tory toxicities can occur. We report three cases with significant respiratory toxicity. METHODS: An IRB approved chart review was performed of three children with recurrent medulloblastoma on MEMMAT treatment and meaningful pulmonary toxicity. Literature review found no reports of similar findings. RESULTS: Patient ages ranged from 3 to 11 years old. Patients completed a mean of 6.33 months on treatment. There was no history of chronic respiratory disease prior to starting MEMMAT. Patient #1 developed chronic cough requiring multiple respiratory and anti-infective treatments; CT scan demonstrated airspace opacities concerning for chronic inflammatory change. Each new viral infection led to significant respiratory distress. He eventually died from respiratory failure with large cystic lesions noted on CT. Patient #2 developed a chronic cough not responsive to antibiotics or respiratory treatments. Images reported airspace disease, bronchiectasis, and chronic inflammatory state. Patient #3 developed chronic cough without improvement despite antibiotics and inhaled respiratory treatments; images were suggestive of small airway disease. All three patients required numerous hospitalizations and additional treatment. CONCLUSION: With MEMMAT, many side effects are expected though respiratory symptoms have rarely been reported. Our cases highlight the possible important correlation of pulmonary toxicity while being treated on MEMMAT, and its impact on patients' overall health and quality of life.

MBCL-34. EFFICACY OF METHOTREXATE (MTX) ACCORDING TO MOLECULAR SUB-TYPE IN YOUNG CHILDREN WITH MEDULLOBLASTOMA (MB): A REPORT FROM CHILDREN'S ONCOLOGY GROUP PHASE III TRIAL ACNS0334

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ACNS0334, a Phase 3 trial, compared outcomes of children <36 months treated with intensive chemotherapy +/-high-dose methotrexate. Nodular-desmoplastic M0-stage MB were excluded. Treatment included 3 induction cycles (cyclophosphamide/etoposide/vincristine/cisplatin+/-mtx) and 3 consolidation cycles (carboplatin/thiotepa with stem cell rescue). Radiation (RT) was at physician discretion. Molecular sub-typing was by DNA-methylation. Log-rank testing was used to compare survival differences. Molecular subtyping of 38 MB identified 11 Sonic Hedgehog (SHH), 25 Group 3 (GP3), 2 Group 4 (GP4). Five-year survival (OS) was 100% for 5 SHH with MTX and 4 SHH without MTX; 80% for 10 GP3 with MTX, 40% for 15 GP3 without MTX (p=0.025). Only 6/14 survivors received RT: 4 for residual following therapy (1 SHH and 3 GP3) and 2 GP3 salvaged after progression. Two GP3 deaths were associated with toxicity; all others were due to disease. Histology among SHH was nodular-desmoplastic (8) or classic (3); GP3 histology was classic (17) or anaplastic (7). Whole-exome sequencing identified 6 somatic PTCH1 and 1 germline SUFU alteration(s) among 9 SHH. Among GP3, no p53 mutations were found; copy-number analysis identified 5/25 with myc-amplification, 5/25 iso17q, 11/25 with 8 loss, 14/25 with loss of 11. Among GP3, 14/19 had no significant germline mutation. ACNS0334 achieved 100% survival for metastatic SHH. Benefit of methotrexate was observed in GP3 MB supporting incorporation of methotrexate into standard therapy for GP3. Upfront central pathology review and molecular sub-typing are critical for future clinical trial risk stratification of young children with embryonal tumors.

MBCL-35. SALVAGE RADIATION THERAPY FOR PROGRESSIVE AND/OR RELAPSED PEDIATRIC MEDULLOBLASTOMA

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Medulloblastoma (MB) has a dismal prognosis after progression or relapse, and there is no standard of care for salvage therapy. Medical records of pediatric patients with progressive/relapsed MB were reviewed for clinical characteristics. We identified 23 patients with recurrent MB with median age at diagnosis of 3.8 years, 14 males (60%). At diagnosis, 16 patients had gross total resection, 1 near total, 5 subtotal, and 1 had biopsy alone. Fifteen patients (66%) had metastatic disease. Tumor histology was classic/nodular in 10, 4 desmoplastic, 8 anaplastic and 1 myogenic. Ten patients (43%) ages < 3 years, were treated with induction chemotherapy followed by high dose chemo and stem cell rescue. Other 13 patients were treated with chemoradiation (11 craniospinal and 2 posterior fossa radiation). Progression free survival after initial treatment was 11 months (range, 3–58 months); 8 patients (34%) had local recurrence, 10 patients (43%) had distant metastasis, 4 patients (17%) had local and distant, and one patient had CSF only recurrence. Salvage therapy was surgery followed by radiation in 12 patients (52%), radiation alone in 3 patients (13%), chemoradiation in 7 patients (30%), and chemotherapy alone in 1 patient. Thirteen patients (56%) received CSI, 6 (26%) received focal and 2 received spinal radiation only. Five year progression free survival and overall survival from the time of relapse were 25% and 45%, respectively. Multidisciplinary care is essential for patients with relapsed MB. Salvage radiation that accounts for the patient's initial treatment volumes should be considered for these patients.

MBCL-36. HOW TO INCREASE SURVIVAL IN 7 TO 10% OF PATIENTS WITH AVERAGE-RISK MEDULLOBLASTOMA WITHOUT NEW THERAPIES: EARLY PROSPECTIVE NEURORADIOLOGY SCREENING EXPERIENCE FROM THE CHILDREN'S ONCOLOGY GROUP

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BACKGROUND: Previous Children's Oncology Group (COG) average-risk medulloblastoma studies retrospectively identified that 7 to 10% of patients were wrongly staged; either due to the presence of unequivocal residual disease greater than 1.5cm^2 or metastatic disease. Notably, these patients had an inferior survival. The current COG front-line average-risk study for WNT-driven medulloblastoma patients, ACNS1422, is a reduced-intensity therapeutic protocol. Given the potentially devastating consequences of dose reduction in a wrongly staged patient, ACNS1422 is utilizing optimized MRI sequences, including thin slices with no gap and post contrast T2 FLAIR sequences, combined with a rapid central neuroradiology review. RESULTS: The study opened on October 2 2017. As of 31 December 2019, a total of 34 patients have undergone central neuroradiology review. In 27/34 (79%) repeat scans were requested due to technically inadequate sequences (majority due to missing post contrast T2 FLAIR, slice thickness and gap issues). Of 19 repeat scans received, four patients (12%) were wrongly staged as average-risk; three patients were identified with residual disease >1.5cm^2 (in 2 residual disease was confirmed at second resection) and one patient had widespread spinal metastases previously obscured by motion. In addition, metastatic disease was excluded in another patient, reported as having metastatic disease. CONCLUSION: Our data is consistent with previous reports revealing that approximately 10% of patients are wrongly staged as average-risk. The early experience of ACNS1422 reveals that the optimized MRI sequences combined with a rapid central neuroradiology review are very valuable in a cooperative group setting to more accurately stage patients.

MBCL-37. CHEMOTHERAPY STRATEGIES FOR YOUNG CHILDREN NEWLY DIAGNOSED WITH CLASSIC (CLMB) OR ANAPLASTIC/LARGE CELL (A/LCMB) MEDULLOBLASTOMA UP TO THE ERA OF MOLECULAR PROFILING – A COMPARATIVE OUTCOMES ANALYSIS

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BACKGROUND/OBJECTIVE: The introduction of German regimens, supplementing "standard" chemotherapy with both intravenous high-dose (HD-MTX) and intraventricular (IVENT-MTX) methotrexate, and North American regimens incorporating marrow-ablative chemotherapy with autologous hematopoietic cell rescue (HDCx+AuHCR), report encouraging outcomes for young children with medulloblastoma. We performed a comparative outcomes analysis of treatment strategies for young children with ClMB or A/LCMB. DESIGN/METHODS: Data from 12 prospective multi-center trials published between 2005 and 2019 for children <six-years-old with ClMB or A/LCMB were reviewed; survivals were compared. RESULTS: COG-9921, UKCCSG-CNS9204, COG-P9934 and SJYCO7 employing standard chemotherapy with either no or risk-based irradiation, reported 3-5-year event-free survival (EFS) of 17+/-5%, 33+/-28% (ClMB), 14+/-7% and 13.8+/-9% (ClMB) respectively, with reported EFS of 0% for A/LCMB in UKCCSG-CNS9204 and SJYCO7. HIT-SKK'87, HIT-SKK'92 and HIT-SKK'00 incorporating HD-MTX and IVENT-MTX reported 2-10-year EFS of 30–34+/-10–11% for ClMB and 33+/-27% (HIT-SSK'00) for A/LCMB. Head Start HS-I-II combined, CCG-99703 and HS-III employing induction chemotherapy, with or without HD-MTX, followed by single or tandem HDCx+AuHCR reported 3-5-year EFS of 42+/-14%, 50+/-11% and 27+/-6% for ClMB, with EFS for A/LCMB of 38+/-13% (HS-III). Finally, 5-year overall survivals for ACNS0334, without or with induction HD-MTX, are 39% and 69% respectively for ClMB and A/LCMB combined. CONCLUSIONS: A trend towards better outcomes for young children with ClMB and A/LCMB is observed in trials including *either* HD-MTX and IVENT-MTX *or* including HD-MTX-containing induction chemotherapy and HDCx+AuHCR. Trials excluding HD-MTX, IVENT-MTX and HDCx+AuHCR have poorer outcomes.

MBCL-38. UNUSUAL EXTRANEURAL METASTASIS OF PEDIATRIC EMBRYONAL TUMORS: TWO CASE REPORTS

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We report two cases of unusual extraneural metastasis in patients with embryonal tumors without central nervous system disease progression and prolonged survival. The first patient presented at 16 years of age with atypical teratoid rhabdoid tumor of the cervical spine. The tumor was confirmed to have loss of INI1, SMARCB1 deletion of exons 1–3, and heterozygous deletion of 22q11.2. The patient received treatment initially per ACNS0333 with high dose chemotherapy and tandem autologous transplants. The patient developed a biopsy-confirmed liver metastasis six months from diagnosis and, subsequently, had disease progression including liver metastases, bony lesions, muscle involvement, and lung nodules. Two and a half years from diagnosis the patient has still not had a relapse in the CNS. The second patient presented with medulloblastoma isolated to the posterior fossa at 11 years of age and was treated on SJMB03 protocol with craniospinal irradiation and high dose chemotherapy. He had his first recurrence in the temporal lobe three years post treatment. He had multiple recurrences in the brain over the next five years treated with re-resections, adjuvant chemotherapy, and gamma knife radiotherapy. He then developed cervical lymphadenopathy, bony lesions, liver lesions, and lung nodules. Cervical lymph node biopsy confirmed medulloblastoma. Next generation sequencing from recurrent tumor showed somatic mutations in *p53*, *KDM6A*, and *PPP2R1A*. Fourteen years from treatment, he has now developed a temporal lobe lesion. These cases are notable for prolonged survival despite widely metastatic disease and genomics predicting poor prognosis as well as metastatic disease disproportionate to CNS disease.

MBCL-41. LYMPHOHEMATOPOIETIC TOXICITY IDENTIFIED IN PATIENTS WITH MEDULLOBLASTOMA RECEIVING CRANIOSPINAL IRRADIATION

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BACKGROUND: Medulloblastoma (MB) is the most common malignant brain tumor of childhood. MB easily disseminates through the spinal fluid. Surgery followed by radiotherapy, applied to the entire craniospinal axis (CSI), and adjuvant chemotherapy, represent the treatment of choice for patients aged ≥3 years. Since the bone marrow of the skull and vertebral column are the major hematopoietic organs, we investigated the myelosuppressive effect of irradiation treatment in patients with MB retrospectively. METHODS: Medical records of newly diagnosed MB patients treated at our hospital from 2007–2019 were analyzed. Children <3 years old were excluded because they did not receive CSI to avoid potential neurotoxicity. RESULTS: Medical records of 18 patients (11 males and 7 females, aged 6–26, median 11 years) were reviewed. Eight patients were stratified as high-risk disease and 10 patients with standard risk. All patients received CSI (dosage range 23.4–39.6 Gy based on disease risk) and posterior fossa boost. All patients developed lymphocytopenia (<0.5×109/L) during irradiation, and for 11 of 18 patients, lymphocytopenia (<0.2×109/L) was severe. Although 13 patients recovered from the lymphocytopenia before the initiation of chemotherapy, five patients underwent chemotherapy without recovery. Conversely, only six patients developed neutropenia (<1.0×109/L), and five of the six patients were <10 years old. CONCLUSION: Although infectious episode associated with lymphocytopenia was not observed in this study, CSI treatment in children and adolescents may induce immunodeficient condition particularly in the lymphocytic system. Pediatric oncologists should pay attention to the impaired immunity of patients with MB who receive CSI.

MBCL-43. RECURRENT MEDULLOBLASTOMA – LONG-TERM SURVIVAL WITH A "MEMMAT" BASED ANTIANGIOGENIC APPROACH

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INTRODUCTION: Patients with recurrent medulloblastoma have a poor prognosis with only around 8% of patients surviving at 5 years irrespective of salvage therapy used. We report on 29 patients from four institutions treated with a "MEMMAT" based antiangiogenic combination therapy. PATIENTS AND METHODS: From 11/2006 to 06/2016, 29 patients were diagnosed with a recurrent medulloblastoma (19 first, 10 multiple recurrences). Median age at start of antiangiogenic therapy was 10 years (range 1–27). Subgroup of medulloblastoma was available in 18 patients and was group 3 or 4 in all except two (one WNT, one SHH-infant). For their current relapse patients received an antiangiogenic combination therapy consisting of bevacizumab, thalidomide, celecoxib, fenofibrate, and etoposide, alternating with cyclophosphamide and augmented with intraventricular therapy (etoposide and liposomal cytarabine). RESULTS: As of 01/2020, 8/29 patients are alive at a median of 44 months after recurrence. 6/8 surviving patients are currently in CCR between 66 and 134 months after recurrence that prompted MEMMAT therapy. Two patients are again in remission after intercurrent relapses 105 and 102 months after first starting MEMMAT therapy. Five patients died of another cause (accident, leukemia, septicemia). OS (median 44 months) was 44±10% at 5 years and 39±10% at 10 years, PFS was 33±10% at 5 years and 28 ±9% at 10 years. Therapy was well tolerated and toxicities were manageable. CONCLUSION: Our results suggest that antiangiogenic metronomic chemotherapy has clinical activity in recurrent medulloblastoma. Further investigation with an international phase II study is ongoing (MEMMAT; ClinicalTrials.gov Identifier: NCT01356290).

MBCL-46. TREATMENT OF RECURRENT WINGLESS-ACTIVATED MEDULLOBLASTOMA (WNT-MB) INCORPORATING MARROW-ABLATIVE THIOTEPA AND CARBOPLATIN CHEMOTHERAPY (HDCX) AND AUTOLOGOUS HEMATOPOIETIC PROGENITOR CELL RESCUE (AUHPCR): A DUAL REPORT

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BACKGROUND: Wnt-MB infers an excellent prognosis, and metastatic disease is rare. However, specific treatment strategies and patterns of failure for patients with recurrent Wnt-MB are unknown. We report two cases of