

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 sub-typing 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<sup>2</sup> 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<sup>2</sup> (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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