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

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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

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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

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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

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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-

tial (PR) or complete response (CR) was achieved after induction chemotherapy, children received 2 courses of thiotepa (600mg/m²) with stem cell rescue. For patients in CR after high-dose chemotherapy, they received one course of Cyclophosphamide – Busilvex with stem cell rescue (Phase I part). The others patients (not in PR after induction or in CR after thiotepa) were treated with 2 cycles of Temozolomide-Irinotecan followed by age-adapted craniospinal irradiation and maintenance treatment. RESULTS: 28 children (2 to 4 years; median: 3.0 years) were enrolled. Group 3 MB were most common (57%). The response rate to Etoposide-Carboplatine was 60.7%. Among 20 patients treated with Thiotepa, 13 children were in CR and received Cyclophosphamide – Busilvex without radiotherapy. Out of them, 9 patients (45%) are alive in CR without craniospinal irradiation (median follow-up 5 years). Among 15 patients treated with radiotherapy, 8 patients are alive (median follow-up 3.8 years). The study was prematurely stopped for an excess of events. The median follow-up was 4 years (range 1.5 - 6.1). The 3-year EFS and OS were 42.3% [25.9 - 60.6] and 71.3% [52.7 - 84.7], respectively. CONCLUSIONS: This risk-adapted strategy did not improve EFS in young children with high-risk MB. However, the study shows that good responders to chemotherapy can be cured without recourse to irradiation.

MBCL-30. NOVEL SMO MUTATION IN DESMOPLASTIC/NODULAR MEDULLOBLASTOMA: A CASE REPORT

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Smoothened (SMO) is a transmembrane protein which is regulated by SHH (Sonic hedgehog) protein binding to PTCH1. SMO activation controls GLI which then translocates into the nucleus and activates target genes. The SHH subtype of medulloblastoma has been extensively studied to have mutations within the SHH signaling pathway, often in PTCH1, SUFU, and SMO. We present a case of desmoplastic/nodular medulloblastoma with the mutation SMO c.1810G>A. The patient presented at 11 years old with a two-week history of headaches and morning vomiting. His neuroimaging revealed a T2 hyperintense, enhancing mass centered at the fourth ventricle. He underwent gross total resection and had no metastatic spread. There were no alterations in PTCH1, SUFU, Tp53, GLI2, MYC/MYCN, CTNNB1, or the WNT pathway. The SMO c.1810G>A alteration has not been previously identified as a somatic mutation in a CNS tumor. The functional effect of this mutation has not been studied. It is known that desmoplastic/nodular histology in medulloblastoma is associated with the SHH subtype and given the fact that SMO is regulated by SHH signaling, this patient was ultimately diagnosed with SHH subtype medulloblastoma. Findings of novel somatic mutations in patients raises the question of whether the mutation is in fact the driver of neoplasia.

MBCL-31. TREATMENT RESULTS AMONG 106 PATIENTS WITH MEDULLOBLASTOMA OF MOLECULAR SUBGROUP 3

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OBJECTIVE: To evaluate the treatment results among 106 patients of molecular subgroup 3 and to determine the factors affecting the prognosis. PATIENTS AND METHODS: In all the patients, initial removal of the tumor was performed. All the patients got chemoradiotherapy according to the HIT protocol. There were 34girls and 72boys. Most patients were over 3 years:74 compared to 32 younger than 3. The majority of the patients had stage M+: 65; in 38 stage M0 was determined; in 3patients, stage was not specified, Mx.MYC amplification was found in 20 patients; MYCN amplification, in 4 patients. Classic medulloblastoma was predominant: 65, and 41 patients had anaplastic/large cell medulloblastoma. RESULTS: The five-year progression-free survival was 0.51±0.05, the five-year overall survival was 0.52±0.04.The median survival was 82months,and the median progression-free survival was 37 months. There were no significant variations of PFS depending on the sex and age. The treatment results depended on the histological subtype: for classic medulloblastoma, the five-year PFS was 0.57; for the anaplastic/largecell,0.38(p = 0.02030). The presence of metastases significantly affected the survival: PFS for stage M0 was 0.77; for stage M+,0.35(p = 0.00062). Patients with MYC amplification had a significantly worse survival compared to MYCN patients and those without MYC amplification: 0.1, 0.75, and 0.58, respectively (p = 0.00002). Three patients with MYC amplification are alive: two patients had MGMT methylation detected. CONCLUSIONS: The results of treatment among the patients with molecular subgroup 3 depended on the tumor subtype, presence of metastases, MYC amplification and MGMT methylation. In the absence of unfavorable factors, the survival was the same as in molecular subgroup 4.

MBCL-32. HIGH-DOSE CHEMOTHERAPY WITH STEM CELL RESCUE FOR RECURRENT PREVIOUSLY IRRADIATED MEDULLOBLASTOMA

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BACKGROUND/OBJECTIVES: Relapse of medulloblastoma (MB) is highly lethal in previously irradiated patients. As one of therapeutic options for recurrence MB, high-dose chemotherapy with stem cell rescue (HDSCR) is suggested. The aim of our work was to evaluate the effectiveness of this therapy. DESIGN/METHODS: We retrospectively analyzed the data of 8 pts with previously irradiated relapse MB using HDSCR. Initially, M0-stage was verified in 4 cases. Histological diagnoses were desmoplastic (2 pts), classic (2 pts), anaplastic (2 pts) and MB NOS (2 pts). Molecular genetic analyses was performed in 6 cases: Group 3 was verified in 2 cases (1-classic, 1-anaplastic), Group 4 – in 3 cases (1-classic, 1-anaplastic, 1-desmoplastic). Time to first PD was from 15 to 86 months (median=29,4 months). Local relapse was revealed in 1 pt, metastatic – in 5 pts, mixed – in 2 pts. RESULTS: All pts were treated according HIT-REZ 2005 (3–5 cycles without/with intraventricular etoposide), with CR achieved in 3 pts and PR in 5 pts. HDCT regimens consisted of carboplatin, etoposide, thiotepa and temozolomide. 2 pts received re-irradiation – focal RT (1) and CSI (1). 7/8 patients died, 1 pt alive with PD. Time from HDCT to death was 5–15 months (median=9,6 months). CONCLUSIONS: HDSCR for recurrent previously irradiated MB is ineffective. Use of other methods should be considered in these cases.

MBCL-33. RARE PULMONARY TOXICITY IN THREE MEDULLOBLASTOMA PATIENTS UNDERGOING ANTIANGIOGENIC METRONOMIC COMBINATION THERAPY

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BACKGROUND: Metronomic and targeted anti-angiogenesis therapy (MEMMAT) has emerged as a promising treatment for recurrent/progressive medulloblastoma. This treatment includes bevacizumab, oral agents (thalidomide, celecoxib, fenofibrate, etoposide & cyclophosphamide) and intrathecal chemotherapy (etoposide & cytarabine). Common toxicities include myelosuppression, nausea, and infection. Mild respira-