have an excellent Performance Status (ECOG score 0 or Lansky/Karnofsky ≥ 90), 5 (14.2%) scored ECOG 1–2 and only 4 (11.4%) scored ECOG 3–4. CONCLUSIONS: A multidisciplinary approach with a focus on Performance Status and the potential for neurological recovery is essential in the management of pediatric patients with CNS tumors. Efforts should be aimed at reducing post-surgical morbidity and early rehabilitation to reintegrate patients into society in the long term.

LINC-40. VERY YOUNG PATIENTS AND CENTRAL NERVOUS SYSTEM TUMORS: A SINGLE-CENTER EXPERIENCE IN AN UPPER-MIDDLE-INCOME COUNTRY

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Tumors of the central nervous system comprise nearly a quarter of all childhood cancers and are the most frequent solid tumor in the pediatric population. Primary central nervous system tumors (PCNST) are a rare and heterogeneous group of tumors responsible for high mortality and morbidity. Around 10% of primary CNS tumors occur during the first year of life with almost half of them during the first six months. About 18% of these tumors appear before the age of two years. Very young children differ from older children and adolescents regarding the incidence and location of different histological entities of CNS tumors. We aimed at providing descriptive epidemiological data and report the outcome in a tertiary center from December 2013 to January 2020 for all histological subtypes of primary central nervous system tumors in very young patients, defined as patients younger than three years. We collect data from 19 patients treated in an oncology exclusive tertiary center in Mexico between 2013 and 2020. This study aims to relate factors such as age, radiotherapy, surgery, chemotherapy with Lansky Performance Scale and determine the impact, not only in the overall survival but also in the quality of life.

LINC-41. TREATMENT OF RECURRENT MEDULLOBLASTOMA IN CHILDREN IN LOW INCOME SETTINGS

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INTRODUCTION: Children with recurrent medulloblastoma after initial therapy have very poor prognosis due to limited second line treatment options and significant treatment-related morbidity. METHODS: A retrospective chart review of 18 children with recurrent or progressive medulloblastoma, treated initially with risk-adapted therapy in Western Ukrainian Specialized Pediatric Medical Centre from 2012 to 2019, was performed. RESULTS: All patients received first line multimodal treatment: surgery, distant beam radiotherapy and chemotherapy. Recurrent disease in 11 patients presented with metastatic dissemination and in 7 patients as local relapse. The median time to recurrence was 10 months. The median follow-up after diagnosis of recurrent disease diagnosed was 2 years and 2 months. Second line therapy included re-surgery (5 cases), radiation therapy (10 cases) and various cytostatic agents as monotherapy or combination - carboplatin, cisplatin, cyclophosphamide, etoposide, methotrexate, temozolomide, lomustine. Patients treated with radiotherapy for salvage had prolonged local control compared to those that received chemotherapy only. On follow-up 8 children are currently alive. CONCLUSION: Recurrent and progressive medulloblastoma had a poor prognosis with a 2-year overall survival (OS) of 28% on different salvage therapy. The variety in the treatment of all patients experiencing recurrence was observed due to low income country settings. The factors that influenced higher survival after recurrence of medulloblastoma were longer time to relapse, and local pattern of relapse/progression.

LINC-42. EPIDEMIOLOGICAL OVERVIEW OF CHILDHOOD CNS TUMORS IN THE NEUROSURGICAL UNIT IN YEREVAN, ARMENIA

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BACKGROUND: Central nervous system (CNS) tumors are the second most common malignant neoplasms among children worldwide. The current paper aims to analyze the situation in pediatric neuro-oncology in Armenia from the neurosurgical perspective. METHODS: We have collected data of pediatric patients with CNS tumors treated in the Neurosurgery department of "Surb Astvasamayr" Medical Center from 01.01.2010 till 01.12.2019. Incidence by gender, age at diagnosis, and histopathology results were calculated. Survival rates were calculated based on the follow-up results performed until 30.12.2019. RESULTS: Hospital-based data showed that during the previous 10 years 47 patients with CNS tumors received neurosurgical treatment in the unit, among them 66% were females. 38.3%, 31.9% and 29.8% of diagnosed patients were aged 0–4, 5–9, and 10–18 respectively. In 41 cases, the disease was not disseminated at diagnosis. The most common observed malignancies were low-grade gliomas (21.3%) and embryonal tumors (19.1%), followed by high-grade gliomas (14.9%) and ependymal tumors (8.5%). Follow-up information only for 33 patients is available. From them, 14 are dead and 19 alive. Survival rates in most common groups were 62.5%, 80%, 50%, and 50% respectively. The median follow-up time was 18 months (range 1–113 months). CONCLUSION: Similar to the data reported in the literature, low-grade gliomas, and embryonal tumors are the most frequent pediatric CNS tumors in Armenia. On the other hand, the pediatric CNS tumor survival rates are lower compared to those reported in developed countries.

LINC-43. FACTORS LEADING TO DIAGNOSTIC DELAY FOR CHILDREN WITH PRIMARY TUMORS OF CENTRAL NERVOUS SYSTEM (CNS) IN QATAR

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INTRODUCTION: Median time to diagnosis for primary CNS tumors for children in Qatar has been reported to be 28 days. However, a wide variation in diagnostic times is seen. This study was undertaken to analyze the factors leading to delay in diagnosis. METHODS: Data were retrospectively analyzed for children who had diagnostic delay (more than 28 days) from September 2006 to February 2020. Presenting symptoms, number and type of healthcare contacts and presenting symptom interval (PSI) were reviewed. Parental delay (PSI-1) was defined as the date of onset of first symptom to the date of first healthcare contact. Healthcare delay (PSI-2) was defined as date of first healthcare contact to the date of diagnostic scan. RESULTS: Twenty-four patients were identified with diagnostic delay. Median age at diagnosis was 48.2 (range 5.4–171.6) months with an equal sex distribution. Fifteen (62.5%) patients were older than 3 years, 13(54%) patients had low grade glioma, 16 (66.7%) had supratentorial tumors and 12 (50%) presented with raised intracranial pressure. Diagnosis was made after a median 3 (range 1–8) healthcare contacts. Nineteen (79%) patients presented to primary care. Median PSI was 132 (31–783) days. Parental delay (PSI-1) was 35 (0–496) days, while healthcare delay (PSI-2) was 41 (0–562) days. Endocrine (241 days) and oculo-visual (184 days) symptoms were associated with the longest PSI. CONCLUSIONS: There was no significant difference between parental and healthcare delay. Endocrine and oculo-visual symptoms were associated with longest PSI. Increased awareness is required for early recognition of signs suggestive of CNS tumors.

MEDULLOBLASTOMA (CLINICAL)

MBCL-01. METHYLATION PROFILING OF PEDIATRIC MEDULLOBLASTOMA IN SAUDI ARABIA IN A CLINICAL SETTING PERMITS SUB-CLASSIFICATION AND REVEALS NEW OUTCOME PREDICTIONS

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Medulloblastoma (MB) is the most common childhood malignant brain tumor. DNA methylation profiling has rapidly advanced our understanding of MB pathogenesis at the molecular level, MBs can be sub-grouped according to methylation patterns from FPPE samples into Wingless (WNT-MB), Sonic Hedgehog (SHH-MB), Group 3 (G3) and Group 4 (G4) WNT-MB and SHH-MB subgroups are characterized by gain-of function mutations that activate oncogenic cell signalling whilst G3/G4 tumors show recurrent chromosomal alterations. each subgroup has distinct clin-

ical outcomes, the ability to subgroup SA-FPPE samples holds significant prognostic and therapeutic value. We performed the first assessment of MB-DNA methylation patterns in Saudi Arabian SA cohort using archival biopsy materials (FPPE n=49). Of the 41 materials available for methylation assessments, 39 could be classified into the major DNA methylation subgroups (SHH, WNT, G3 and G4). Methylation analysis was able to reclassify tumors that could not be sub-grouped through NGS testing, highlighting its improved accuracy for MB molecular classifications. Independent assessments demonstrate clinical relationships of the subgroups, exemplified by the high survival rates observed for WNT tumors. Surprisingly, the G4 subgroup did not conform to previously identified phenotypes, with a high prevalence in females, high metastatic rates and a large number of tumor-associated deaths. DNA methylation profiling enables the robust sub-classification of four disease sub-groups in SA-MB patients. Moreover, the incorporation of DNA methylation biomarkers can significantly improve current disease-risk stratification schemes, particularly concerning the identification of aggressive G4 tumors. These findings have important implications for future clinical disease management in MB cases across the Arab world.

MBCL-02. ROLE OF PREOPERATIVE CHEMOTHERAPY IN METASTATIC MEDULLOBLASTOMA: A COMPARATIVE STUDY IN 92 CHILDREN

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BACKGROUND: Previous pilot studies have shown the feasibility of preoperative chemotherapy in patients with medulloblastoma, but benefits and risks compared with initial surgery have not been assessed. METHODS: Two therapeutic strategies were retrospectively compared in 92 patients with metastatic medulloblastoma treated at Gustave Roussy, France, between 2002 and 2015: surgery at diagnosis (n=54; group A) and surgery delayed after carboplatin and etoposide-based preoperative therapy (n=38; group B). Treatment strategies were similar in both groups. RESULTS: The rate of complete tumor excision was significantly higher in group B than in group A (93.3% versus 57.4%, p=0.0013). Post-operative complications, chemotherapy-associated side effects and local progressions were not increased in group B. Preoperative chemotherapy led to a decrease in the primary tumor size in all patients, 4/38 patients experiencing meanwhile a distant progression. The histological review of 19 matched tumor pairs (before and after chemotherapy) showed that proliferation was reduced and histological diagnosis feasible and accurate even after preoperative chemotherapy. The 5-year progression-free and overall survival rates were comparable between groups. Comparison of the longitudinal neuropsychological data showed that intellectual outcome tended to be better in group B (the mean predicted intellectual quotient value was 6 points higher throughout the follow-up). CONCLUSION: Preoperative chemotherapy is a safe and efficient strategy for metastatic medulloblastoma. It increases the rate of complete tumor excision and may improve the neuropsychological outcome without jeopardizing survival.

MBCL-03. RESULTS OF HIGH-DOSE THIOTEPA, CARBOPLATIN AND ETOPOSIDE WITH AUTOLOGOUS HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR PATIENTS WITH RECURRENT MEDULLOBLASTOMA

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AIM: Medulloblastoma is a highly lethal disease when it recurs. Very few patients survive with second line conventional treatment after relapse. This study evaluated the use of high-dose thiotepa, carboplatin and etoposide with autologous hematopoietic stem-cell transplantation (HSCT) in patients with recurrent medulloblastoma. METHODS: From 2010 to 2019, 60 patients at the age 4–32 years (median, 12) with recurrent medulloblastoma were received high-dose chemotherapy (HDCT) with auto-HSCT after induction second line chemotherapy. HDCT included thiotepa 150 mg/m^2 #4; carboplatin 500 mg/m^2 #4; etoposide 250 mg/m^2 #4 and +/- etoposide 1 mg intraventricular on days #5 if patient had Ommaya reservoir; followed by HSCT. At the moment of HDCT 24 patients were in complete response (CR), 31 patients were in partial response (PR) and 5 patients had stable disease (SD) after second line conventional chemotherapy. RESULTS: The median follow-up is 65 months (range, 24–227). The median time to engraftment after auto-HSCT was day +11 (range, 8–39). Five-year overall survival (OS) was 58% and disease free survival (DFS) was 46%. DFS was significantly better among patients in CR or PR 50% in compared to children in SD 20% at the moment of HDCT (p=0,002). Transplant related mortality were 12%, there were 7 patients died because of severe complications within 14 days after transplantation. CONCLUSIONS: HDCT with auto-HSCT in pediatric patients with recurrent medulloblastoma may be a feasible option for cases who had CR or PR after induction chemotherapy. It is ineffective as a salvage therapy in refractory patients.

MBCL-04. 5 – AZACYTIDINE IN TREATMENT OF CHILDREN WITH DE NOVO AND RELAPSED METASTATIC MEDULLOBLASTOMA: RESULTS OF INTERCENTER PILOT STUDY

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The aim of this study was to estimate treatment toxicity and event-free survival (EFS) according to therapeutic program, *MYC/MYC-N* gene amplification and MGMT/DNMT (1, 3a, 3b) proteins expression in tumor cells. From 2016 to 2018 twenty four patients were included in trial. Children underwent adjuvant therapy: craniospinal radiation (CSI) or local radiation therapy (RT) to the relapsed site up to 23.4Gy with 5-azacytidine, 2 cycles methotrexate/5-azacytidine/cisplatin/etoposide, 3 cycles 5-azacytidine/temozolomide - for relapsed group (arm A, n = 5); for patients with de novo medulloblastoma: arm B, n = 11 – vincristine/cyclophosphamide/cisplatin/etoposide (OPEC) - based induction, CSI 36Gy + local RT to the tumor bed up to 54Gy with 5-azacytidine, 1 cycle OPEC and 2 cycles thiophosphamide/carboplatin with auto stem cell transplantation (auto-SCT); arm C, n = 8 – cyclophosphamide/cisplatin - based induction, CSI 23.4 Gy followed by 2 cycles 5-azacytidine/thiophosphamide/carboplatin with auto-SCT, local RT with 5-azacytidine. The combination of 5-azacytidine with local RT or temozolomide was safety and tolerability. Arm C was discontinued due to severe gastrointestinal grade 3/4 toxicity, hemorrhagic syndrome after combination of 5-azacytidine with thiophosphamide/carboplatin. EFS was 0% in arm A, 53.0 ± 15.5%, 50.0 ± 17.7% in arms B and C, a median follow-up 8.8 ± 1.1 months (arm A), 18.8 ± 2.5 months (arm B), 25.0 ± 4.4 months (arm C). Addition of 5-azacytidine to RT or chemotherapy did not improve EFS of patients with *MYC/MYC-N* gene amplification positive tumor. There was not determined any prognostic significance of MGMT/DNMT (1, 3a, 3b) proteins expression in this cohort.

MBCL-05. TREATMENT OF CHILDREN WITH MEDULLOBLASTOMA WITHOUT METASTATIC INVOLVEMENT IN THE AGE GROUP OLDER THAN 3 YEARS: RESULTS OF INTERCENTER TRIAL

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The aim of this study was to identify a group of patients aged 3 to 7 years for whom there is the possibility for reducing of craniospinal radiation dose (CSI). From 2008 to 2018 fifty one pediatric patients with primary diagnosed medulloblastoma in the age group 3 - 18 years were included in trial, 38 in standard risk group, 13 in high risk group. Treatment program consisted of surgical removal of the primary tumor site with subsequent radiation therapy (with CSI of 23,4 Gy or 36 Gy, depending on the risk group) and high-dose chemotherapy (with high-dose cyclophosphamide or thiophosphamide). As a result of this study, sufficiently high rates of overall survival and progression/relapse - free survival (PFS) were achieved in standard and high-risk groups patients, which amounted to 76,0 ± 8,8% and 83,3 ± 10,8% with median follow-up 62,9 ± 6,2 months and 52,2 ± 7,8 months, respectively. There was revealed patients group in the age 3 - 7 years with 100% PFS and median follow-up 66,9 ± 8,9 months. Morphological and molecular biological factors of an unfavorable outcome of the