planned protocol therapy but relapsed 6 months following the completion of therapy. In both cases, relapse was local and disseminated. Further recurrence was halted. Both subjects were salvaged with CSXRT followed by adjuvant chemotherapy at the remaining 4 years of follow-up. They completed planned protocol therapy at the time of study closure and received CSXRT while in remission and remain in remission approximately one year from the completion of treatment. One subject aborted protocol therapy and received second surgery and adjuvant chemotherapy. The remaining subject remains in remission approximately one year 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 CSXRT but subsequently relapsed and is now receiving salvage chemotherapy. CONCLUSIONS: Chemotherapy following ACNS031, among CSXRT, 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 medulloblastoma subtypes treated as 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 1.21, 0.91, and 3.09 years in SHH, Group 5, and Group 4 respectively. Group 4 patients had longer post-recurrence survival than others (p-value=0.005). 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-resection, 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 factors 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, but the pathologically diagnosed as desmoplastic medulloblastoma. He received chemotherapy according to the HIT protocol, however, developed severe peripheral neuropathy in the initial stage of the treatment. Reninversion of family history revealed his mother, grand-mother, 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 remission for four years and two had received chemotherapy. In the literature, there are reports of patients with CMT who developed MBL were complicated with severe peripheral neurotoxicity due to the use of vincristine. The present case, along with previous reports, suggests that vincristine-induced peripheral neurotoxicity is successfully treated by chemotherapy without 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 cm2 or large cell/anaplastic histology) over 3 years of age were enrolled in this study. Two cycles of pre-RK chemotherapy and 4 cycles of post-RK chemotherapy were used. Patients who experienced progression during the induction chemotherapy underwent HDCT. Relapse/recurrence occurred 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) related to radiation toxicity, high TRM rate was 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-tumor 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/recurrence 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 II STUDY OF SEQUENTIAL HIGH-DOSE CHEMOTHERAPY WITH STEM CELL SUPPORT FOR 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+Carboplatin. If par-
tial (PR) or complete response (CR) was achieved after induction chemotherapy, children received 2 courses of thiopeta (600mg/m²) with stem cell rescue. For patients in CR after high-dose chemotherapy, they received one course of Cyclophosphamide – Busulphan with stem cell rescue (Phase I part). The patients (not in PR after induction or in CR after thiopeta) were treated with 2 cycles of Temozolomide-Ifotecan followed by age-adjusted craniospinal irradiation and maintenance treatment. RESULTS: 28 children (3 girls; 25 boys; median age 3.0 years) were treated with thiopeta. Group 3 MB was most common (57%). The response rate to Etoposide-Carbolipin was 60.7%. Among 20 patients treated with Thiopeta, 13 children were in CR and received Cyclophosphamide – Busulphan without radiation therapy. Out of them, 9 patients (80%) 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 SMO antagonists (SMOIs), whose high expression is observed in MBCL and 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. The desmoplastic/nodular subtype of medulloblastoma has several unique features: firstly, a wide age distribution (1–40 years); secondly, a higher proportion of patients (50%) present with metastases, making it the most lethal MB sub-type; thirdly, there is a trend towards higher mortality rates in patients with advanced-stage disease (IIIb–IV). We describe a case of SMO mutation in MBCL, which is not previously described in the literature.

A 13-year-old male presented with headache, nausea, and right-sided weakness. MRI showed a left frontal mass with effacement of the lateral ventricles. The patient 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 described in MBCL, and was identified in the primary tumor tissue. This mutation was not present in matched normal tissue. The patient continues to do well 2 years after surgery, with no evidence of disease.

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

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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 were performed in 6 cases: 1) PTCH1, 2) SUFU, 3) myc, and MGMT methylation. RESULTS: All pts were treated according HIT-REZ (median=29,4 months). Local relapse was revealed in 1 pt, metastatic – in 3 pts. 7 pts died (4 pts died – in 3 pts and 3 pts in 5–15 months), 1 pt alive with PD. 3 pts died from infection. CONCLUSIONS: HDSCR for recurrent previously irradiated MB is effective. Use of other methods should be considered in these cases.

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

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BACKGROUND/OBJECTIVES: The purpose of this study was to evaluate the efficacy of high-dose chemotherapy with stem cell rescue (HDSCR) for recurrent previously irradiated MB. 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 were performed in 6 cases: 1) PTCH1, 2) SUFU, 3) myc, and MGMT methylation. RESULTS: All pts were treated according HIT-REZ (median=29,4 months). Local relapse was revealed in 1 pt, metastatic – in 3 pts. 7 pts died (4 pts died – in 3 pts and 3 pts in 5–15 months), 1 pt alive with PD. 3 pts died from infection. CONCLUSIONS: HDSCR for recurrent previously irradiated MB is effective. Use of other methods should be considered in these cases.

MBCL-33. RARE PULMONARY TOXICITY IN THREE MEDULLOBLASTOMA PATIENTS UNDERGOING ANTIANGIOGENIC 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 and cyclophosphamide) and intrathecal chemotherapy (etoposide & cytarabine). Common toxicities include myelosuppression, nausea, and infection. Mild respiratory