etic predisposition for pediatric MB_{SHH} to 40%. These results mark MB_{SHH} as an overwhelmingly genetically-predisposed disease and implicate disruption of protein homeostasis in MB_{SHH} development.

MBCL-22. EFFICACY OF DOUBLE-CONDITIONING REGIMEN COMPRISING THIOTEPA AND MELPHALAN FOR RELAPSED MEDULLOBLASTOMA – A SINGLE INSTITUTION EXPERIENCE

Kai Yamasaki[1], Kazuki Tanimura[1], Yuki Okuhiro[1], Kota Hira[1], Chika Nitani[1], Keiko Okada[1], Hiroyuki Fujisaki[1], Noritsugu Kunihiro[2], Yasuhiro Matsusaka[2], Hiroaki Sakamoto[2], and Junichi Hara[1]; [1]Department of Pediatric Hematology and Oncology, Osaka City General Hospital, Osaka, Japan, [2]Department of Pediatric Neurosurgery, Osaka City General Hospital, Osaka, Japan

BACKGROUND: The prognosis of relapsed medulloblastoma was dismal. Recently, we published the promising outcome of metastatic medulloblastomas treated with a double-conditioning regimen comprising high-dose thiotepa and melphalan (HD-TM). Here, we report a single-center study of HD-TM for relapsed medulloblastomas. MATERIALS AND METHODS: From April 2006 to January 2019, 17 consecutive medulloblastoma patients with the first relapse were identified, and of which 10 received HD-TM were retrospectively reviewed. RESULTS: The median age at first relapse was 11.9 years (range 1.8–31.7). The median follow-up period was 23.5 months after 1st relapse. Four localized relapses at the posterior fossa and 6 metastatic relapses including 3 with multiple sites were observed. Surgical resection and re-irradiation were administered in 5 and 9 patients, respectively. Two-year PFS and OS after relapse were 21±18.1% and 60±21.9%, respectively, and significantly better than in patients who did not receive HD-TM. Among 7 evaluable patients, tumor shrinkage was observed in 6 after HD-TM administration including 3 patients who were resistant to prior chemotherapy. At the present time, 5 patients are alive with no evidence of disease (NED). The last 5 patients received re-irradiation including 12 Gy craniospinal irradiation (CSI), and 4 are alive with NED. In multivariate analysis for all patients, both HD-TM and re-irradiation were associated with improved OS and PFS, but disseminated relapse had no prognostic value (p=0.56). CONCLUSION: HD-TM contributes to prolonged survival when combined with re-irradiation. HD-TM might become a curative approach for relapsed medulloblastoma, especially when combined with CSI.

MBCL-23. PRELIMINARY ANALYSIS OF TREATMENT-RELATED TOXICITIES DURING INDUCTION CHEMOTHERAPY FOR PATIENTS ON THE HEAD START 4 TRIAL

Vibhuti Agarwal[1], Joseph Stanek[2], Megan Jaeger[2], Girish Dhall[3], and Jonathan Finlay[2]; [1]Nemours Children's Hospital, Orlando, FL, USA, [2]Nationwide Children's Hospital, Columbus, OH, USA, [3]Children's Hospital of Alabama, Birmingham, AL, USA

The currently active, prospective multi-center Head Start 4 (HS4) trial for CNS embryonal tumors differs from prior HS I-III trials by utilizing absolute phagocyte count (APC) as a measure of myeloid recovery instead of absolute neutrophil count. The aim of this study was to determine if utilization of APC resulted in unanticipated treatment-related toxicities during induction chemotherapy for patients enrolled on HS4. Review of the RedCap database was conducted for treatment-related CTCAE grade 3 and 4 toxicities. Data were summarized descriptively. Nonparametric statistical methods were used for comparisons. At the time of this most recent analysis, a total of 180 induction cycles were completed for the 57 patients enrolled. Of the 57 patients, nine voluntarily discontinued therapy after completing a median of three cycles each. These patients had a higher number of documented infections (59% *versus* 24%, p=0.0004). Veno-occlusive disease (VOD) occurred in five patients, three of whom voluntarily discontinued therapy. Since the protocol amendment utilizing milligram per kilogram dosing for patients less than six years of age, there have been no documented episodes of VOD. The overall toxicities for this cohort were comparable to those reported for induction chemotherapy in HS I-II trials. The toxic death rate is lower for HS4 compared to HS I-II (0.018% *versus* 4.7–6%) (Chi et al 2004). Other than the high rate of infection, possibly associated with shorter duration of the immediately prior cycles, the use of APC as part of a dose-compression strategy in HS4 does not appear associated with more significant toxicities.

MBCL-24. CAN YOUNG CHILDREN WITH RELAPSED MEDULLOBLASTOMA BE SALVAGED AFTER INITIAL IRRADIATION-SPARING APPROACHES?

Craig Erker[1,2], Valérie Larouche[3], Ashley Margol[4,5], Chantel Cacciotti[6], Sébastien Perreault[7,8], Kenneth J. Cohen[9,10], Mohamed S. AbdelBaki[11,12], Juliette Hukin[13,14], Shahrad Rod Rassekh[13,14], David D. Eisenstat[15,16], Beverly Wilson[15,16], Jeffrey Knipstein[17,18], Anna L. Hoppmann[19], Eric S. Sandler[20,21], Kathleen Dorris[22,23], Taryn B. Fay-McClymont[24,25], Ralph Salloum[26,27], Virginia L. Harrod[28,29], Bruce Crooks[1,2], Jonathan L. Finlay[11,12], Eric Bouffet[30,31], and Lucie Lafay-Cousin[24,25]; [1]Dalhousie University, Halifax, Nova Scotia, Canada, [2]IWK Health Centre, Halifax, Nova Scotia, Canada, [3]CHU de Québec-Université Laval, Québec City, Québec, Canada, [4]Keck School of Medicine of University of Southern California, Los Angeles, California, USA, [5]Children's Hospital of Los Angeles, Los Angeles, California, USA, [6]Dana-Farber/ Boston Children's Cancer and Blood Disorders Center, Boston, Massachusetts, USA, [7]Université de Montréal, Montreal, Québec, Canada, [8]CHU Sainte-Justine, Montreal, Québec, Canada, [9]The Sidney Kimmel Comprehensive Cancer Center, Baltimore, Maryland, USA, [10]Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [11]Ohio State University, Columbus, Ohio, USA, [12]Nationwide Children's Hospital, Columbus, Ohio, USA, [13]University of British Columbia, Vancouver, British Columbia, Canada, [14]BC Children's Hospital, Vancouver, British Columbia, Canada, [15]University of Alberta, Edmonton, Alberta, Canada, [16]Stollery Children's Hospital, Edmonton, Alberta, Canada, [17]Medical College of Wisconsin, Milwaukee, Wisconsin, USA, [18]Children's Hospital of Wisconsin, Milwaukee, Wisconsin, USA, [19]University of Alabama at Birmingham, Birmingham, Alabama, USA, [20]Nemours Children's Specialty Care, Jacksonville, Florida, USA, [21]Wolfson Children's Hospital, Jacksonville, Florida, USA, [22]University of Colorado School of Medicine, Aurora, Colorado, USA, [23]Children's Hospital Colorado, Aurora, Colorado, USA, [24]University of Calgary, Calgary, Alberta, Canada, [25]Alberta Children's Hospital, Calgary, Alberta, Canada, [26]University of Cincinnati, Cincinnati, Ohio, USA, [27]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA, [28]University of Texas, Dell Medical School, Austin, Texas, USA, [29]Dell Children's Medical Center of Central Texas, Austin, Texas, USA, [30]University of Toronto, Toronto, Ontario, Canada, [31]The Hospital for Sick Children, Toronto, Ontario, Canada

INTRODUCTION: Irradiation-sparing approaches are used in young children with medulloblastoma (MB) given the vulnerability of the developing brain to neurocognitive impairment. Limited data are available following relapse for these patients. We aimed to describe the management and outcomes of young children with MB who relapsed after initial treatment without craniospinal irradiation (CSI). METHODS: International retrospective study including patients with MB diagnosed between 1995–2017, ≤ 72 months old, initially treated without CSI, who subsequently relapsed. RESULTS: Data are available for 52 patients (32 male). Median age at initial diagnosis was 27 months (range, 6–72) with 24 being metastatic. Initial therapy included conventional chemotherapy alone or high-dose chemotherapy (HDC) in 21 and 31 subjects, respectively. Three received upfront focal irradiation. Molecular subgrouping, available for 24 tumors, included 9 SHH and 15 non-WNT/non-SHH. Median time to relapse was 13 months (range, 3–63). Relapse was local, disseminated or combined in 20, 15, and 16, respectively. Salvage therapy with curative intent was given in 42/52 patients, including CSI in 28 subjects (median dose 36Gy, 18–41.4) or focal irradiation in 5 others. Three received HDC only. At a median follow-up time of 46 months (range, 4–255), 25 (48%) were alive, including 7/9 SHH and 7/15 non-WNT/non-SHH. The 2- and 5-year OS was 67% and 56% (SE, 7%), respectively. Two of 3 patients with SHH who did not receive salvage radiotherapy are survivors. CONCLUSION: A substantial proportion of young children who relapse following irradiation-sparing strategies can be salvaged. Neurocognitive and ototoxicity outcomes are being evaluated.

MBCL-25. PILOT STUDY OF A SURGERY AND CHEMOTHERAPY-ONLY APPROACH IN THE UPFRONT THERAPY OF CHILDREN WITH WNT-POSITIVE STANDARD RISK MEDULLOBLASTOMA: UPDATED OUTCOMES

Kenneth Cohen[1], Susan Chi[2], Cynthia Hawkins[3], Fausto Rodriguez[4], Wendy London[2], Robert Craig Castellino[5], Dolly Aguilera[5], Stacie Stapleton[6], David Ashley[7], Daniel Landi[7], and Pratiti Bandopadhayay[2]; [1]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA, [2]Dana-Farber Cancer Institute, Boston, MA, USA, [3]Hospital for Sick Children, Toronto, Ontario, Canada, [4]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [5]Children's Healthcare of Atlanta, Atlanta, GA, USA, [6]Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA, [7]Duke University Medical Center, Durham, NC, USA

BACKGROUND: Wnt+ medulloblastoma (WPM) is a favorable subtype with EFS > 90% when treating postoperatively with craniospinal irradiation and posterior fossa boost (CSI/XRT) followed by adjuvant chemotherapy. This pilot study explored the safety of omitting radiation in standard-risk WPM. METHODS: Subjects had to meet standard-risk criteria (< 1.5 cm2 residual tumor, no metastatic spread, no anaplasia) and have a WPM. Subjects received chemotherapy following the COGACNS0331 AAB-AAB-AAB (A=cisplatin/CCNU/VCR; B=cyclophosphamide/vincristine) backbone. RESULTS: Six children were enrolled on study treatment prior to early study closure. Subject #1 completed planned protocol therapy but relapsed 3 months following the completion of therapy. Subject #2 completed

planned protocol therapy but relapsed 6 months following the completion of therapy. In both cases, relapse was local and disseminated. Further accrual was halted. Both subjects were salvaged with CSI/XRT followed by adjuvant chemotherapy. Of the remaining 4 subjects, two had recently completed planned protocol therapy at the time of study closure and received CSI/XRT while in remission and remain in remission approximately one year from the completion of treatment. One subject aborted protocol therapy and transitioned to a Head Start regimen and remains in remission 10 months from completion of therapy. The final subject had just completed protocol therapy and had new areas of restricted diffusion concerning for early relapse. Went on to receive CSI/XRT but subsequently relapsed and is now receiving salvage chemotherapy. CONCLUSIONS: Chemotherapy following ACNS0331, omitting CSI/XRT, appears to be insufficient for the treatment of non-metastatic WPM.

MBCL-26. FACTORS ASSOCIATED WITH LONGER SURVIVAL AFTER FIRST RECURRENCE IN MEDULLOBLASTOMA BY MOLECULAR SUBGROUP AFTER RISK-BASED INITIAL THERAPY

Murali Chintagumpala[1], Colton Terhune[2], Lin Tong[3], Eric Bouffet[4], Ute Bartels[4], Michael Fisher[5], Tim Hassall[6], Shridharan Gururangan[7], Kristin Schroeder[8], Jordan Hansford[9], Dong Anh Khuong Quang[9], Richard Cohn[10], Stewart Kellie[11], Geoffrey McCowage[12], Kyle Smith[3], Paul Northcott[3], Giles Robinson[3], and Amar Gajjar[3]; [1]Texas Children's Hospital, Houston, TX, USA, [2]University of South Hampton, South Hampton, United Kingdom, [3]St. Jude Children's Research Hospital, Memphis, TN, USA, [4]Hospital for Sick Children, Toronto, Ontario, Canada, [5]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA, [6]Children's Health Queensland, Brisbane, Queensland, Australia, [7]University of Florida, Gainsville, FL, USA, [8]Duke University, Durham, NC, USA, [9]Royal Children's Hospital, Melbourne, Victoria, Australia, [10]Sydney Childre, Sydney, New South Wales, Australia, [11]Westmead Children's, Sydney, New South Wales, Australia, [12]Westmead Children's, Sydney, NSW, Australia

OBJECTIVE: To evaluate differences in time to recurrence among molecular subgroups of medulloblastoma treated on a single protocol and to identify factors associated with survival after first recurrence. METHODS: Time to recurrence following SJMB03 treatment was compared across methylation subgroups among relapsed patients. Therapies received subsequent to relapse were noted. Kaplan-Meier methods and log-rank tests were used for statistical analyses. RESULTS: 74 of 330 medulloblastoma patients developed recurrence after initial therapy. (38 Standard-Risk; 36 High-Risk). The 2- and 5-year survival after first recurrence was 30.4% and 14.6% respectively. DNA methylation-based subgroups from initial diagnosis were SHH (n=14), Group 3 (n=24), Group 4 (n=26), and unclassified (n=8). None of the pts with WNT MB had recurrent disease. Median time to first recurrence was 1.23, 0.91, and 3.09 years in SHH, Group3, and Group 4 respectively. Group 4 patients had longer post-recurrence survival than others (p-value=0.0169). Clinical risk at diagnosis (p-value=0.337), anaplasia (p-value=0.4032), *TP53* (p-value=0.1969), *MYC* (p-value=0.8967), and *MYCN* (p value = 0.9404) abnormalities were not associated with post progression survival. Patients who received any therapeutic modality (chemotherapy, re-radiation and second surgery) had longer survival and those who had all three (n=10) had the best outcome (p-value<0.0001). CONCLUSION: Outcome after recurrence in medulloblastoma is dismal, however, association with subgroups is still present. Group 4 patients had a longer time to recurrence and post progression survival. No other prognostic factor at initial diagnosis was associated with outcome after recurrence. Patients who received all 3 types of conventional therapy had better survival.

MBCL-27. ASSOCIATION OF MEDULLOBLASTOMA WITH CHARCOT-MARIE-TOOTH DISEASE

Kenichiro Watanabe[1], Kazuyuki Komatsu[1], Koji Kawaguchi[1], Risa Makino[1], Takayuki Takachi[1], Taemi Ogura[1], Yasuo Horikoshi[1], Ryuji Ishizaki[2], Hideto Iwafuchi[3], and Yuzuru Tashiro[2]; [1]Department of Hematology and Oncology, Shizuoka Children's Hospital, Shizuoka, Japan, [2]Department of Neurosurgery, Shizuoka Children's Hospital, Shizuoka, Japan, [3]Department of Pathology, Shizuoka Children's Hospital, Shizuoka, Japan

Charcot-Marie-Tooth disease (CMT) is one of the most common hereditary neurological disorders and damages peripheral nerves that results in motor and sensory disturbance. Association of medulloblastoma (MBL) with CMT has been rarely reported. A one-year-old male was referred to our hospital because of cerebellar mass. He had partial resection of the tumor, and was pathologically diagnosed as having desmoplastic nodular medulloblastoma. He received chemotherapy according to the HIT protocol, however, developed severe peripheral neurotoxicity in the initial stage of the treatment. Reinvestigation of family history revealed his mother, grandmother, and aunt had muscle weakness. We suspected he had an inherited neurological disease including CMT, and discontinued administration of vincristine. Fluorescence in situ hybridization analysis detected duplication of PMP22 gene located on 17p11.2, confirming the diagnosis of CMT1A. He completed the rest of chemotherapy without vincristine, and remained in complete remission for four years from the end of treatment. In the literature, there are reports of patients with CMT who developed MBL and were complicated with severe peripheral neurotoxicity due to the use of vincristine. The present case, along with previous reports, suggests that medulloblastoma can develop in patients with CMT and reminds the importance of recalling the possibility of CMT when patients develop severe chemotherapy-induced peripheral neurotoxicity upon use of vincristine. Desmoplastic nodular medulloblastoma may be successfully treated by chemotherapy without vincristine.

MBCL-28. LONG-TERM FOLLOW-UP RESULTS OF REDUCED DOSE CRANIOSPINAL RADIOTHERAPY AND TANDEM HIGH-DOSE CHEMOTHERAPY IN PATIENTS WITH HIGH-RISK MEDULLOBLASTOMA

Ji Won Lee[1], Do Hoon Lim[2], Meong Hi Son[1], Ki Woong Sung[1], Hee Won Cho[1], Hee Young Ju[1], Ju Kyung Hyun[1], Keon Hee Yoo[1], Hye Lim Jung[3], Hong Hoe Koo[1], Yeon-Lim Suh[4], Yoo Sook Joung[5], and Hyung Jin Shin[6]; [1]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [2]Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul,Republic of Korea, [3]Department of Pediatrics, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [4]Department of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [5]Department of Psychiatry, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [6]Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

BACKGROUND: In this study, we report the follow-up results of reduced-dose of craniospinal radiotherapy (CSRT) followed by tandem high-dose chemotherapy (HDCT) in patients with high-risk medulloblastoma (MB). METHODS: Newly diagnosed high-risk MB patients (metastatic disease, postoperative residual tumor > 1.5 cm^2 or large cell/anaplastic histology) over 3 years of age were enrolled in this study. Two cycles of pre-RT chemotherapy, RT including reduced-dose CSRT (23.4 or 30.6 Gy), 4 cycles of post-RT chemotherapy and tandem HDCT were given. NanoString and DNA sequencing were done with archival tissues. RESULTS: Forty patients were enrolled, and molecular subgrouping was possible in 21 patients (2 WNT, 3 SHH, 8 Group 3 and 8 group 4). All patients including two patients who experienced progression during the induction chemotherapy underwent HDCT. Relapse/progression occurred only in four patients (10-year cumulative incidence 10.4 ± 0.3%). However, six patients died from treatment-related mortality (TRM) (4 acute TRMs and 2 late TRMs) resulting in 18.5 ± 0.5% of 10-year cumulative incidence. Taken together, the 10-year event-free survival and overall survival were 71.1 ± 8.0% and 68.9 ± 8.5%, respectively. Late effects were evaluated in 25 patients and high-tone hearing loss, endocrine dysfunction, dyslipidemia, and growth retardation were common. CONCLUSIONS: Strategy using tandem HDCT following reduced-dose CSRT showed promising results in terms of low relapse/progression rate, however, the high TRM rate indicates that modification of HDCT regimen and careful selection of patients who can have benefit from HDCT will be needed in the future study.

MBCL-29. PHASE I/II STUDY OF SEQUENTIAL HIGH-DOSE CHEMOTHERAPY WITH STEM CELL SUPPORT IN CHILDREN YOUNGER THAN 5 YEARS OF AGE WITH HIGH-RISK MEDULLOBLASTOMA

Christelle Dufour[1], Julien Masliah-Planchon[2], Marie-Bernadette Delisle[3], Anne Geoffray[4], Rachid Abbas[1], Franck Bourdeaut[2], Anne-Isabelle Bertozzi[3], Cecile Faure-Conter[5], Celine Chappe[6], Emilie De Carli[7], Natacha Entz-Werle[8], Fanny Fouyssac[9], Nicolas Andre[10], Christine Soler[11], Claire Pluchart[12], Gilles Palenzuela[13], Pierre Leblond[14], and Jacques Grill[1]; [1]Gustave Roussy, Villejuif, France, [2]Curie Institute, Paris, France, [3]Toulouse University Hospital, Toulouse, France, [4]Fondation Lenval Children's Hospital, Nice, France, [5]Institut d'Hématologie et d'Oncologie pédiatrique, Lyon, France, [6]Rennes University Hospital, Rennes, France, [7]University Hospital, Angers, France, [8]CHU of Strasbourg, Strasbourg, France, [9]Children's Hospital, Nancy, France, [10]CHU Timone, Marseille, France, [11]CHU of Nice, Nice, France, [12]CHU of Reims, Reims, France, [13]CHU of Montpellier, Montpellier, France, [14]Oscar Lambret, Lille, France

PURPOSE: To assess the 3-year EFS rate of children younger than 5 years of age with high-risk medulloblastoma (MB) treated according to the prospective multicenter trial HR MB-5. PATIENTS AND METHODS: After surgery, all children received 2 cycles of Etoposide- Carboplatine. If par-