASTOMA PATIENTS RECEIVING IMMUNOTHERAPY

D. McIntosh[1], C. Reilly[2], M. Canning[2], G. Paton[1], M. Ronghe[1], J. Sastry[1], D. Murphy[1]

[1]Paediatric Oncology, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom; [2]Pain Team, Royal Hospital for Sick Children Yorkhill, Glasgow, United Kingdom

Objectives: Assessment of ketamine efficacy and tolerability in patients receiving immunotherapy for Neuroblastoma.
Methods: Retrospective case note and pain database review of patients on the HR-NBL-1/SIOPEN protocol.
Results: Nine patients, 4 male, median age 36months (IQR: 25-70months) received a total of 42 cycles of immunotherapy between 2009 and 2013. 2 of the 6 patients who received CH14.18/CHO antibody with aldesleukin (IL2) completed all 5 cycles of treatment. 20 of a possible 30 antibody cycles were delivered in total. 1 patient relapsed and died following cycle 2. All 4 patients receiving ketamine as second line analgesia were in the combined antibody/IL2 group. These patients had high pain scores despite multiple Nurse Controlled Analgesia boluses or clinician overrides. Pain scores fell to 0 soon after ketamine infusions were commenced despite greater than 50% decreases in opiate requirements. Ketamine was administered prophylactically in all subsequent cycles and significant pain was not experienced thereafter.
Conclusions: Ketamine is a safe and effective adjunct to morphine when administered to High Risk Neuroblastoma patients receiving immunotherapy. Ketamine facilitates a decrease in morphine dosage and toxicity. Following ketamine commencement the median morphine dose was reduced by 50-75% when compared to the peak morphine dose prior to its introduction. The use of ketamine improves tolerability of immunotherapy allowing maximal delivery which may positively impact on High Risk Neuroblastoma survival.

EP-649

THE BENEFIT OF COMMUNITY ENGAGEMENT IN PUBLIC HEALTH AND PALLIATIVE CARE SERVICES FOR CHILDREN WITH CANCER IN LOW RESOURCE SETTINGS

W. Mwashala[1], D.R.M. Murtadha[2]

[1]Nursing/Palliative care, St. Lucia Nursing Home, Arusha, Tanzania; [2]Pediatric, Mount Meru Hospital, Arusha, Tanzania

Objectives: To facilitate early referral of identified at risk sick children to the local district hospital for clinical referral to Ocean Road cancer hospital in Tanzania for further diagnosis and treatment.
Methods: The Global Fund supported St. Lucia Nursing Home to identify 35,000 children and their families for community health fund, which included a payment scheme for vulnerable children to attend hospital services with special card named TIKA, TREATMENT PER CARD. The local government authorities identified children, as well as individuals in need of training to assist with identification, engaging participatory services of government hospitals for treatment. The training module offered was "Introduction to Palliative care", using tool such as HELPFUL to identify early signs of cancer in children and to create awareness in the general public of the importance of urgent referrals and early attendance to the hospitals. The HELPFUL tool was adapted from Muhimbili Cancer institute describing early diagnosis of Cancer which was translated in the local vernacular language. Between 2009 to 2013, 13,867 children were enrolled in 8 district hospitals for various medical conditions and recorded in each hospital registry.
Results: After a mean of 5yrs, 13,867 children were followed, 9740 were males 4127 females aged 1-19 yrs. Out of 13, 867 cases, 735 children needed palliative care as 3 children had hydrocephalus, 3 cerebral palsy, 9, mental retardation, 717, HIV/AIDS, 1 Albino. 8 children with cancer were referred to Ocean Road Cancer hospital for management of cancer 4 male were diagnosed with Burkitts lymphoma, 1 male with Acute lymphoblastic leukemia while 1 female had Burkitts lymphoma, 1 female had brain tumor.
Conclusions: The trained community members enhanced quality of care through early referrals, creating community awareness regarding cancer care, and eradication of stigma in settings where resource and infrastructures are limited.

EP-650

A REVIEW OF TREATMENT OUTCOMES OF KAPOSI'S SARCOMA IN CHILDREN ATTENDING HOSPICE AFRICA UGANDA AND ITS IMPLICATIONS FOR THE PROVISION OF PALLIATIVE CARE

S. Nandaula[1]

[1]Clinical, Hospice Africa Uganda, Kampala, Uganda

Objectives: To associate between the prevalence of antibodies against sarcoma-associated HIV/AIDS
To find out the response of treatment s once given to patients
Methods: A chart review of 10 children with HIV/AIDS and KS at Hospice Africa Uganda was carried out. All the children had been on programme for at least a month prior to review.
Results: Of the children reviewed, 6 (60%) were male and 4 (40%) female, the age of the children ranged from 3 to 15 years with the mean age being 9.4 years. In reviewing their histology, the most common presentation was lymphadenopathic KS. 5 of the children were receiving treatment in terms of both chemotherapy and ARVs whereas 5. of the children were unable to start either treatment. Three out of the 5 children receiving chemotherapy had earlier shown signs of clinical improvement but following treatment default, they had presented with rapidly progressing symptomatology. These three children fared poorly on retreatment courses of chemotherapy with one fatality.
Conclusions: Children commonly get lymphadenopathic KS and this is more common in the older children although this review is small in scale, it does seem to suggest that combination of therapy with chemotherapy and ARVs is beneficial. On the other side, treatment default can lead to rapidly progressing symptomatology, poor response to retreatment regimens and possibilities of high fatality rates. Within the provision of palliative care, this has implications for both management of KS but also for the palliation of symptoms associated with both treatments for the disease as it progresses. Bigger studies are recommended in the pediatric population to study this in more depth.

EP-651

PALLIATIVE CARE SERVICES IN CHILDHOOD CANCER IN BANGLADESH – CURRENT SITUATION AND CHALLENGES

A.S.M. Nurunnabi[1]

[1]Research and Publication, Bangladesh Medical Research Council, Dhaka, Bangladesh

Objectives: Palliative care is a major priority in childhood cancer care strategy as it provides compassionate support both for the children and their families. The aim of the present study was to observe the current situation of palliative care services in childhood cancer in Bangladesh and its challenges.
Methods: A survey was done between July and December of 2013 in some specialized pediatric oncology units of different public and private hospitals in Dhaka city of Bangladesh, based on a semi-structured questionnaire. A total of 300 respondents including physicians, nurses, caregivers, hospital managers who deal with childhood cancer, and parents of children suffering from cancer took part in this survey. Queries addressed are access to treatment, availability of drugs, palliative care, pain management, cost of treatment, quality of care and perceived challenges.
Results: Difficulty in access to treatment (86%), out-of-pocket payment for oncology therapies (88%), palliative care (91%) were evident. 93% reported that availability of specialized palliative care services, pain management and psychological plus decision-making support were inversely related to income level. Overall, 96% of respondents indicated that palliative care is important for their patients and 79% indicated that they were competent to provide this care; however, only 64% indicated that they had enough time to deliver quality palliative care. Challenges include less availability of facility, high cost, limited and inefficient manpower, low quality of care, less communication between health professionals and parents/family members of the patient.
Conclusions: In Bangladesh, pediatric oncology is usually practiced in resource-strained oncology units of pediatric divisions in different public hospitals along with few private hospitals. However, this survey confirmed that many of the children lack access to quality palliative care. Effective palliative care requires establishment of more facilities with cancer registry, availability of drugs for therapies and pain management, manpower development, communication with patients and families in decision-making.

EP-652

BODY MASS INDEX FOR SCREENING BACTEREMIA AMONG PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA

R. Ojha[1], M. Aviles-Robles[2], K.M. Johnson[3], B. Phillips[4], M.A. Caniza[3]

[1]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, USA; [2]Department of Infectious Diseases, Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico; [3]Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, USA; [4]Centre for Reviews and Dissemination, University of York, York, United Kingdom

Objectives: Currently available clinical prediction models are suboptimal for screening bacteremia among pediatric cancer patients with febrile neutropenia. The addition of better markers of bacteremia may improve screening. Given evidence supporting an association between body mass index (BMI) and infection, we explored whether BMI could improve screening of bacteremia among pediatric cancer patients with febrile neutropenia in Mexico.
Methods: We prospectively collected data for febrile neutropenia episodes among pediatric cancer patients admitted to Hospital Infantil de Mexico Federico Gomez (Mexico City) between November 2009 and September 2010 ($n = 115$; 147 episodes of febrile neutropenia). Generalized estimating equation logistic regression was used to predict bacteremia for one model with 2 markers commonly used in previous studies (C-reactive protein [CRP] and hypotension), and a second model with CRP, hypotension, and BMI. We subsequently estimated the area under the receiver operating characteristic curve (AUC) and corresponding 95% confidence limits (CL) for each model, and used decision curve analysis to assess the clinical net benefit of adding BMI.
Results: Bacteremia was microbiologically confirmed in 14% (21/147) of febrile neutropenia episodes. The addition of BMI improved clinical discrimination of bacteremia (with BMI: AUC = 0.77, 95% CL: 0.68, 0.85; without BMI: AUC = 0.74, 95% CL: 0.64, 0.84). The model with BMI also yielded a greater clinical net benefit compared with the model without BMI between risk thresholds of 7% and 17%.
Conclusions: Our results suggest that BMI may be a promising complementary marker for screening bacteremia among pediatric cancer patients with febrile neutropenia, particularly for individuals with predicted bacteremia risks in an otherwise clinically ambiguous range. The added value of BMI for screening bacteremia should be explored in other geographic areas, and could be particularly useful in low- and middle-income countries given the feasibility of measuring BMI.

EP-653

DEVELOPING AN INTEGRAL PEDIATRIC PALLIATIVE CARE PROGRAM: THE ROLE OF PARENTS, VOLUNTEERS AND PERIPHERAL CLINICS IN NICARAGUA.

R. Ortiz[1], S. Moya[2], L. Paredes[1], A. Orozco[1], F. Baltodano[3], R. Carranza[4], N. Ribera[5]

[1]Pediatric Hematology-oncology Department, Manuel de Jesus Rivera La Mascota Children's Hospital, Managua, Nicaragua; [2]MAPANICA Parents' Association, Manuel de Jesus Rivera La Mascota Children's Hospital, Managua, Nicaragua; [3]Pediatric Hematology-oncology Peripheral Clinic, Matagalpa Regional Hospital, Matagalpa, Nicaragua; [4]Pediatric Hematology-oncology Peripheral Clinic, Victoria Mota Regional Hospital, Jinotega, Nicaragua; [5]Pediatric Hematology-oncology Peripheral Clinic, Esteli Regional Hospital, Esteli, Nicaragua

Objectives: Background/Purpose: Manuel de Jesus Rivera, La Mascota, Children's Hospital is the only pediatric cancer unit in Nicaragua. Since the early 90's the pediatric oncology staff have implemented palliative care. The National Ministry of Health introduced Palliative care in 2010 as a Health strategy by recommendation of the World Health Organization (WHO). Although a National Palliative Care Protocol exists, most of the medical staff remains unaware of its presence. As in most low income country patients arrived with advance disease, for this reason this program was developed aiming to provide integral palliative care since diagnosis to alleviate suffering, and to improve the quality of life of children in the hospital setting and at home.
Methods: A survey assessing symptom control and physician report with families in the palliative care setting was performed on 45 progressive disease, oncology patients out of the 181 newly diagnosed from January-December 2010. Findings of the survey were used to establish the work plan of the multidisciplinary palliative care team.
Results: In 50% of patients, disturbing symptoms were moderately controlled; half of families interviewed referred to be satisfied with the communication of bad news that prepared them for the terminal phase. Multidisciplinary meetings including parents' association, volunteers and members of the hemato-oncology staff were conducted to train in communication skills, and to review family needs assessed by home visits from members of MAPANICA. Medical, nursing staff, psychologists and social workers from five peripheral clinics were trained in palliative care. Three out of the five clinics are providing palliative care follow up to children near their homes.
Conclusions: Integrating efforts of medical personnel, parents and volunteers can contribute to provide good palliative care practices in countries with limited resources. Assessment of the needs of the children and their families contribute to improve the quality of care.

EP-654

A FEASIBLE COMPUTER-BASED EXERCISE PROGRAM FOR DAILY CLINICAL PRACTICE IN PAEDIATRIC ONCOLOGY INCREASES MOTIVATIONAL BENEFITS

A.M. Platschek[1], L. Kehe[1], F. Berthold[2], F.T. Baumann[3], H.K. Strüder[1]

[1]Institute of Movement and Neurosciences, German Sport University Cologne, Köln, Germany; [2]Children's Hospital, University Hospital of Cologne, Köln, Germany; [3]Institute of Cardiology and Sports Medicine, German Sport University Cologne, Köln, Germany

Objectives: The benefits of physical activity in cancer therapy in adults are well documented. In addition to an increase of physical performance there can be positive effects on quality of life and reduction in fatigue syndrome. However, in paediatric oncology this approach has not been sufficiently explored, well controlled exercise programms are still missing. The purpose of our PAPO-Study (Physical Activity in the Paediatric Oncology) was to investigate the integration of a child-friendly computer-based exercise program in paediatric oncology and furthermore to research effects of the intervention on motivational benefits. Results could underline the need for exercise therapy as an useful supportive care in paediatric oncology.
Methods: Ten subjects with malignant neoplasm (ICD10 C00-C97) between 9-14 years were included. The intervention included a weekly computerized exercise program over three months. Intensity and duration were dependent on individual day's form and contained different sport games. A brief emotional questionnaire (MoodMeter®) was answered before and after a sport unit every month. Integrability of the intervention was determined by dropout and analysis of the number of interventions.
Results: Subjects performed on average approximately 10 sport units with about 45 minutes, no dropouts. During the sport units mean heart rate was approximately 136 beats per minute. Pre-post comparison showed a significant increase in the overall motivational states (including self-confidence, social acceptance, readiness to strain and willingness to seek contact) ($p < 0.05$).
Conclusions: The PAPO-Study shows that physical activity can be well integrated into paediatric oncology clinical practice and furthermore the exercise intervention produces verifiable motivational benefits. The results indicate the importance of physical activity for the quality of survival in paediatric oncology. Exercise could restore a piece of normality to children's lives and help in handling with psychological side effects of chemotherapy. More studies exploring this approach and supporting natural need for movement will be needed.

EP-655

EFFECTS OF MALNUTRITION ON TREATMENT RELATED MORBIDITY (TRM) AND SURVIVAL IN CHILDREN WITH CANCER IN NICARAGUA

A. Pribnow[1], R. Ortiz[2], S. Luna-Fineman[3], F. Baez[2], L. Mendieta[4]

[1]Department of Pediatrics, Stanford University, Palo Alto, USA; [2]Department of Hematology/Oncology, Children's Hospital Manuel de Jesus Rivera "La Mascota", Managua, Nicaragua; [3]Hematology/Oncology/SCT/Cancer Biology, Stanford University, Palo Alto, USA; [4]Department of Nutrition, Children's Hospital Manuel de Jesus Rivera "La Mascota", Managua, Nicaragua

Objectives: Most children with cancer live in low- and middle-income countries where rates of malnutrition are often high. This study aimed to identify the relationship between malnutrition and treatment related morbidity (TRM), abandonment of therapy, relapse, and death of children with cancer in Nicaragua to better inform targeted nutritional interventions.
Methods: A retrospective study of patients ages 6 months-18 years newly diagnosed with ALL, AML, Wilms tumor, Hodgkin disease, or Burkitt lymphoma between January 1st 2004 and December 31st 2009 and treated at Children's Hospital Manuel de Jesus Rivera in Managua, Nicaragua. Children were included only if nutritional evaluation was recorded at diagnosis. Statistical analysis examined the relationship between nutritional status and cancer type, risk category, TRM and event-free survival (EFS) using de-identified data from the POND database.
Results: Of the 282 patients included in the study, 67% were malnourished at diagnosis. Malnutrition was highest among Wilms tumor (85.7%), Burkitt lymphoma (75%), and AML (74.3%), and lowest in Hodgkin disease (58.3%). Malnourished patients had inferior EFS (2.25 vs. 5.58 years) with significance across the distribution ($p = 0.049$), and malnutrition was associated with abandonment at 2 years ($p = 0.015$). Of the 244 patients included in the TRM analysis, almost all (92.2%) experienced morbidity during the first 90 days of treatment, and 84% experienced severe (grade $\geq$3) morbidity. Malnutrition was significantly associated with severe infection ($p = 0.033$) but not other specific morbidity types. Malnourished patients had severe morbidity on a higher proportion of days ($p = 0.023$); and were more likely to experience severe morbidity during >50% of days ($p = 0.032$, OR 3.27 [95% CI 1.05-10.16]).

Conclusions: Pediatric oncology patients from Nicaragua with malnutrition at diagnosis experience increased TRM, particularly severe infection, and have inferior EFS. Standardized nutritional evaluation of all newly diagnosed patients with targeted provision of nutritional support is essential to decrease TRM and improve outcomes.

EP-656

IDENTIFICATION OF ISSUES INVOLVED IN THE ROAD TO DIAGNOSIS OF CHILDHOOD CANCER IN A DEVELOPING COUNTRY

J. Pulivadula Venkatasai[1], J.X. Scott[1], A. Rajendran[1], R. Manipriya[1], M.S. Latha[1]

[1]Dept. of Pediatrics Division of Hemato-oncology, Sri Ramachandra Medical College And Research Institute, Chennai, India

Objectives: Cure rates for children with childhood malignancies are 80–85% in high-income countries (HICs). However, cure rates are much lower in many low income countries (LICs). Globally, an estimated 250,000 children develop cancer each year, and 80% of them live in developing countries. Unfortunately, late presentation and delayed diagnosis of childhood cancers remains a problem in developing countries. The principle objectives of this study is to assess the referral pattern and identification of issues related with road to diagnosis of childhood cancer in India
Methods: 70 families with children undergoing treatment participated in the study. The parents/guardians were interviewed in a prepared questionnaire session. Study Period - Aug 2012 -Aug 2013.
Results: Of the 70 patients with hematological malignancies, with 69% males and 31% females, the mean age was 7.8 ± 2.2 years. The diagnostic delay, in most patients, was attributed to healthcare system delay with a median delay of 18 days (Mean – 26 days) (Range 5-39). Parental delay was significantly higher with patients from rural areas and whose parents had lower levels of education (highest being 44 days). Diagnosis and physician delay was relatively shorter for patients who visited a pediatrician than for patients whose first health contact was a general physician or other specialties. Number of different contacts and hospital admissions in the health system is significant factor causing delay in diagnosis. The median number of healthcare visits by parents is 4 and average number of days of admission is 9 days, before they were evaluated by a specialist. Geographical distance from access to tertiary healthcare is also positively associated with diagnostic delay.
Conclusions: Prompt and early diagnosis of cancer is considered the corner stone of a healthy prognosis for the patient.

EP-657

OUTCOME OF SURGICAL INSERTIONS OF TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES: AN INSTITUTIONAL EXPERIENCE FROM PAKISTAN

A.Q. Qazi[1], Z.Q. Feroza[1], M. Zia-ul-Miraj[2], T. Latif[1]

[1]Surgical Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan; [2]Department of Paediatric Urology, The Children's Hospital, Lahore, Pakistan

Objectives: To determine outcomes of surgical insertions of totally implantable venous access devices (TIVAD) in children in a cancer hospital in developing world.
Methods: This is retrospective study of patients with TIVAD in children requiring chemotherapy for cancer. All these procedures were performed in a specialized cancer hospital in Pakistan. Period of study was from June 2005 to June 2013. Data was retrieved from hospital information system using identified parameters and analysed using SPSS.
Results: A total of 370 patients underwent TIVAD insertion during the study period. Indication of insertion of device was chemotherapy for cancer in all patients. There were 62% males. One hundred seventeen patients were lost to follow up with TIVAD in place. All other lines were either removed at completion of treatment (42.4%) or due to infection or blockage of line. A total of 94 (25%) devices were removed prior to completion of therapy. Out of these 29 (7.8%) TIVADs were removed due to infection proven by microbiology cultures from of the line tip. Mean life of device in our patient was 278 days. In our study we could not find a correlation between neutropenia and line infection ($P = 0.88$). We have studied factors responsible for early removal of line and a large number of patients being lost to follow up. Role of nursing care, long distances from hospital and advanced stage of cancer in device care is also highlighted.
Conclusions: Benefits of central venous device for chemotherapy can not be denied. However it is challenging to care for these devices in a charity cancer hospital in a developing country setting. In our study we have proven that TIVADs can be safely inserted and managed for chemotherapy in children in a low resource setting with extra vigilant care while devices are in place.

EP-658

VANCOMYCIN RESISTANT ENTEROCOCCI COLONIZATION AND INFECTION IN CHILDREN WITH CANCER

S. Farid[1], I. Ragab[1], S. Girgis[2], W. Sarhan[1]

[1]Pediatrics, Ain-shams University, Cairo, Egypt; [2]Clinical Pathology, Ain-shams University, Cairo, Egypt

Objectives: Vancomycin-resistant enterococci (VRE) were previously reported to be responsible for a serious hospital-acquired infection. This study aimed to identify risk factors and resistance profile associated with VRE intestinal colonization and infection in a cohort of children with cancer.
Methods: Seventy five children were included in this case-control study. They were divided into 3 groups; group (1) includes 25 cancer outpatient having no symptoms and signs suggestive of infection and having a neutrophil count more than 500/uL, group (2) includes 25 cancer inpatient who were admitted for febrile neutropenia, group (3) includes 25 healthy, age and sex matched children as a control. Stool analysis, rectal swab and blood culture were performed for inpatient on admission, at 3 and 7 days later. Outpatients and controls were studied by rectal swab and stool analysis. The analysis of samples includes culture, isolation, identification and detection of susceptibility of isolates to antibiotics.
Results: The median duration of admission was 15 days (9-60); 20% of blood culture showed VRE isolates. VRE were detected in one inpatient on admission, compared to 5 patients after one week ($p = 0.01$). Infected inpatients had significant lower neutrophil count compared to non-infected ones ($p < 0.001$), meanwhile there was no significant difference in age, sex, duration of neutropenia and duration of admission between infected and non-infected inpatients ($p > 0.05$), The use of vancomycin, metronidazole and imipinem antibiotics were significantly higher in those infected with VRE compared to non-infected ones ($p < 0.05$). Twenty eight percent of inpatients had a positive stool culture after one week, enterococci were found in 4% of inpatient 3 days post admission, compared to 28% one week post admission.
Conclusions: We conclude that children with cancer are at high risk for VRE colonization and infections. Severity of neutropenia and excess use of vancomycin are important risk factors.

EP-659

INVASIVE POSITIVE PRESSURE VENTILATION IN CHILDREN WITH FEBRILE NEUTROPENIA: FIVE YEARS OF EXPERIENCE IN A PAEDIATRIC ONCOLOGY INTENSIVE CARE UNIT

K. Riad[1], S. Abdel Hadi[2], M. Ghazally[3], M. Mokhtar[4]

[1]pediatric oncology, South Egypt Cancer Institute, Assiut, Egypt; [2]pediatric oncology, Natinal Cancer Institute, cairo, Egypt; [3]pediatric hematolgy, faculty of medecine, assiut, Egypt; [4]pediatric ICU, faculty of medecine, assiut, Egypt

Objectives: To evaluate the feasibility and outcome of -invasive positive pressure ventilation (IPPV) in children with febrile neutropenia due to haematological malignancy.
Methods: Design: Observational retrospective cohort study. Setting: Pediatric intensive care unit in a university hospital. Patients: children with hematological cancer with febrile neutropenia treated by IPPV, regardless of the indication, during five consecutive 5 years (2008-2013).
Results: A total of 101 patients were included, and 61of the 101 patients (60%) were successfully treated by IPPV. The success rate of IPPV was significantly lower (22%) in the patients with acute respiratory distress syndrome ($p < .05$) than in the other patients
Conclusions: This study demonstrates the feasibility and efficacy of IPPV in the daily practice of a pediatric oncology intensive care uni, but. This ventilatory support could not be proposed as a first-line treatment in children with acute respiratory distress.

EP-660

THE ROLE OF PROCALCITONIN IN DIAGNOSIS OF SEVER SEPSIS AND CLINICAL OUTCOME IN CRITICALLY ILL FEBRILE NEUTROPENIC CHILDREN WITH CANCER

K. Riad[1], S. Amr[2], S. Abdel Hady[3], M. Ghazally[4], M. Mokhtar[5], E.M.A.N. Zaki[6]

[1]Pediatric Oncology, South Egypt Cancer Institute, Assiut, Egypt; [2]Anathesea and ICU, South Egypt Cancer Institute, Assiut, Egypt; [3]Pediatric Oncology, National Cancer Institute, Cairo, Egypt; [4]pediatric oncology, Faculty of medecine, Assiut, Egypt; [5]pediatrics, Faculty of medecine, Assiut, Egypt; [6]Clinical pathology, South Egypt Cancer Inestitute., Assiut, Egypt

Objectives: Evaluate the significance of early diagnostic serum procalcitonin (PCT) in febrile neutropenic children and its value for ICU admission and outcome.
Methods: The study was conducted on 200 episodes of febrile neutropenic children with hematological malignancies who presented to the South Egypt Cancer Institute (SECI) diagnosedwith fever and neutropenia with no prior treatment with antimicrobial therapy for the present episode. The patients were divided to two equal groups, group A and group B. Both groups were further classified into high risk group (HR) and low risk group (LR) 50 patients in each group. complete blood count, serum procalcitonin (PCT) in the first day of admission, blood culture and other cultures (sputum, urine, wounds), liver function, kidney function, random blood sugar, serum electrolytes, and chest radiograph were done.
Results: The number of unimproved patients in our study were 35.21patients had gram -ve isolates (60%), 9 patients had gram +ve isolates (25.7%) (5 died and 4 alive) and 5 had no growth (14.3%). From the 35 unimproved patients, 23 patients had sepsis level of PCT, 7 patients had systemic infection and 5 patient had local infection level of PCT, the difference

was statistically significant, ($P < 0.001$). From 50 high risk patients treated inside ICU, 11 patients not improved, and those treated outside ICU, 17 patients not improved, the difference was statistically not significant. In the studieded groups, 15 cases put on mechanical ventilation (7.5%), 13 patients had profound neutropenia (86.6%) and 10 patients had sepsis level of serum PCT level (75%), and only 9 patients improved (60%).
Conclusions: Sepsis level of serum PCT is a useful marker for suggesting sever sepsis and estimation of serum PCT support the decision to start antibiotics therapy and ICU admission.

EP-661

INFECTION PATTERN OF NEUTROPENIC CHILDREN IN POST-CHEMOTHERAPY PHASE OF HEMATOLOGICAL MALIGNANCIES TREATMENT

K. Riad[1], S. Abdel Hadi[2], H. Ghazally[3], M. Mokhtar[4], E.M.A.N. Zaki[5]

[1]Pediatric Oncology, South Egypt Cancer Institute Assiut, Egypt; [2]Pediatric Oncology, National Cancer Inestitute, Cairo, Egypt; [3]Pediatrics, Assiut University Chidren Hospital, Assiut, Egypt; [4]Pediatric ICU, Assiut University Chidren Hospital, Assiut, Egypt; [5]Clinical Pathology, South Egypt Cancer Inestitute, Assiut, Egypt

Objectives: Neutropenia following chemotherapy regimens in hematological malignancies children is of major concern since it makes these patients vulnerable to infections.
In this study, we tried to identify the pattern of infections and their antibiotic resistance.
Methods: This retrospective multi-center study took place in 2012 and included patients with hematological malignacies who had been febrile for at least 12 hours. In order to assess the type of infection, This study took place in 3 places in Egypt.
Results: From all our positive cultures, it was seen that 80.4% of them had gram-negative bacteria with a dominance of E. coli of 22.8% over the other colonies. Also, antibiograms revealed the sensitivity of almost all the gram-negatives to amino glycosides. In contrast with most of the literature.
Conclusions: in our patients, gram-negatives are the most common cause of infection and, therefore, administering amino glycosides would be the safest antibiotic therapy to prescribe before culture results are available.

EP-662

THE IMPACTS OF ESTIMATION OF SERUM PCT LEVEL AS EARLY DIAGNOSTIC MARKER OF BACTEREMIA IN FEBRILE NEUTROPENIC CHILDREN

K. Riad[1], S. Abdel Hadi[1], H. Ghazally[1]

[1]Pediatric Oncology, South Egypt Cancer Institute, Assiut, Egypt

Objectives: Many studies have succeeded in identifying a subset of children with febrile neutropenia (FN) who are at lower and higher risks of infectious complications and eventual death. but small of them that discuss the impacts of estimation of a diagnostic marker of bacteremia which is the procalcitonin (PCT).
Methods: Between January 2010 and July 2012, 200 episodes of FN in 143 children were included in a prospective study in South Egypt Cancer Institute Assiut University, Assiut, Egypt to evaluate the outcome of febrile neutropenia in children with hematological malignancies and to determine the impacts of estimation of a diagnostic marker of bacteremia which is the procalcitonin (PCT).
Results: In the present study profound neutropenia (ANC less than 100 cell/m3) was significantly observed in high risk febrile neutropenic patients and observed also in patients with high PCT level (sepsis level i.e more than 10 ng/ml and systemic infection level more than 0.5 ng/ml,) and with patients with positive blood cultures in comparison to pateints with mild to moderate neutropenia (ANC more than 100cell/m3). Profound neutropenia also was signfcantly observed to be associated with monocytopenia (96%) in comparison to mild and moderate neutropenia (3%). Patients with profound neutropenia were also signfcantly observed to be more laible to develop shock (86.6%) more than of that of higher ANC (5%). Bacteriologically documented infection were detected in 162 neutropenic episodes (81%), of them gram positive infection were detected in 111 patients (55.5%) and gram negative were detected in 52 (25.5%) and 38 (19%) patients had no growth. Grame negative infection were signifcantly observed in high risk febrile neutropenia epesodes and associated with poor prognosis.
Conclusions: -It was concluded that sepsis level of serum PCT is a useful marker strongly suggestive of sever sepsis and bacteriologically documented infection.
-High serum level of PCT may help in stratification of patients with febrile neutropenia in high risk and low risk group.

EP-663

VENOUS CATHETERIZATION AS A MIRROR OF RUSSIAN PEDIATRIC ONCOLOGY

M. Rykov[1], E. Gyokova[1], V. Polyakov[1]

[1]General Oncology, Institute of Pediatric Oncology and Hematology N. N. Blokhin, Moscow, Russia

Objectives: The treatment of any oncologic disease is impossible without a venous access. What kind of properties should it possess? It has to be safe, easy to use, implanted only once during the treatment course and have minimal risks associated with implantation and use.
Methods: From 2010 to 2013 we were monitoring the treatment of 228 children (aged 3 months to 17 years) with oncologic diseases. 110 patients underwent 605 subclavian vein catheterization, 118 patients – 118 venous port implantation.
Results: Complications and technical difficulties during catheter insertion were observed in 98.3% of cases, during venous port implantation – in 23% of cases. Complications of subclavian catheter and venous port use were observed in 97.3% and in only 11% of cases, respectively. Subclavian catheters compromised cancer treatment in 45.9% of patients, implantable venous ports – in 1.7% of patients. Each patient with a subclavian catheter underwent central venous catheterization 4 to 19 times (mean 6 times) during treatment. Catheter dwell time exceeded the recommended limit in all patients except for cases of catheter removal by patients. On multiple occasions all patients were discharged with a subclavian catheter in place.
Conclusions: Venous ports obviously match the criteria mentioned in the introduction. Subclavian catheter use resulted in cancer treatment protocol deviation in almost 50% of cases, thus leading to a poorer prognosis and significantly increasing the number of invasive procedures and instances where general anesthesia was needed.

EP-664

APPLICATION OF EPIDURAL IMPLANTABLE ACCESS SYSTEMS FOR PAIN MANAGEMENT IN INCURABLE PATIENTS

M. Rykov[1], V. Polyakov[1]

[1]General Oncology, Institute of Pediatric Oncology and Hematology N. N. Blokhin, Moscow, Russia

Objectives: Domiciliary chronic pain syndrome management in incurable patients with disseminated cancer is of paramount importance in improving their quality of life.
Methods: In the period of 2012-2013, 5 incurable patients with various types of cancer (aged 10 to 15 years; mean age 12.7 years) underwent epidural access system implantation. Epidural space catheterization at the $L_3 – L_4$ interspace was performed followed by x-ray to ensure the catheter proper placement. A 1 cm skin incision and blunt dissection of the subcutaneous tissue was made at the catheter exit site. A clip for catheter fixation was then inserted into the created subcutaneous space and sewn to the adjacent tissues. The port was implanted into the soft tissues above right ribs 10-12. The catheter was threaded through the subcutaneous tunnel up to the port. The incision above the clip and port was closed in layers. Only Huber needles were used to access the port. The choice of type and dosage of the analgesic was based on the pain syndrome severity, as well as cancer localization and stage.
Results: The patients noted the improvement in quality of life, improved emotional state, and almost complete pain relief. 1 patient (20%) is currently alive, 4 (80%) died due to cancer progression. The epidural implantable access system was used for up to 5 months. No infection or occlusion of the system was observed. One patient (20%) experienced blood pressure drop due to an opioid analgesic overdose.
Conclusions: Epidural access systems facilitate pain syndrome management, improve the quality of life, and reduce the opioid dose. Besides, these routes of opioid administration are commonly associated with adverse effects. However the introduction of epidural access systems in the Russian medical setting is stalled due to the absence of qualified medical staff in hospices as well as in outpatient departments which provide in-home care for incurable patients.

EP-665

RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN IS SAFELY AND EFFICIENTLY USED FOR DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN CHILDHOOD ACUTE PROMYELOCYTIC LEUKEMIA (APL)

Y. Saito[1], Y. Yuza[1], S. Ishimaru[1], Y. Yokokawa[1], T. Kaneko[1]

[1]Haematology/Oncology, Tokyo Metropolitan Children's Medical Hospital, Tokyo, Japan

Objectives: Patients with APL are usually complicated with DIC at onset, which occasionally lead to life-threatening hemorrhage. Efficacy of heparin, other anticoagulants, or antifibrinolytic therapy remains questionable for the management of DIC complicated with APL. In 2008, a new anticoagulant, recombinant human soluble thrombomodulin (rTM) was approved for the treatment of malignancy- or infection-associated DIC in Japan. So we retrospectively evaluated the safety and efficacy of rTM for the treatment of DIC in childhood APL.
Methods: We reviewed three patients with DIC associating underlining untreated APL, who were treated with rTM from October 2010 to February 2014. rTM were used at the recommended dosage in adults, 380 U/kg/day. Toxicity profiles were graded based on CTCAE ver.4.0. Diagnosis of DIC was based on the criteria released from Japanese Ministry of Health, Labor and Welfare. Concurrent treatment with fresh frozen plasma and platelet transfusion are administered, but no other anticoagulant therapies were performed. Endpoint for efficacy was

complete resolution of bleeding disorders, such as petechiae, purpura, gingival hemorrhage and intramuscular bleeding.
Results: Three patients with APL presented bleeding disorders at the onset of APL. Median age at diagnosis was 6 years (range 5-6). Duration of rTM treatment was 13 days (range 7-19). DIC status were resolved with the median of 8 days (range 6-14) and bleeding disorders were recovered with the median of 6 days (range 5-7) after initiation of rTM. No patient experienced severe hemorrhagic complication as well as grade 3-4 non-hematologic toxicities related with rTM. Neither of dose-escalation nor dose-reduction was clinically needed.
Conclusions: Administration of rTM for the treatment of DIC related with childhood APL appears safe and probably effective to control hemorrhagic complication of DIC. A large prospective trial is necessary to confirm efficacy and safety of rTM treatment for DIC of childhood APL.

EP-666

PROPHYLACTIC USE OF OCTREOTIDE FOR ASPARAGINASE-INDUCED ACUTE PANCREATITIS

S. Sakaguchi[1], T. Higa[2], M. Suzuki[1], J. Fujimura[1], T. Shimizu[1]

[1]Department of Pediatrics, Juntendo University Faculty of Medicine, Tokyo, Japan; [2]Department of Pediatric Hematology and Oncology, Okinawa Prefectural Nanbu Medical Center Children's Medical Center, Okinawa, Japan

Objectives: Acute pancreatitis develops in up to 18% of patients with acute lymphoblastic leukemia who are treated with asparaginase. Re-administration of asparaginase is often avoided because of the risk of pancreatitis recurrence. Octreotide is a synthetic somatostatin analogue that has been suggested for use in the treatment of acute pancreatitis, although its ability to prevent asparaginase-induced pancreatitis has not been fully evaluated. The purpose of this study is to evaluate the prophylactic use of octreotide for asparaginase-induced acute pancreatitis.
Methods: We performed a retrospective chart review in two institutions to evaluate pediatric patients who had experienced asparaginase-induced pancreatitis and underwent prophylactic octreotide treatment with re-administration of asparaginase. We also performed a literature review using PubMed with the following search terms: octreotide, pancreatitis, and asparaginase.
Results: We identified seven patients who received prophylactic octreotide in the two institutions between 2008 and 2013. Of these patients, four experienced recurrence of pancreatitis after asparaginase re-administration, and three completed treatment without recurrence. Our literature review yielded three additional cases with no recurrence. Among the six patients without recurrence, the severity of the first episode of pancreatitis was grade 2 for four patients and grade 3 for two patients. Among the four patients with recurrence, pancreatitis severity was grade 3 for three patients and grade 4 for one patient. No adverse events associated with octreotide were reported for any patient.
Conclusions: Our results suggest that the prophylactic use of octreotide prevents asparaginase-induced pancreatitis. Therefore, re-administration of asparaginase with octreotide may be warranted for patients with mild to moderate asparginase-induced pancreatitis. For patients with severe pancreatitis, however, the re-administration of asparaginase requires caution.

EP-667

CATATONIA IN COURSE OF HSCT IN A 17 YEAR-OLD PATIENT WITH AML

M. Samardakiewicz[1], K. Drabko[1], A. Zaucha-Prazmo[1], A. Makarewicz[2], J. Kowalczyk[1]

[1]Pediatric Hematology Oncology&Transplantology, Medical University, Lublin, Poland; [2]Chair and Department of Psychiatry, SPSK 1, Lublin, Poland

Objectives: Catatonic disorders in a form of inertness, negativism and mutism or hyperactivity, echolalia, echopraxia, occur rarely during treatment serious somatic diseases. Sometimes catatonia may develop as a result of psychic trauma.
Aim of the study: Presentation of catatonia case study in 17 year-old female with AML treated with HSCT.
Methods: Analysis of medical history, available lab tests as well as interdisciplinary consultations, on basis of which catatonic disorder was diagnosed among the patient hospitalized due to several post transplant complications.
Results: The patient with AML derivative to MDS was treated according to AML BFM Interimphase protocol, and required two MUD PBSCT. During treatment complications occurred (kidney and multiorgan failure requiring hemodialysis). From 36th day after Ist MUD PBSCT on, paroxysmal disorders were observed in form of head and arm shaking, anxiety, without losing conscience, without sleepiness after the seizure as well as an episode of sight perception disorder. From 60th day after IInd MUD PBSCT progressive loss of verbal contact, with periods of agitation, active resistance in attempt to move and feed, catalepsy. Due to this, the patient was multiple times consulted. In EEG, MRI and CT examinations organic basis of disorders was excluded. Patient's state was impossible to explain also because of balanced metabolic state. After secondary psychiatric opinion the patient was classified to pharmacological treatment and electroshock therapy was in question. Due to deteriorating somatic state of the patient and progressive symptoms of muscle flaccidity, the psychiatric treatment was canceled 3 weeks after its start.
Conclusions: 1. Catatonic disorders during treatment of an aggravating somatic disease are rarely diagnosed. 2. Due to diagnostic difficulties, especially among patients with various complications, there is a risk of not diagnosing this disorder. 3. The diagnosis of catatonia among adolescents during cancer treatment requires multidimensional diagnostics prior to difficult therapeutic decisions. 4. Not undertaking the proper catatonia treatment is a threat to a patient's life.

EP-668

FREQUENCY OF OCCURENCE OF MENTAL DISORDERS AMONG ADOLESCENTS TREATED FOR CANCER

M. Samardakiewicz[1], A. Makarewicz[2], K. Faber[3], A. Zaucha-Prazmo[1], J. Kowalczyk[1]

[1]Pediatric Hematology Oncology&Transplantology, Medical University, Lublin, Poland; [2]Chair and Department of Psychiatry, SPSK 1, Lublin, Poland; [3]Department of Psychology, University of Maria Sklodowska Curie, Lublin, Poland

Objectives: Pediatric cancer is an intense emotional and physical experience for patients and their families. Comprehensive psychiatric assessment of these children is complicated by symptoms of medical comorbidities that overlap mental health conditions.
Aim of the study. The analysis of frequency of symptoms of mental disorders among adolescents treated for cancer.
Methods: Between Jan 2010 to Feb 2014, 101 consecutive adolescents diagnosed with cancer were hospitalized at single pediatric oncology centre in Lublin, Poland. Following patients were excluded from the study: patients hospitalized once due to neutropenia, stem cells separation, and with mental retardation. 80 patients entered the study (45% females), with average age at the diagnosis 14.9. The List of Psychiatric Symptoms (LPS) was used to assess mental functioning.
Results: 26.3% of patients showed symptoms of mental disorders and were consulted with psychiatrist. Among 21 children psychiatric treatment was used. Average time of occurring symptoms from the moment of diagnosis was 6.05 months. Among females following symptoms were more frequent: Talking about death, Frequent cry, Low self-esteem, Refusal to eat, Decrease of concentration, Mutism ($p < 05$). Moreover, among patients with treatment complications aggravation of psychiatric symptoms was observed: Talking about death (72,4%), Irritability (74,2%), Affective instability (51,7%), Sadness, Low mood (89,7%), Anxiety (62,1%), Social withdrawal (69%), Lack of interest in environment (62,1%), Anhedonia (44,8%) – $p < 0.5$. Talking about death and Anhedonia were most frequently observed in patients with oeteosarcoma ($p < 0.5$). The most alarming symptoms were observed in patients with leukemia. Among 20,7% of them conscience and orientation disorders occurred, which was not observed in patients with lymphoma and solid tumors.
Conclusions: 1. More then one fourth of adolescents with cancer revealed different psychiatric symptoms. 2. All patients consulted with psychiatrist was treated with antidepressants. 3. LPS questionnaire is a useful clinical tool but we need further research on methods with better psychometric features.

EP-669

PREVALENCE OF SYMPTOMATIC AND ASYMPTOMATIC THROMBOSIS IN PEDIATRIC ONCOLOGY PATIENTS WITH TUNNELED CENTRAL VENOUS CATHETERS

R. Schoot[1], M. van de Wetering[1], T. Stijnen[2], W. Tissing[3], H. Heij[4], J. Lieverst[5], L. Spanjaard[6], H.N. Caron[7], C.H. van Ommen[8], S. SKION-aristocaths[9]

[1]Paediatric Oncology, Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands; [2]Medical Statistics And Bioinformatics, University of Leiden, Leiden, Netherlands; [3]Paediatric Haematology/Oncology, University of Groningen, Groningen, Netherlands; [4]Paediatric Surgery, Academic Medical Centre and Vu Amsterdam, Amsterdam, Netherlands; [5]Data Management, Dutch Childhood Oncology Group, The Hague, Netherlands; [6]Microbiology, Academic Medical Centre, Amsterdam, Netherlands; [7]Paediatric Oncology, Emma Children's Hospital/Academic Medical Centre, Amsterdam, Netherlands; [8]Paediatric Haematology, Emma Children's Hospital/Academic Medical Centre, Amsterdam, Netherlands; [9]Paediatric Supportive Care, Dutch Childhood Oncology Group, The Hague, Netherlands

Objectives: Pediatric oncology patients are at increased risk to develop venous thrombo-embolic events (VTE); up to 500 times higher than in the general pediatric population. The incidence of VTE in pediatric cancer patients with CVCs varies widely among studies between 2.1 and 50%.
Objective in this study; To determine the prevalence of (a) symptomatic venous thrombo-embolic events (VTE) in pediatric oncology patients with tunneled central venous catheters (CVC).
Methods: We systematically screened for (a) symptomatic VTE in patients included in the Aristocaths study: a randomized controlled trial investigating the prophylactic effect of 70% ethanol locks on CVC-associated bloodstream infections (CABSI). Patients were monitored

clinically for symptomatic VTE and with ultrasound (US) at the end of the study. Follow-up was six months, unless patients developed one of the following events: symptomatic VTE, CABSI, CVC removal, or death.
Results: We included 305 patients (hematologic malignancy, N = 148; solid tumor, N = 157) for symptomatic VTE and 182/305 patients were evaluated for asymptomatic CVC-related VTE. Twenty patients developed VTE: 8/305 (2.6%) patients developed symptomatic VTE (CVC-related, N = 3), 11/185 (6.0%) patients evaluated with US had asymptomatic CVC-related VTE and one patient was diagnosed with asymptomatic non CVC-related VTE. There was no significant difference in symptomatic and asymptomatic CVC-related VTE between the ethanol and heparin treatment group ($p = 0.25$ and $p = 0.17$ respectively).
Conclusions: This was the first systematic assessment of (a) symptomatic VTE in a large cohort pediatric oncology patients. Prevalence of symptomatic VTE was 2.6% and of asymptomatic CVC-related VTE (6.0%). These rates were lower than the prevalence reported in literature. This may in part be explained by the inclusion of patients with solid tumors, but also the reduction of CABSI by ethanol locks may have influenced the development of asymptomatic CVC-related VTE.

EP-670

CLINICAL EVALUATION OF ORAL MUCOSITIS IN CHILDREN WITH LYMPHOMA AND SOLID TUMORS

B. Sevinir[1], M. Demirkaya[1]

[1]Pediatric Oncology, Uludag University Medical Faculty, Bursa, Turkey

Objectives: The aim of this study is to compare the demographic and clinical characteristics of children with and without oral mucositis receiving chemotherapy for cancer.
Methods: This study is conducted prospectively in a total of 106 children receiving chemotherapy for lymphomas and solid tumors, between May 2012 and May 2013. Age, sex, diagnosis, the chemotherapy regimen, the presence of daily oral care, the time between the beginning of chemotherapy and oral mucositis, duration of oral mucositis were recorded. Severity of oral mucositis assessed by WHO oral toxicity scale.
Results: The mean age of patients is 80 ± 64 months (median 64 m, range:1 m-17 yrs) Of all patients 34% are lymphomas, 19% are CNS tumors, 10.5% are bone tumors, 36.5% are other solid tumors. 43.3% of the cases developed chemotherapy-induced oral mucositis. More than 80% of them were severe. When compared according to tumor subgroups there was significant difference between patients with and without oral mucositis. Mucositis observed in 91% of patients with non-Hodgkin lymphomas, 72% of the patients with bone sarcomas. Mucositis ratio was only 8% for Hodgkin's lymphoma cases (p:0.02). Of patients without oral mucositis 92.7%, applied daily oral care. This rate was 67% in patients with mucositis (p:0.004). The mean time between the onset of chemotherapy and development of oral mucositis is found 11.3 ± 8.1 days, and the mean duration of oral mucositis is found as 6.14 ± 8.15 days respectively. Recurrent oral mucositis is observed in 56.5% of patients.
Conclusions: Patients with non-Hodgkin lymphomas and bone tumors are major risk groups for developing oral mucositis. Daily oral care is another factor which lowers mucositis ratio in this study.

EP-671

EXPERIENCES AND OPINIONS ON BREAKING BAD NEWS; A SURVEY ON CHILDHOOD CANCER SURVIVORS AND THEIR PARENTS

E. Song[1], S. Park[1], C. Hong[1], H. Joo[1], J. Lee[1], H. Kang[1], K. Park[1], H. Shin[1]

[1]Department of Pediatrics Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea

Objectives: The purpose of this study is that childhood cancer survivors and their parents who had diagnosed cancer in relation to awareness of how to know about the cancer diagnosis, and the preference for cancer diagnosis disclosure is intended to identify.
Methods: A survey was conducted of patients and their family members who were diagnosed with childhood cancer by pathologic diagnosis at 10 cancer institutes from July of 2011 to January of 2012. Patients with multiple original carcinogenesis of tumor and a history of psychiatric illness were excluded. All patients experienced one or more treatments of chemotherapy, radiation therapy, or surgery.
Results: We survey 283 dyads of pediatric cancer survivors aged 10 to24 years and their parents answered multiple choice questions, respectively. Two hundred five parents (76%) knew about their child's diagnosis, cancer survivors were 99 survivors (35%) knew about their diagnosis. One hundred thirty-four parents (45.7%) wanted physicians to explain the treatment plan and prognosis, and also to inform the survivors. In contrast, 106 parents (36.2%) wanted to hear the diagnosis first and to explain their children by themselves. Fifty parents (17.1%) wanted physicians to explain directly to their children, and the other 3 parents (0.01%) didn't want to inform about the diagnosis to the children. Among the 193 survivors, 112 survivors (39.5%) was informed the cancer diagnosis by the parents, and 35survivors (12.4%) was informed by the physician, respectively.
Conclusions: Health care providers should effectively convey information that is tailored to the emotional needs of patients and their families who have experienced a never before experience of being diagnosed with cancer. The role of being able to motivate their active participation for treatment is important.

EP-672

IN-HOSPITAL SUPERVISED EXERCISE TRAINING PROGRAM TO ENCOURAGE CHILDREN AND ADOLESCENTS WITH CANCER TO PRACTICE SPORTS

F. Spreafico[1], M. Murelli[2], A. Ferrari[1], M. Terenziani[1], P. Fanelli[2], B. Giacon[3], L. Veneroni[3], L. Gandola[4], F. Gariboldi[5], M. Massimino[1]

[1]Pediatric Oncology Unit Hematology and Pediatric Onco-Hematology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [2]Studio Fisioterapico Murelli Vergnaghi s.r.l., Studio Fisioterapico Murelli Vergnaghi s.r.l., Milano, Italy; [3]Pediatric Onco-Hematology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [4]Pediatric Radiotherapy Unit Department of Diagnostic Imaging and Radiation Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; [5]Palliative Care Pain Service and Riabilitation Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Objectives: Evidence for the positive effects of physical activity in children and adolescents with cancer is growing. In the past, the dogma that cancer diagnosis precludes participation in exercise training prevailed. Primary objective of our hospital & outdoor exercise interventions was to explore an effective strategy in promoting physical activity in cancer patients during and soon after treatment.
Methods: Characteristics of the exercise training program developed at our Institution: 1) 30 m^2 gym installed on the floor (treadmill, exercise bike, other training equipment); 2) supervision by the treating clinical care team and three sports professionals, providing individual training programs (phases: cardiovascular training, toning exercises; cool-down/relaxation exercises; muscle stretching); 4) connection with the institutional physiotherapy service; 5) joint with structured outdoor adventure activities (sailing).
Results: During pilot 10-month period, 100 (in- and out-) patients participated. Giving the high demand, we moved from once to twice weekly 3-hour attendance. The delicate relation between individual whishes and capabilities (possibly altered by cancer) sometimes called for parallel psychosocial intervention, or for adaptive sports to meet needs of patients with disabilities. Reported benefits of active sport engagement included a recovered self-estimation of a lively and working body, new opportunities to relate comfortably and without frustration with peers. Limitation stays in difficulties to measure physical and mental conditioning through exercise-oncology studies.
Conclusions: Hospital exercise training demonstrated to be feasible during treatment and improved accessibility to play and exercise spaces for our patients. Despite physical activity was linked to physical and psychosocial integrity, on a patient-by-patient base, harmonized recommendations that guide participation to sport activities of patients during and after treatments might help. Treating oncologists (who have an in-depth knowledge of the individual's medical history) can provide exercise guidance to move safely, which nearly every patient can do.
Aknowledgments: Associazione Bianca Garavaglia.

EP-673

ANALYSIS OF RISK FACTORS BACTERAEMIA AMONG CHILDREN WITH CANCER AND EARLY DIAGNOSTIC

J. Suvada[1], M. Plesko[2], T. Sykora[2], E. Kaiserova[2], D. Sejnova[2], L. Perdochova[3]

[1]Children Hematology and Oncology, St. Elizabeth University of Public Health and Social Science, Bratislava, Slovakia; [2]Children Hematology and Oncology, Children's Teaching Hospital, Bratislava, Slovakia; [3]HPL, Dept. of Microbiology, Bratislava, Slovakia

Objectives: The most common complication during cancer therapy occurs bacterial infection. The key factor in risk prediction for bacterial infection is to consistently andreliably identify patients "at risk." Of the several risk prediction models proposed, few apply to pediatric patients.
Methods: This study was retrospective analytic study. There were enrolled according to the criteria patients with cancer who received treatment during January 2009 and February 2014 in Clinic of Children Hematology and Oncology in Bratislava, Slovakia. We evaluated patients with hematological and non-hematological malignancies as well. In the study group were 342 patients with positive hemoculture.
Results: Patients with coagulase-negative staphylococci (CoNS) were responsible for 61% of positive hemocultures with 33% of clinical presentation. Median of the patients was 7.0 years. The non-CoNS were 132 bacteraemias. 73% of the patients with non-CoNS developed Hospital-aquired Infection (HAI) and 27% developed infection up to 48 hrs after admission to the hospital and were enrolled in group of comunity-aquired infection (CAI). CRP and procalcitonin were not statisticaly significant predictors of bacterial inflamation and markers for differencial diagnosis. More than 38% of those who had central venose catheter from group of HAI, have confirmed multidrug resistant strain in hemoculture. 73% of the patients received during prior admission an antimicrobial therapy. The most frequent isolates were coagulase-positive staphylococci (18%); Corynebacterium spp. (14%); Ps. aeruginosa (12%); Enterobacter spp. (12%); Klebsiella spp. (9%), E. coli (6%), Enterococci (7%). In our study only 2 patients with laboratory confirmed bloodstream infection died.
Conclusions: In our study was observed that the frequent use of antimicrobial drugs prior blood culture may have crucial impact on detection of the micro-organism, antibiotic testing and susceptibility to commonly used antibiotics.

EP-674

LACK OF TREATMENT-RELATED MORTALITY DEFINITIONS IN STUDIES OF CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH LYMPHOMAS, SOLID TUMORS AND BRAIN TUMORS: A SYSTEMATIC REVIEW

T.H. Tran[1], M. Lee[2], S. Alexander[1], P. Gibson[3], U. Bartels[1], D. Johnson[4], C. Portwine[5], M. Silva[6], J. Pole[7], L. Sung[1]

[1]Haematology/Oncology, The Hospital for Sick Children, Toronto, Canada; [2]Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada; [3]Pediatrics, London Health Sciences Center, London, Canada; [4]Haematology/Oncology, Children's Hospital of Eastern Ontario, Ottawa, Canada; [5]Haematology/Oncology, McMaster Children's Hospital, Hamilton, Canada; [6]Haematology/Oncology, Cancer Center of Southeastern Ontario, Kingston, Canada; [7]Haematology/Oncology, Pediatric Oncology Group of Ontario, Toronto, Canada

Objectives: There is a lack of standardized definition for treatment-related mortality (TRM), which represents an important endpoint in cancer. Our objectives were (1) to determine the frequency with which TRM has been defined; and (2) to describe the utilized TRM definitions among studies of lymphomas, solid tumors and brain tumors.
Methods: We conducted a systematic review of studies enrolling children, adolescents and young adults with lymphomas, solid tumors and brain tumors in which an anti-cancer intervention was randomized, or all study designs in which TRM was a primary or secondary outcome. We searched Ovid MEDLINE, EMBASE and Evidence-Based Medicine Reviews from 1980 to June 2013. Two reviewers evaluated study eligibility and abstracted data.
Results: A total of 19,129 titles and abstracts were reviewed; 131 full articles were retrieved for detailed evaluation; 62 randomized therapeutic studies and 5 studies in which TRM was a primary or secondary outcome (TRM studies) satisfied eligibility criteria to be included in the systematic review. None of the studies (0/67) provided a definition for TRM. 12 therapeutic and 3 TRM studies reported their TRM rate. Among therapeutic studies, TRM rates ranged from 0.2% to 7.0% (mean 2.7%) in these patient populations that consisted of neuroblastoma (n = 996), rhabdomyosarcoma (n = 2,073), medulloblastoma (n = 364), soft tissue sarcomas (n = 1,115), Hodgkin lymphoma (n = 1,572), and non-Hodgkin lymphoma (n = 280). Hodgkin lymphoma patients had the lowest TRM rate while the highest TRM rate was reported among neuroblastoma patients. For TRM studies, reported TRM rates were much higher, ranging from 8.0% to 27.1% (mean 15.6%).
Conclusions: We were unable to identify any TRM definitions used in studies of children, adolescents and young adults with lymphomas, solid tumors and brain tumors. Given that a proportion of this patient population may receive intensive treatment, there is an urgent need for consensus-based definitions of TRM for use across clinical trials.

EP-675

A PROSPECTIVE PILOT STUDY TO DESCRIBE THE OUT-OF-POCKET EXPENSES INCURRED BY FAMILIES OF CHILDREN NEWLY DIAGNOSED WITH CANCER IN GUATEMALA

M. Bustamante[1], S. Rivas[1], A. Cáceres[1], M. de Pernillo[1], S. Luna-Fineman[2], A. Martiniuk[3], A. Tsimicalis[4]

[1]Oncology, Unidad Nacional de Oncologia Pediatrica, Guatemala, Guatemala; [2]Hem/Onc/SCT/Bio Cancer Division Department of Pediatrics, Stanford University, Stanford, USA; [3]Faculty of Medicine, Sydney University, Sydney, Australia; [4]Ingram School of Nursing, McGill University, Montreal, Canada

Objectives: In resource poor countries, parents may abandon their child's cancer treatment to ensure the financial sustainability of the family; however, the precise magnitude of their out-of-pocket (i.e. direct) costs remains unknown in Guatemala. The study objectives were to identify the costs incurred by families of children diagnosed with cancer during (a) the period prior to the diagnosis and (b) the three-month period following the diagnosis.
Methods: After ethical approval, a prospective cost of illness design with 13 repeated assessments over a 3-month time frame was piloted from a family household perspective. Parents met 13 times with a member of the research team to record their costs and resource utilization with a validated cost diary. Descriptive statistics were used to express costs in 2013 Guatemalan quetzal (GTQ; 1USD = 7.8GTQ). Costs were analyzed according to a uniformly determined set of 17 cost categories. Total cost was computed as the sum of all cost categories.
Results: Eleven families with a mean monthly income QTQ3,333 (SD 3,245) reported utilizing 9 cost categories and 28 cost items/resources. Ten families were eligible for a hospital subsidy following the child's cancer diagnosis. Collectively, families incurred a total sum of GTQ11,808 in direct costs. Nearly 90% of costs were attributed to food, travel, and communication. Families received over GTQ14,214 in donations from the cancer community and their support network. Over 75% of donations were payments for the child's treatment (e.g. use of health services prior to diagnosis, medications, and complementary medicine). Nearly 25% of donations were monetary given by the families' support networks.
Conclusions: The reliance on family's scarce resources and philanthropy subsidies/donations are essential for the diagnosis and treatment of children with cancer in Guatemala. A subsequent grant submission will ensue for a larger study to correlate family costs with abandonment and therapy outcomes.

EP-676

DEVELOPMENT OF CLINICAL PRACTICE GUIDELINES REGARDING SUPPORTIVE CARE IN CHILDHOOD CANCER IN THE NETHERLANDS - PRIORITIZATION OF TOPICS USING A DELPHI QUESTIONNAIRE

E. Loeffen[1], R.L. Mulder[2], vd Wetering, M[2], L.C.M. Kremer[2], W.J.E. Tissing[1]

[1]Department of Pediatric Oncology/Hematology, Beatrix Children's Hospital University Medical Center Groningen University of Groningen, Groningen, Netherlands; [2]Department of Pediatric Oncology, Emma Children's Hospital Academic Medical Center, Amsterdam, Netherlands

Objectives: Currently, nationwide Dutch guidelines for supportive care for children with cancer are over 10 years old and not evidence based. There is growing support and need for clinical practice guidelines (CPGs), which bridge the gap between research and clinical practice. However development of CPGs is time consuming, therefore it is important to prioritise subjects for which the clinical importance is the greatest. Thus, our objective is to prioritise childhood cancer supportive care topics for development of CPGs.
Methods: A core research group formed a list of relevant topics regarding supportive care in childhood cancer. These topics were incorporated in a modified two-round Delphi questionnaire to determine the order of development of CPGs for all topics in supportive care in childhood cancer (see figure 1). The Delphi method is a well-recognized process to achieve consensus among a group of experts (pediatric oncologists, pediatric oncology nurses and pediatricians involved in care for childhood cancer patients), based on anonymity, iteration, controlled feedback and statistical group response.

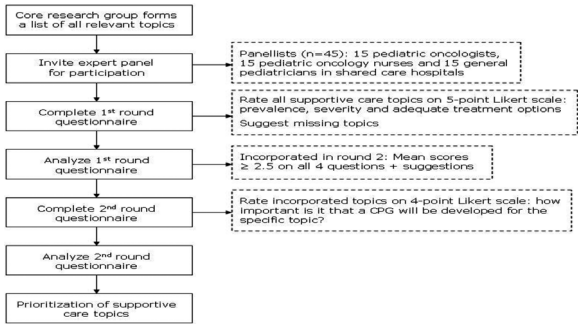


Figure 1. Outline of the Delphi method used in the questionnaire

Results: In both rounds, 36 panellists (80%) responded. The five topics with the highest score in round 2 were infection, sepsis, febrile neutropenia, pain and nausea/vomiting.
Conclusions: We successfully used a Delphi questionnaire to prioritize childhood cancer supportive care topics for the development of clinical practice guidelines. This is a first step towards uniform and evidence based Dutch guidelines in supportive care in childhood cancer.

EP-677

WHY DO PARENTS NOT TALK WITH THEIR TERMINALLY ILL CHILD WITH CANCER ABOUT DEATH?

I. van der Geest[1], M. van den Heuvel-Eibrink[1], L. Van Vliet[2], S. Pluijm[1], I. Streng[1], E. Michiels[1], R. Pieters[1], A. Darlington[3]

[1]Pediatric Oncology/Hematology, Erasmus University Medical Center - Sophia Children's Hospital, Rotterdam, Netherlands; [2]Department of Palliative Care Policy and Rehabilitation, Cicely Saunders Institute King's College, London, United Kingdom; [3]School of Health Sciences, University of Southampton, Southampton, United Kingdom

Objectives: Limited data is available about parents' reasons for not talking with their terminally ill child about death. This study explores parents' reasons for not having a conversation with their terminally ill child with cancer.
Methods: Parents were asked whether they had talked with their terminally ill child with cancer about death, and how they felt about this decision. Parents who did not talk were subsequently asked to indicate their reasons for not talking and parents who had talked were asked to indicate how the conversation took place. Descriptive and qualitative analyses were performed identifying emerging themes.
Results: Fifty-five parents (67%) did not talk with their child about death. The following themes were identified for not talking about death: parent-related reasons (e.g. unable to cope, not feeling confident, fearing consequences, preventing painful moments), child-related reasons (e.g. child does not want to talk, never started conversation, avoided conversation) and parental perception of child (e.g. already aware, too young). Parents who talked about death used stories or indicated simply telling the child that they would not be cured. Allthough the

majority of parents felt good about their decision, ten parents did not, predominantly based on the subsequent negative emotional response of their child.
Conclusions: The majority of parents did not talk with their terminally ill child about death. Parental confidence and uncertainty about consequences played an important part in reasons for not talking to the child. In addition, children may avoid or not want to talk, or already be aware of their impending death. Our findings highlight the complexity of engaging in these conversations and the role for clinicians in supporting parents who will find these conversations difficult.

EP-678

EUTHANASIA IN MINORS: A PROBLEM OF THE PATIENT, THE PEDIATRICIAN OR THE COMMUNITY?

S. Van Gool[1], J. De Lepeleire[2]

[1]Microbiology and Immunology, KU Leuven, Leuven, Belgium; [2]General Medicine, KU Leuven, Leuven, Belgium

Objectives: The discussion on euthanasia in minors flared up in Belgium by the call of 16 pediatricians ("Euthanasia for children. Now!) to develop a legal framework for practicing euthanasia in minors. We posed the question to what extent in neighboring countries a need is perceived by pediatric oncologists.
Methods: Three questions with four pre-defined answers were sent to 253 colleagues from pre-existing email lists. We asked only about the situation in adolescents. We asked not to express a personal opinion but only afterwards.
Results: Fifty-four colleagues from 19 countries answered. A legal framework for euthanasia in minors exists only in the Netherlands. There is no legal framework in Australia, Austria, Czech Republic, Denmark, France, Hungary, Ireland, Israel, Italy, Norway, Portugal, Slovenia, Spain, Sweden and the UK. Euthanasia is regulated by State in the US. For Germany, one pediatrician believed that discussions were started to develop a legal framework. The other German colleagues replied that there was no legal framework, and no initiative to develop one. In Austria, Czech Republic, Denmark, Hungary, Ireland, Israel, Italy, Norway, Portugal, Slovenia and Sweden pediatricians estimated that there is no question to develop a legal framework in the general population or in their own professional category. Only a minority of the general population and of the pediatricians was estimated for asking for a legal framework in Australia, France, Germany, Spain, UK and US. No conclusive answers came from Canada. Forty two pediatricians took the chance to write a personal comment.
Conclusions: In most countries there is no legal framework for euthanasia in minors, and there is no need for it felt in the general population and the pediatric community. Nevertheless, a debate in SIOP might be needed. We will sum up some objective arguments that can be of help in discussions on this issue.

EP-679

TIME-TREND, OVER 10 YEARS, OF INCREASING MULTI-DRUG RESISTANT SUPERBUGS IN PEDIATRIC ONCOLOGY UNIT OF A TERTIARY CANCER CENTRE: CORRELATION WITH ANTIBIOTIC UTILIZATION AND COMMUNITY COLONIZATION

T. Vora[1], G. Surwade[1], N. Shah[1], S. Tandon[1], M. Prasad[1], G. Chinnaswamy[1], B. Arora[1], S. Banavali[1]

[1]Pediatric Medical Oncology, Tata Memorial Centre, Mumbai, India

Objectives: Multi drug resistant organisms (MDRO) colonization and infections are of serious concern due to the associated high morbidity and mortality. This study was undertaken to determine the temporal trends in prevalence of MDRO in pediatric oncology unit at a tertiary cancer centre, over last decade and correlate these with antibiotic utilization and community colonization.
Methods: We analyzed the prevalence of extended spectrum beta-lactamase positive (ESBL), carbapenem resistant (CRE) and Vancomycin resistant enterococci (VRE) in blood cultures from 2005 to 2013 by audit of microbiology records of alternate years.
Results: In 2005, 1587 blood cultures were sent, of which 199 (12.54%) were positive and incidence of ESBL and VRE was 32 (16.08%) and 2 (0.50%) respectively. CRE were 27 (13.57%). In 2007, 2011 blood cultures were sent, of which 179 (8.9%) were positive and prevalence of ESBL and CRE was 29 (16.76%) and 12 (6.7%) respectively. In 2009, 154 (7.38%) out of 2087 cultures were positive, 17 (11.04%) and 27 (17.53%) were CRE and ESBL respectively. In 2011, of 1600 blood cultures, 112 (7%) were positive. Of these, 21 (18.75%) were ESBL, 32 (28.57%) were CRE, and 50 (44.64%) were pan sensitive bacteria. In 2013, a total of 1597 blood cultures were sent, of these total 107 (6.7%) showed positivity. Of these, 20 (18.69%) were ESBLs, 31 (28.97%) were CRE, and 56 (52.73%) were pan sensitive organisms. Correlation with antibiotic utilization revealed increasing use of carbapenems as well as colistin. 923 patients on admission in pediatric oncology unit were assessed for stool culture by rectal swabs. 644 (69.77%) showed bacterial growth, of which 265 (41.15%) were ESBL, 202 (31.37%) MDRO and 72 (11.18%) were VRE. Rectal swabs from newly registered outpatients (62) showed 8 (12.9%) MDRO and 30 (53.22%) ESBL positivity.
Conclusions: This study shows the increasing trend of multidrug resistance in a tertiary cancer care centre in a developing country. Colonization of MDRO in the community is a dangerous trend and would require stringent policy decisions to curb this epidemic.

EP-680

A RETROSPECTIVE CLINICAL ANALYSIS OF NEUTROPENIC ENTEROCOLITIS IN CHILDHOOD ACUTE LEUKEMIA

H. Xiong[1], J. Fan[1], J. Li[1], H. Li[1], W. Cai[1]

[1]Hematology and Oncology, Wuhan children's Hospital, Wuhan, China

Objectives: To summarize the clinical characteristics of neutropenic enterocolitis (NE) secondary to childhood acute leukemia (AL)
Methods: 10 pediatric AL patients diagnosed with NE from January 2007 to December 2013 were retrospectively analyzed the clinical features, management experience and outcome.
Results: Among the 10 patients, 8 were diagnosed as acute lymphoblastic leukemia (ALL) and 2 with acute myeloid leukemia (AML). The average age at diagnosed was 3.4 years old. All 10 patients presented enterocolitical symptoms as fever, abdominal distension with rigidity and neutropenia. Abdominal imaging revealed different severity of intestinal cavity expansion or bowel wall thickening. Treatment procedures were including fasting and total peripheral nutrition maintained till the recovery of neutrophil count and intestinal peristalsis function; given powerful broad-spectrum antibiotics (G+/G-, anti fungal when necessary); transfusion of blood component (IVIG, concentrated red cells, apheresis platelets, and apheresis granulocyte). The average recovery time was 13.2 days. 3 patients had been suffered again from NE immediately after neutrophil count recovery and liquid diet restored as abdominal distension with pain and digestive tract hemorrhage. Among them, 1 patient received surgical operation for intestinal necrosis. *Enterococcus faecium* infection had been confirmed on the culture of this patient's blood and fecal samples. NE symptoms repeated in 4 patients were identified in the follow-up chemotherapy, and 3 patients died from pulmonary fungal infection, sepsis, or septic shock, another one patient had been reduced 1/3 formal chemotherapy dosage. A total of seven patients survived.
Conclusions: NE is a rare but life-threatening complication of chemotherapy in childhood AL patients. Clinical symptoms and abdominal imaging would be helpful to the early diagnosis. Immediate powerful support treatment is necessary when NE diagnosed. Subsequent chemotherapy could be interfered negatively by NE, which might be recurrent and need be taken a high premium by clinics.

EP-681

AGGRESSIVENESS OF END OF LIFE CARE FOR NEUROBLASTOMA PATIENTS

T. Yanai[1], K. Miyata[1], S. Ochi[1], A. Saito[1], A. Kozaki[1], T. Ishida[1], D. Hasegawa[1], K. Kawasaki[1], Y. Kosaka[1]

[1]Hematology and Oncology, Kobe Children's Hospital, Kobe, Japan

Objectives: Patterns of end of life care are poorly understood in pediatric cancer population. This study aimed to elucidate aggressiveness of end of life care for children with neuroblastoma that is the most common life-threatening solid tumor in Japan.
Methods: Patients who were diagnosed as neuroblastoma in our institute and died between September 1, 1995 and December 31, 2013 were enrolled. Medical records were retrospectively reviewed. Chemotherapy, life-sustaining treatment such as mechanical ventilations or CPR in the last month of life, the period between the last chemotherapy and death and place of death were investigated as indicators for aggressiveness of end of life care.
Results: Fifteen patients (6 males and 9 females) were identified. The median age at death was 3.5 years (range, 3 months-12.2 years). Thirteen patients (87%) died of neuroblastoma, and 2 (13%) died of treatment-related toxicity. Chemotherapy was performed for 10 patients (67%) in the last month of life and 5 patients (33%) continued to receive chemotherapy in the last week of life. Our hospital was the sole place of death. Three patients (20%) received life-sustaining treatments due to treatment-related toxicity and died in ICU. Fourteen patients (93%) did not receive cardiac or cardiopulmonary resuscitation. The median period between the last chemotherapy and death was 14 days (range, 0-498).
Conclusions: The proportion of terminally ill cancer patients who received chemotherapy was higher than the previous reports. Meanwhile, cardiac or cardiopulmonary resuscitation was not performed in the majority. Further large research is required to determine aggressiveness of end of life care for pediatric cancer patients in Japan.

EP-682

PROSPECTIVE AND RANDOMIZED STUDY OF FIXED VS FLEXIBLE SCHEDULE OF POST CHEMOTHERAPY ADMINISTRATION OF GRANULOCYTE COLONY-STIMULATING FACTOR (G-CSF): PRELIMINARY DATA

M. Yankelevich[1], M. Henry[1], K. Bhambhani[1], J.W. Taub[1]

[1]Hematology/Oncology, Children's Hospital of Michigan, Detroit, USA

Objectives: G-CSF is commonly used after chemotherapy to shorten neutropenic periods. Administration of G-CSF contributes to the cost of treatment and may cause some side effects. Based on our studies of kinetics of post chemotherapy bone marrow recovery we hypothesized that doses of G-CSF given during the first few days after chemotherapy do not significantly contribute to the final neutrophil recovery due to the absence of myeloid progenitors in the bone marrow.
Methods: To evaluate this in the clinical setting, we have initiated a prospective randomized clinical study of two different prophylactic G-CSF schedules in children with solid tumors: a "fixed" schedule where G-CSF is started 24 hours after the completion of chemotherapy and a "flexible" schedule where G-CSF is not started until the absolute neutrophil count (ANC) falls below 1,000/mm^3. We used a crossover study design with each patient receiving 2 cycles of the same chemotherapy followed by the fixed or the flexible schedule of G-CSF chosen in random order.
Results: To date, 6 patients have been enrolled since October 2013 and the study continues to enroll patients. There was no significant difference in the time to neutrophil recovery (number of days from the start of chemotherapy to ANC $>$ 1,000/mm^3 post nadir) between the two schedules of G-CSF: 14.6 ± 1.1 days with the fixed vs. 14.6 ± 0.6 days using the flexible schedule. The patients received 4.7 less G-CSF injections (5.3 ± 2.1 vs. 10.0 ± 2.0 daily injections) after cycles followed by the flexible schedule which would translate into an average of $1,700 direct savings from reduced injections of G-CSF per chemotherapy cycle.
Conclusions: Our preliminary data show that the flexible schedule of post chemotherapy G-CSF administration resulted in a significant reduction in the treatment cost without compromising of G-CSF effects on neutrophil recovery after myelotoxic chemotherapy in children with solid tumors.

EP-683

THE NEED FOR PEDIATRIC PALLIATIVE CARE IMPLEMENTATION IN MEXICO: A CASE REPORT

G. Zúñiga-Villanueva[1], L.V. Uribe-Ortiz[1], J. Azpilcueta-García[2]

[1]Multicenter Pediatric Residency Program, Escuela de Medicina y Ciencias de la Salud Tecnologico de Monterrey, Monterrey, Mexico; [2]Pediatric Oncology, Hospital San José - TEC de Monterrey, Monterrey, Mexico

Objectives: To analyze the missed opportunities of a case report in which Pediatric Palliative Care (PPC) could have been integrated in order to create a framework for Mexican pediatric oncologists to recognize the need for implementing palliative care in their patients.
Methods: A case of high-risk medulloblastoma of the cerebellum occurring in a 14-year-old patient is presented. He was first diagnosed and treated at 13 years of age with partial surgical resection of the tumor and ventriculoperitoneal shunt placement. During the next 6 months he concluded 6 cycles of chemotherapy. He developed worsening brain edema and in his last hospitalization he was admitted with progressive intracranial hypertension. The patient himself asked to continue with chemotherapy and begged the team to not give up on him. He received chemotherapy until the last day of his life with few or almost none palliative care for him or his family.
Results: Within the patient's evolution (from diagnosis until his death) 5 opportunities were identified in which PPC could have been initiated.
Conclusions: More than 85% pediatric cancer cases occur in developing countries. In low resource settings mortality is approximately 80%, or even 90% in the world's poorest countries. In Mexico, being a developing country, it is estimated that childhood cancer has an incidence of more than 3,800 per year, and a mortality rate of approximately 90,000 per year, meaning every 4 hours a Mexican child dies because of cancer. PPC reduces the morbidity and improves the quality of life at any stage of the disease. Clearly all this patients could benefit from PPC, however, this situation will not improve until we get Mexican pediatric oncologists to recognize this need and integrate PPC into their medical practice.
Acknowledgments: Sebastian Rodríguez Llamazares for his invaluable help.

SURGERY (IPSO)

EP-684

GANGLIONEUROMA: BECOMING SYMPTOMATIC TUMOR?

P. Abad Calvo[1], M. Melo Valls[2], R.M. Isnard Blanchar[3], F. Almazán[4], J.A. Blanco[3], A. Castellvi Gil[3], M. Curbelo Rodriguez[3], M. De Diego Suarez[3]

[1]Paediatric Surgery, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; [2]Pediatrics Oncology, Hospital de Sabadell. Corporacio Parc Tauli, Sabadell, Spain; [3]Pediatric Surgery, Hospital Universitari Germans Trias I Pujol, Badalona, Spain; [4]Pediatric Oncology, Hospital Universitari Germans Trias I Pujol, Badalona, Spain

Objectives: Ganglioneuromas are commonly defined as a benign silent tumor more frequent in adults than children. Very often misdiagnosed before surgery because radiological appearance could be non-specific. However surgical approach still the mean treatment when becoming symptomatic. But is really a silent tumor or is becoming symptomatic?
Methods: We review all the pathologic reports about neuroblastic tumors in two pediatric departments. We focus on ganglioneuroma diagnosis after complete surgery in the last 10 years. Also reviewing the literature in adults to compare with children.
Results: We describe 4 cases of ganglioneuroma in this institutions: 1 neck and thorax and 3 abdominal (1 retroperitoneal, 1 adrenal and 1 liver hilum). This cases were hormonally silents. Ultrasound was taken because of persistent abdominal pain in 3. A neck mass was the iceberg of the bilateral thoracic tumor. The one located in the liver hilum has spontaneous eye movements although had been operated for optokinetic nistagmus as a child. Misdiagnosis before surgery in 3 (ganglioneuroblastoma, suprarrenal adenoma, and cyst duplication). No complications after open surgery in those cases.
Conclusions: A few cases reported about symptomatic ganglioneuroma in children if we compare with adults, where pain is the main indication for surgery in the early 40s. Difficult to obtain the diagnosis previously at surgery because the imaging characteristics are very similar to other tumors. Maybe we have to became more active doing surgery in this 'benign tumor' before the symptoms appear in adults. Long follow up and a common registrer also for benign lesions might be considered.

EP-685

COMBINED APPROACH FOR THE MANAGEMENT OF REFRACTORY CHYLOUS ASCITES IN PEDIATRIC ONCOLOGY PATIENTS

A. Alkudayri[1], Z. Habib[1], S. Koussayer[1]

[1]Department of Surgery, King Faisal Hospital & Research Center, Riyadh, Saudi Arabia

Introduction: Postoperative chylous leak is a rare result of lymphatic channels disruption or obstruction following surgical resection of retroperitoneal tumors that represent a difficult management problem due to the serious mechanical, nutritional and immunological consequences of the constant loss of protein and lymphocytes. The management of chylous leak is either conservative or interventional (surgical and/or radiological).
Methods: We are reporting two pediatric patients with refractory chylous ascites following retroperitoneal tumor resection (neuroblastoma and nephroblastoma). They were managed successfully using the combined approach (Intra operative lymph-angiogram and laparoscopy). The intervention was dictated by the failure of conservative treatment (Total parental nutrition, Octerotide, and low fat diet), and/or timing of scheduled chemotherapy cycle. Our combined approach was utilized to identify and treat the source of lymphatic leak simultaneously. The Modalities of intervention included diagnostic laparoscopy, Intra-operative ultrasound localization of the inguinal lymph nodes followed by lymph angiogram under fluoroscopic guidance. The identified sites of the lymphatic leak were handled by Mini-laparotomy, suture ligation, omental patch and hemostatic agents. The patients continued their chemotherapy regimen within one week of the intervention.
Results: No Recurrences were observed on six months of follow up.
Conclusion: The usual conservative management of lymphatic leak for long time should be discouraged from being an option in oncologic patients, as it may delay the completion of the chemotherapeutic regimen, which might theoretically increase the risk of recurrence. With the Available advanced resources, an early intervention for the lymphatic leak is recommended in these patients.

EP-686

CONGENITAL JUVENILE GRANULOSA CELL TUMOR OF THE TESTIS: CASE REPORT AND REVIEW OF THE LITERATURE

A. Aranha Jr[1], F. Vargas[1], L. Noronha[2], E. Gugelmin[2], L. Matoso[3], R. Galli[4], K. Barszcz[4], R. Possagno[4], E. Mol[4], L. Garbuio[4]

[1]Surgery, Hospital Pequeno Príncipe, Curitiba, Brazil; [2]Pathology, Hospital Pequeno Príncipe, Curitiba, Brazil; [3]Pediatrics, Hospital Municipal de Araucária, Curitiba, Brazil; [4]Medicine, Universidade Estadual de Ponta Grossa, Ponta Grossa, Brazil

Objectives: Even though represents the most common stromal cord tumor of the infant testis, juvenile granulosa cell tumor (JGCT) is a very rarely diagnosed benign tumor, accounting for 1.2% of all prebubertal testicular tumors.
Methods: We retrospectively reviewed the data of one patient diagnosed in the first day of life.
Results:
Case report: A full-term healthy neonate was diagnosed with a painless left escrotal mass. During evaluation it was identified to have about two times the volume of the contralateral testis, presenting a firm consistency, not so hard as the consistency of a prenatal testicular torsion. Doppler ultrasound detected a multicystic left testicular mass, with normal blood flow, but failed in detecting normal-appering testis. Human chorionic gonadotropin (b-HCG) and serum alpha-fetoprotein (AFP) were normal. Inguinal approach was performed, exposing the testis and spermatic cord. After cord clamping, a section of the lesion was sent to frozen biopsy and excluded yolk sac tumor, however the impossibility of detecting normal testis tissue indicated orchiectomy with high ligation of the spermatic cord. Histological evaluation demonstrated gray testicular parenchima with multicystic aspect fullfiled with yellow fluid. Postoperative evolution was uneventfull. Six months after surgery the patient is assymptomatic and being followed by pediatric oncology.
Conclusions: The usual clinical presentation of JGCT is a painless scrotal mass, detected during clinical routine examination or perceived by the parents. Prenatal diagnosis has been described. Radiological imaging demonstrates a multicystic circunscribed tumor. Tumoral markers levels are normal and the standart treatment is the inguinal orchiectomy. As the tumor

presents as a benign tumor, testicular sparing surgery can be performed in cases normal parenchima is identified. Adjuvant therapy is not indicated.

EP-687

URETEROSIGMOIDOSTOMY IN A CASE OF BLADDER RHABDOMYOSARCOMA WITH TOTAL CYSTECTOMY

S. Bhatnagar[1]

[1]*Pediatric Surgery, B.J. Wadia Hospital for Children, Mumbai, India*

Objectives: Urinary diversion with Mitrafanoff and neo-bladder formation is the most utilized option for bladder rhabdomyosarcoma in a child who has undergone total cystectomy. Presenting here a child who underwent Ureterosigmoidostomy - a continent urinary diversion 5 years following total cystectomy and subtotal urethrectomy.
Methods: Retrospective case study wherein all details of the patient were retrieved from the records
Results: 2 day old male neonate presented with poor stream of urine and palpable bladder, was suspected to have posterior urethral valves, underwent cystoscopy and fulguration of valves. 2 months later, child was brought in severe urosepsis with a fungating mass from the hypocondrium, which was found to originate from the urinary bladder. Total cystectomy with bilateral end ureterostomies were performed, and post-operative chemotherapy was given after confirmation of diagnosis of rhabdomyosarcoma. Tumor recurred in the bladder neck/prostatic urethra and later in distal urethra for which subtotal urethrectomy was done. 5 years later with no evidence of recurrence, the child underwent ureterosigmoidostomy as a continent urinary diversion. The child is able to pass urine every 2-3 hours per rectally and is also continent for stools. No evidence of renal upper tract damage has been found.
Conclusions: With the myriad complications of bladder augmentation/neo-bladder creation from ileal or sigmoid loop and life-long catheterization of the neo-bladder via the Mitraffanoff, ureterosigmoidostomy seems to be better option wherein the child can voluntarily void urine per rectally and remains dry without the need to repeatedly catheterize. In the event of late recurrence of the tumor, redo-ureterostomies would be much more easily carried out till loco-regional control of the tumor is done.

EP-688

IMPORTANCE OF SURGICAL TREATMENT AND PROGNOSTIC FACTORS IN NEUROBLASTOMA STAGE 4S, ACCORDING TO OUR CASE

T. Budi[1]

[1]*2nd Department of Paediatrics, Semmelweis University, Budapest, Hungary*

Objectives: Stage 4S neuroblastoma is said to have very favourable outcome than other patients with metastatic neuroblastoma, often demonstrating spontaneous maturation and regression, and hardly requires any treatment. Is it true really? Stage 4S neuroblastoma is a benign, or a deadly disease? How to treat this “benign” entity? Do we need to do any surgical treatment or to administer chemotherapy? Is there any prognostic factor?
Methods: Case report: A 2 days old, mature newborn has been admitted to our clinic with bilateral advanced tumor in the adrenal regions. She had multiplex liver metastases, extreme hepatomegaly, substantially distended abdomen, and dyspnoea. After the investigation and biopsy, the laesion was proved to be a neuroblastoma, and it was staged to 4S. According to our case we reviewed the literature.
Results: Under 1 month of age, neuroblastoma stage 4S has very bad prognosis, many cases end with death. Most of the deaths are caused by the rapidly worsening abdominal status. Infants must be administered chemotherapy and operated urgently at the first signs of abdominal compartment syndrome.
Conclusions: Stage 4S neuroblastoma’s estimated survival rates of 75% to 90% have been reported. These tumors are usually associated with favourable biologic features, but infants under 1 month of age have very bad prognosis, many cases end with death. It seems that under 1 month of age, the more intense, and earlier the treatment is, the better the results. Studies may identify markers to more accurately predict the clinical outcome of various subtypes of neuroblastoma stage 4S. Moreover, surgeons have an important role to prevent abdominal compartment syndrome, and raise survival rates.

EP-689

CONSERVATIVE SURGERY WITH COMBINED HIGH DOSE RATE BRACHYTHERAPY FOR PATIENTS WITH BLADDER-PROSTATE RHABDOMYOSARCOMA: TECHNICAL ISSUES, CHALLENGES AND INITIAL EXPERIENCE

J. Fuchs[1], **F. Paulsen**[2], **F. Heinzelmann**[2], **S.W. Warmann**[1], **G. Seitz**[1]

[1]*Department of Pediatric Surgery and Pediatric Urology, University Children’s Hospital, Tübingen, Germany;* [2]*Department of Radiation Oncology, University Hospital, Tübingen, Germany*

Objectives: Although treatment of patients suffering from bladder-prostate-rhabdomyosarcoma (BPRMS) has been improved in the past regarding the outcome, the bladder preservation rates in the large multi center trials are still too low. In the past, conservative surgery with combined low dose rate brachytherapy has been advocated as a novel treatment option. Nevertheless, low dose rate brachytherapy is not available in many centers. Therefore, the aim of the study was to establish a new treatment modality combining high dose rate brachytherapy and conservative surgery.
Methods: The principle of the study was to perform an organ preserving microscopical complete (R_0) or incomplete (R_1) tumor resection with intraoperative placement of 4 to 6 brachytherapy tubus around the urethra. Only patients with tumor extension below the bladder neck were treated. After surgery, high dose rate brachytherapy (3 Gy / fraction) was carried out for 6 days (2 fraction / d). After that, brachytherapy tubes were removed. A total number of 4 patients were treated up to now.
Results: In all patients bladder preservation was feasible. Conservative surgery and brachytherapy was well tolerated without significant side effects. All patients are in the first complete remission. One patient developed a neurogenic bladder and required creation of a Mitrofanoff stoma.
Conclusions: Combined conservative surgery and high dose rate brachytherapy is a treatment option for selected patients with BPRMS. The paper highlights the essential technical challenges and clearly shows limitiations of this treatment approach.

EP-690

MANAGEMENT OF WILMS TUMOUR WITH INFERIOR VENA CAVA EXTENSION: A SINGLE-INSTITUTION EXPERIENCE

Y.T. Lee[1], **A.S. Jacobsen**[1], **C.H. Chui**[2], **N.K. Laksmi**[1]

[1]*Paediatric Surgery, KK Women’s and Children’s Hospital, Singapore, Singapore;* [2]*Surgery Centre for Children Pte Ltd, Mount Elizabeth Medical Centre, Singapore, Singapore*

Objectives: Current treatment strategies for Wilms tumour with inferior vena cava (IVC) extension include pre-operative chemotherapy, followed by radical nephrectomy and tumour thrombectomy. Literatures report regression of tumour thrombus with pre-operative chemotherapy facilitating surgery. However there were also reports regarding dense adherence of a tumour thrombus to vessel wall resulting from pre-operative chemotherapy. This study aims to examine management of Wilms’ tumour with IVC extension in our institution.
Methods: Patients diagnosed with Wilms tumour with IVC extension between 1997-2013 were included. Data were collected from patient notes regarding presentation, operative details, and outcome.
Results: Twenty-three cases of Wilms tumour were treated in our institution during the study period. Two patients (8.6%) had tumour extension into infrahepatic vena cava. One patient (4.3%) had thrombus extending from iliac veins to right atrium, and extending into the left renal and right hepatic vein leading to Budd-Chiari syndrome. All 3 patients received pre-operative chemotherapy based on NWTS-5 regime (Duration: 4-9 weeks) followed by radical nephrectomy and tumour thrombectomy. Pre-operative chemotherapy had reduced thrombus extent in 2 cases with infrahepatic vena cava extension and complete thrombectomy achieved. However, for the patient with intra-trial extension the tumor thrombus was only cleared from the atrium with pre-operative chemotherapy. The thrombus in intrahepatic and infrarenal IVC were densely adhered to vessel wall and could not be completely excised. All 3 tumours had favourable histology and the excised thrombus showed no viable tumour. Two patients received post-op radiotherapy. All the 3 children are alive and tumor free.
Conclusions: Management of Wilms tumour with IVC and intra-atrial extension is technically challenging. Pre-operative chemotherapy may cause dense adherence of thrombus to vessel wall, but it may be effective as all thrombus excised reported no viable tumour cells. More careful studies are needed to make recommendations on staging and treatment of Wilms tumour with extensive IVC thrombus.

EP-691

UNUSUAL PRIMARY PAEDIATRIC TESTICULAR TUMOURS

F. Li[1], **J.H.Y. Chua**[1]

[1]*Paediatric Sugery, KK Women’s and Children’s Hospital, Singapore, Singapore*

Objectives: To describe the unique clinical presentation, diagnostic difficulties and uncommon histology in 2 cases of primary paediatric testicular tumour (TT).
Methods: A retrospective clinical chart review of 2 males with rare primary TT.
Results: A 2-year old male presented with a painless left scrotal swelling a year after bilateral inguinal orchidopexies for bilateral undescended testicles. Ultrasound demonstrated an enlarged heterogeneous left testis measuring 5.0 × 3.5 × 2.5 cm with increased vascularity. Serum Alphafetoprotein and Beta-hCG were normal. A left testicular biopsy was performed via an inguinal approach. Intra-operative frozen section was inconclusive but the diagnosis of embryonal rhabdomyosarcom was made on paraffin sections. Radical inguinal orchidectomy and hemi-scrotectomy was performed. Tumour margins were clear except for focal microscopic involvement at the spermatic cord margin. He received adjuvant chemotherapy as per ARM A protocol and has remained disease-free for

3.5years. Another child, 4.5years old, presented with a 3-month duration of painless right scrotal swelling. Ultrasound scan revealed a heterogeneous enlarged right testis measuring 1.9 × 2.8 × 1.6 cm with increased vascularity, raising the possibility of a germ cell tumour (GCT). Tumour markers were normal. Intra-operatively, the right testis measured 4.0 × 2.5 × 2.5c m with no normal testicular tissue evident. A radical orchidectomy was performed. Histopathology diagnosed primary paediatric follicular lymphoma of the testis grade IIIa. He received standard-risk chemotherapy for lymphoma and has remained disease-free for 10.5years.
Conclusions: Traditionally, elevated serum Alphafetoprotein and Beta-hCG play a significant role in pre-operative counselling for primary paediatric TT. Our experience with these 2 patients illustrates the limitations of these tumour markers, and that of intra-operative frozen section to direct the need for radical orchidectomy. While GCT are the commonest primary TT in children, other rare malignancies should be considered when tumour markers are normal. While testis-sparing surgery for primary TT may be possible, these patients should be carefully selected and pre-operative imaging thoroughly evaluated.

EP-692

MULTIMODALITY THERAPY FOR WILMS'TUMOR WITH INFERIOR VENA CAVA AND ATRIAL TUMOR THROMBUS

M. Li[1], S.H.A.N. Xu[2], Y.O.N.G. Huang[2], Q. Shu[1], J. Wang[1], C.A.N. Lai[3], J. Yu[4]

[1]Division of Pediatric Surgical Oncology Department of Pediatric Surgery, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [2]Division of Urology Department of Pediatric Surgery, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [3]Department of Radiology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China; [4]Division of Cardial Surgery Department of Pediatric Surgery, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China

Objectives: We introduce one case of Wilms' tumor with inferior vena cava and right atrial tumor thrombus successfully treated with multimodality therapy.
Methods: A 18 months old female was admitted with history of abdominal distension and hematuria for 5 days. Abdominal ultrasound, CT and MRI showed a right renal mass measured 12.8 cm×10.6 cm×10.2 cm with tumor thrombus extending into inferior vena cava and right atrium. Echocardiogram confirmed a mass (3.3 cm×3.2 cm×2.0 cm) in the right atrium. The histological diagnosis of Wilms' tumor was confirmed by core-needle biopsy. Combined-modality neoadjuvant therapy with transcatheter arterial chemoembolization (TACE) and systemic chemotherapy was taken. The patient subjected to transcatheter arterial chemo-embolization by Seldinger method. Chemoembolization emulsion was injected into the involved renal artery. The chemoembolization emulsion consisted of cisplatin (80 mg/m2), pirarubicin (40 mg/m2), vindesine (3mg/m2), and iodized oil (5 ml). Two sessions of intravenous chemotherapy administered 3 weeks after TACE. That was alternating using ifosfamide (1200mg/m2), etoposide (100 mg/m2), vindesine (3mg/m2) and carboplatin (300mg/m2), pirarubicin (40mg/m2), vindesine (3mg/m2), one each treatment interval of 3 weeks. The tumor decreased in size to 10.8 cm×8.5 cm×8.2 cm on CT images. The tumor thrombus within the IVC and RA also shrunk but has not disappeared.
Results: The patient was operated after twelve weeks Combined-modality neoadjuvant therapy. Complete resection of tumor kidney first, then the right atrium opened and the tumor thrombus completely removed under cardiopulmonary bypass with deep hypothermia and circulatory arrest. Recovery was uneventful. Pathological examination of the resected tumor showed necrosis more than 95%. The child was given radiotherapy to the right flank followed by postoperative chemotherapy. The patient was free of recurrence with a follow-up of 15 months.>
Conclusions: Multimodality Therapy is effective for the treatment of Wilms' tumor with inferior vena cava and right atrial tumor thrombus.

EP-693

SURGICAL INTERVENTION FOR RESIDUAL LUNG NODULES AFTER CHEMOTHERAPY FOR PEDIATRIC MALIGNANCIES

T. Oue[1], S. Uehara[1], K. Nakahata[1], M. Zenitani[1], K. Nara[1], M. Owari[1], T. Ueno[1], N. Usui[1]

[1]Pediatric Surgery, Osaka University Graduate School of Medicine, Osaka, Japan

Objectives: we retrospectively reviewed the surgical managements for residual lung nodules after chemotherapy for pediatric malignancies.
Methods: Eleven pediatric oncology patients who had undergone a resection of pulmonary nodules between 2001 and 2013 were included in the study. They included five hepatoblastomas, three Wilms tumors, two osteosarcomas and one neuroblastoma. All lung nodules were identified on preoperative CT imaging for routine surveillance, and were resected by either thoracotomy or thoracoscopic surgery. Patient demographics, initial diagnosis, location of the lung nodule, procedure performed, and pathology of the lesion were recorded.
Results: Six patients had lung nodules at diagnosis, remaining five developed lung nodules during or after the treatments. Biopsy of the multiple nodules was performed in 3 cases bythoracoscopic surgery. In eight cases, complete resections of the lung nodules were performed. In the bilateral case, each side was resected by separate operation. Five cases were resected by thoracotomy and remaining three were resected by thoracoscopic surgery. In three cases with the small nodules less than 5mm, CT guided marking were successfully performed before surgery. Pathological examination revealed that the nodules were viable metastasis in five cases, complete necrotic metastasis in 3 cases and benign lesions in two cases. Two patients died of recurrence, however remaining nine are alive without disease for 1 to 13 years.
Conclusions: Complete resection of the lung nodules contributed to the achievement of complete remission. Pathological findings of the nodules were useful to decide the further management of these patients and, ultimately, to improve their overall survival. CT guided marking were useful to resect the small nodules less than 5 mm.

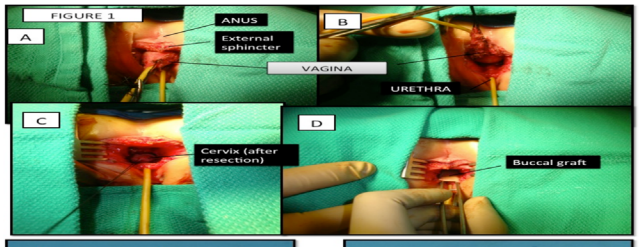
EP-694

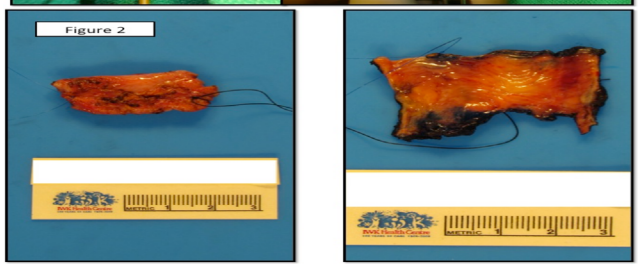
SURGICAL RESECTION AND BUCCAL MUCOSA VAGINOPLASTY FOR LOCAL CONTROL IN VAGINAL BOTRYOID RHABDOMYOSARCOMA

R.L.P. Romao[1], J. Pierce[1], S. Afzal[2], D. Davies[1], C.V. Fernandez[2], M. Bernstein[2], A.J. Lorenzo[3]

[1]Surgery, IWK Health Centre and Dalhousie University, Halifax, Canada; [2]Oncology, IWK Health Centre and Dalhousie University, Halifax, Canada; [3]Surgery, The Hospital for Sick Children University of Toronto, Toronto, Canada

Objectives: Standard treatment for vaginal botryoid rhabdomyosarcoma (RMS) in children encompasses systemic chemotherapy and radiation therapy (RT) for local control with good results. RT to the young pelvis leads to significant long-term complications. Herein, we report a surgical alternative for local control with the goal of sparing RT to the pelvis.
Methods: Case report (after informed consent) of a new surgical technique used for local control in the treatment of vaginal botryoid RMS in a 30-month old female.
Results: The child has been treated on Children's Oncology Group D9803 protocol (VAC chemotherapy) for group III, stage II biopsy-proven vaginal botryoid RMS. At 12 weeks, vaginoscopy depicted very good response with small residual lesions containing rhabdomyoblasts identified in the anterior and posterior vaginal walls. At 24 weeks, instead of standard RT as per protocol, we performed a subtotal vaginectomy using an anterior sagittal approach and buccal mucosa vaginoplasty, with bilateral grafts harvested from the patient's cheeks (figure 1). A 20 fr. chest tube was left in situ as a vaginal mold. The cervix and other internal reproductive organs were left intact and the grafts were anastomosed to the forniceal mucosa. The patient was discharged on postoperative day (POD) 3. Vaginal stent was removed on POD9. Fifteen days after surgery, the patient presented with a superficial dehiscence of the perineal body. Examination under anesthesia revealed well-healed grafts with a patent vagina and no evidence of perineal infection. The wound healed by secondary intention without any further complications. Pathology revealed focal residual rhabdomyoblasts with negative margins (figure 2).





Conclusions: Subtotal vaginectomy and buccal mucosa vaginoplasty using an anterior sagittal approach offers an alternative for local control in children with botryoid RMS that may spare these patients from receiving RT to the pelvis. Long-term follow-up to assess function of the neovagina and oncological outcomes is mandatory.

EP-695

SURGICAL PROBLEMS IN CHILDREN WITH GENITO-URINARY TRACT'S RHABDOMYOSARCOMA

Z. Sabirzyanova[1], A. Pavlov[2]

[1]pediatric urology, Russian scientific center of roentgenradiology, Moscow, Russia; [2]Urology, Russian scientific center of roentgenradiology, Moscow, Russia

Objectives: The prognosis of children with rabdomiosarcomas (RMS) has improved over the last 30 years. Their survival rate gets to 80-85% because the modern algorithm based on chemotherapy and radiotherapy. Surgery comes to the second plan in local therapy but there are a lot of surgical problems based on specific urogenital localization of tumor.
Methods: 19 children (11 males and 8 females) in the age from 9 month to 12 years. Tumors localization was in 4 – paratesticular, in 12- bladder with/without prostate, uterus or/and vulva – 3. Follow up from 1 till 22 years after the treatment.
Results: In all patients there were "surgical" reasons of primary treatment: abdominal pain (8), acute retention of urine or disuria (7), palpable or visual tumor mass (4). Primary laparotomy or laparoscopy were done in all children with abdominal pain by common surgeons, but the biopsy wasn't perform in all cases and in 4 of them the primary resection of tumor was done. Complications of primary surgery were urinous infiltration in 3 patients and large vascular disruption in 1 of them. Primary urine diversion has been done in 3 patients by bladder catheterization and by nephrostomy in 2. All patients undergone XR therapy. Secondary radical resection was done in 7 children after radiotherapy: total cystectomy (4) and/or total prostatectomy (2), uterus- and vaginaectomy in 2. Later reconstruction in 3. Urinary tract obstruction as side effect in long term follows up after radiotherapy was shown in 8 patients. Urethral reimplantation was done in 3 of them, vesicostomy in 1, internal urethral stents were placed in 2
Conclusions: Surgical intervention in the first step of treatment in patients with RSM of genitourinary tract must be more safety and be limited by biopsy and urinary diversion. Delayed reconstructive surgery is necessary for most patients after the both methods of local treatment.

EP-696

RECURRENT MONOPHASIC WILMS' TUMOR IN PELVIC KIDNEY - A THERAPEUTIC CHALLENGE

Y. Sarin[1], S. Sinha[1]

[1]Pediatric Surgery, Maulana Azad Medical College and LN Hospital, Delhi, India

Objectives: To report an unusual case of repeated loco-regional recurrences in a patient with stage I intermediate-risk monophasic (epithelial variant) Wilms' tumor (WT) of pelvic kidney requiring aggressive therapy over a decade.
Methods: Retrospective case study
Results: One-year-old male presented with lower abdominal lump. Investigations showed WT in left ectopic kidney. Left nephroureterectomy was done; HPE confirmed WT with predominant tubule formation, minimal atypia and mitosis (stage I). Repeat CECT a month later showed thrombus in infra-hepatic inferior vena cava (IVC) and right common iliac vein with para-aortic and iliac lymphadenopathy. This was followed by early abandonment of therapy; the patient received only 2 cycles of chemotherapy (VAC regimen). He returned with local relapse in retroperitoneal lymph nodes after 7 years. After 6 cycles of ICE chemotherapy, RPLND was done but HPE showed no tumor. Fourteen months later, he developed second recurrence in mesocolic lymph nodes that was completely excised followed by 6 cycles of IE chemotherapy and 20 Gy whole abdominal irradiation. Histopathology was again epithelial variant of WT. Four months later, he presented with 3rd recurrence - a large pelvic mass (15×8×7 cm); trucut biopsy again showed epithelial predominant WT. He received 6 cycles of Paclitaxel based salvage chemotherapy followed by excision of the retro-vesical tumor and boost radiotherapy of 10.8 Gy to the pelvis. We had planned to excise the persistent calcified thrombus in subhepatic IVC that could be harboring a nidus of tumor cells but he suffered acute renal failure from radiation nephritis 4 months later. He had repeated dialysis over next 10 months before he succumbed to chronic renal failure.
Conclusions: Inert tumor cells in the calcified IVC thrombus has possibly caused the repeated loco-regional recurrences of a low-risk localized monophasic WT. The importance of initial completion of therapy and need for long term follow-up cannot be overemphasized.

EP-697

SYNCHRONOUS IPSILATERAL WILMS' TUMOR AND NEUROBLASTOMA IN AN INFANT

Y. Sarin[1], S. Sinha[1]

[1]Pediatric Surgery, Maulana Azad Medical College and LN Hospital, Delhi, India

Objectives: To report synchronous co-existence of ipsilateral adrenal neuroblastoma and Wilms' tumor
Methods: Retrospective case study
Results: A 10-month-old female was admitted with complaints of abdominal distension since 1½ months, cough and fever since 3 weeks and weight loss. Examination revealed a large right retroperitoneal mass; clinical diagnosis was right Wilms' tumor (WT). Ultrasonography revealed 2 heterogeneous, echogenic masses- a well defined, 4.8 × 4.3 cm mass in right suprarenal region and another 8.9 × 7 cm mass with multiple internal anechoic areas along anterolateral aspect of kidney. CT scan revealed 13 X 9 X 9 cm well defined heterogeneous mass abutting the right kidney with loss of fat planes. Superiorly, the lesion had a well-defined round component, which was seen abutting the undersurface of liver. Inferiorly, it extended till the pelvic brim and medially it crossed the midline causing effacement and displacement of Inferior vena cava, however no encasement of major vessels was noted. WT was confirmed on trucut biopsy. Metastatic workup was negative. She was administered pre-operative chemotherapy (Vincristine+ Adriamycin) over 4 weeks. At surgery, 13 X 8 X 8 cm right renal mass was noted. There was a separate mass of 5 X 5 X 3 cm in the area of the right suprarenal gland with a clear plane of separation between the two masses. Local lymph nodes were enlarged. Complete excision of both masses and lymph node sampling was done. Histopathology revealed co-existing intermediate-risk stage I WT and stage I neuroblastoma (NB). Bone survey, bone scan, bone marrow aspiration and MIBG scan were negative. The child has been started on OPEC regimen, as NB was positive for N-myc amplification.
Conclusions: The co-existence of 2 embryonal tumors in the same patient may merely be a coincidence. However accumulation of data on similar cases may help to clarify if there is an association between these 2 tumors.

EP-698

CHEMOTHERAPY INDUCED CHANGES IN WILMS' TUMOR – OUR EXPERIENCE

Y. Sarin[1], S. Sinha[1], N. Khurana[2]

[1]Pediatric Surgery, Maulana Azad Medical College and LN Hospital, Delhi, India; [2]Pathology, Maulana Azad Medical College and LN Hospital, Delhi, India

Objectives: Preoperative chemotherapy propagated by SIOP renal tumour trials reduces tumor rupture and increases favourable stage distribution of Wilms' tumor (WT). It is known that chemotherapy induced changes (CIC) alter the tumor's histological features and distribution of subtypes, making staging more difficult. We studied CIC in our patients.
Methods: Histopathology slides of 10 children with WT treated in our institute as per SIOP WT 2001 protocol, were reviewed in the light of current knowledge by an experienced senior pathologist. Since a mandatory pre-chemotherapy tru-cut needle biopsy was done in all patients (UKCCG protocol), the tumor morphology was compared before and after chemotherapy.
Results: 6 pre-chemotherapy tru-cut biopsies could be subtyped: mixed (n = 5), epithelial (n = 1). Mean tumor volume decreased from 919 to 564cc after chemotherapy (mean response 38.6%); only 2 patients had a good response (≥40% reduction). The most common histological subtype after chemotherapy was mixed [akin to traditional terminology of triphasic WT] (n = 4); followed by stromal (n = 3), epithelial (n = 1), regressive (n = 1) and cystic partially differentiated nephroblastoma (CPDN) (n = 1). All except 1 were intermediate risk. CPDN was low risk and did not show any CIC. In the remaining 9 cases, CIC was demonstrated involving 25 – 70% (mean 38.8%) of the tumor area. The nephrectomy specimen correlated histologically in epithelial subtype. However, only 2/5 nephrectomy specimens had subtype concurrence in mixed type. The other 3 were subtyped subsequently as stromal (n = 1), regressive (n = 1) and CPDN (n = 1). Fibrous pseudocapsule was seen in 1 epithelial subtype and rhabdomyoblastic differentiation was seen in all 3 stromal subtypes, 1 of which also had focal anaplasia.
Conclusions: It is possible to subtype WT on trucut biopsy preoperatively in majority of specimens. The incidence of regressive subtype was much lower in our series as compared to SIOP study results (10% Vs 37.6%).

EP-699

VASCULAR TUMORS AND MALFORMATIONS-MULTIDISCIPLINARY APPROACH AND OUTCOME IN NORTH INDIAN CHILDREN

D. Yadav[1], S. Acharya[1], T. Khan[1], A. Prasad[1], A. Samie[1], L. Ahmad[1], R. Gupta[2], D. Bagga[1]

[1]Pediatric Surgery, Vardhman Mahavir Medical college and Safdarjung Hospital, Delhi, India; [2]Radiology, Vardhman Mahavir Medical college and Safdarjung Hospital, Delhi, India

Objectives: To evaluate the presentation, treatment and outcome of vascular tumors and malformations in North Indian children.
Methods: Retrospective analysis of consecutive cases of vascular tumors and malformations presenting at VMMC and Safdarjang Hospital, New Delhi from 2008 through 2013 was carried out. The age at presentation, type of vascular tumors and malformations {International Society for the Study of Vascuar Anomalies (ISSVA) Classification), associated abnormalities, treatment options and outcome were reviewed. Protocol based radiological examinations were colour Doppler and CT angiography. Treatment options were conservative, oral propranolol and steroids, intralesional therapy with Bleomycin & Sodium tetradecyl sulphate, laser therapy, compression therapy and surgical excision.
Results: Two hundred six patients (125 female, 81male) were identified. Vascular tumors 118 pt (57%) were Infantile hemangioma 84pt (40%, 52female, 27male, mean age of presentation 4 week, 70% over head and neck, good response to propranolol and 8 required excision),

hepatic hemangoima 4 pt (2%, large, responded well to prednisolone), congenital hemangioma 18 pt {8%, 8RICH, 10NICH (trunk & extremities, required excision, good cosmesis)}, pyogenic granuloma 12 pt (6%, excision). Vascular malformations 88pt (43%) were venous malformation 52 pt (25%, over trunk, extremities and face, age ranges 1month to 12 years, major role of colour Doppler and CT angio for flow pattern and vascular anatomy, responded well to inj sclerotherapy, rarely excision), capillary malformation 6pt (3%), lymphatic malformation 20 pt {10%, 15 cystic hygroma (cervical, responded well to bleomycin, excision in 2 pt), 5 macrocystic lymphangioma, responded well to bleomycin}. Complex vascular malformation was Klippel-Trenaunay syndrmor in 10pt (5%, lower extremities & perineum with bony overgrowth, satisfactory response to compression bandage and local sclerotherapy).

Conclusions: Multidisciplinary approach and treatment, with appropriate clinical and radiological assessment provide satisfactory outcome and accepted morbidity in vascular tumors and malformations cases.

Author/Abstract Index

H