reduced the dose of craniospinal irradiation by 25% to 18 gray with the goal of maintaining the therapeutic efficacy as described in CCG 9892 with maintenance chemotherapy. RESULTS: 28 patients aged 3–30 years were enrolled across three institutions between April 2001 and December 2010. Median age at enrollment was 9 years with a median follow-up time of 11.7 years. The 3-year relapse-free (RFS) and overall survival (OS) were 78.6% (95% CI 58.4% to 89.8%) and 92.9% (95% CI 74.4% to 98.2%), respectively. The 5-year RFS and OS were 71.4% (95% CI 50.1% to 84.6%) and 85.7% (95% CI 66.3% to 94.4%), respectively. Toxicities were similar to those seen in other studies; there were no grade 5 toxicities. CONCLUSIONS: Given the known neurocognitive adverse effects associated with cranial radiation therapy, studies to evaluate the feasibility of dose reduction are needed. In this study, we demonstrate that select patients with average-risk medulloblastoma may benefit from reduced craniospinal radiation dose of 18 gray without impacting relapse-free or overall survival.

MBCL-15. IMPACT OF MOLECULAR SUBGROUPS ON OUTCOMES FOLLOWING RADIATION TREATMENT RANDOMIZATIONS FOR AVERAGE RISK MEDULLOBLASTOMA: A PLANNED ANALYSIS OF CHILDREN'S ONCOLOGY GROUP (COG) ACNS0331

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The COG conducted a randomized trial for average-risk medulloblastoma (AR-MB). Patients age 3–21 years were randomized to a radiation boost to the whole posterior fossa (PFRT) or an involved field volume (IFRT) after receiving CSI. Patients age 3–7 years were also randomized to standard dose CSI (23.4Gy, SDCSI) or low dose CSI (18Gy, LDCSI). 464 evaluable patients were available to compare PFRT vs. IFRT and 226 for SDCSI vs. LDCSI. 380 cases had sufficient tissue for DNA methylation-based molecular classification: 362 confirmed medulloblastoma; 6 non-medulloblastoma; 12 inconclusive. Molecular subgrouping confirmed the following representation amongst the evaluable cohort: 156 Group 4 (43.1%), 76 Group 3 (21.0%), 66 SHH (18.2%), 64 WNT (17.7%). Five-year event-free survival (EFS) estimates were 82.5±2.7% and 80.5±2.7% for IFRT and PFRT, respectively (p=0.44). Five-year EFS estimates were 71.4±4.4% and 82.9±3.7% for LDCSI and SDCSI, respectively (p=0.028). EFS distributions differed significantly by subgroup (p<0.0001). Group 3 had the worst outcome, while WNT had the best outcome. There was a significant difference in EFS by RT group among SHH patients; SHH patients receiving IFRT arm had better EFS compared to PFRT (p=0.018). There was a significant difference in EFS distributions by CSI group in Group 4 patients; young Group 4 patients treated with SDCSI had better EFS compared to LDCSI (p=0.047). As previously reported, IFRT is noninferior to PFRT in all patients with AR-MB but LDCSI is worse than SDCSI in younger children. Significant differences in outcome by study randomization and molecular subgroup are observed.

MBCL-16. EFFICACY OF CARBOPLATIN GIVEN CONCOMITANTLY WITH RADIATION AND ISOTRETINOIN AS A PRO-APOPTOTIC AGENT IN MAINTENANCE THERAPY IN HIGH-RISK MEDULLOBLASTOMA: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

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BACKGROUND: Metastasis, residual disease, and diffuse anaplasia are high-risk features in medulloblastoma. METHODS: This was a randomized phase 3 study. Patients age 3–21 years with high-risk medulloblastoma received (+/-) daily carboplatin with 36Gy craniospinal radiation and weekly Vincristine followed by six cycles of maintenance chemotherapy with Cisplatin, Cyclophosphamide and Vincristine (+/) 12 cycles of isotretinoin during and following maintenance. The primary endpoint was event-free survival, with exact log-rank test to compare arms. Retrospective molecular analysis included DNA methylation and exome sequencing. RESULTS: Of 294 medulloblastoma patients enrolled, 261 were eligible by central review of radiology and pathology, median age 8.6 years (range 3.3–21.2), 70% male, 189 (72%) with metastatic disease, 58 (22%) with diffuse anaplasia, 14 (5%) with >1.5cm2 residual disease. The 5-year EFS and OS for all subjects was 63%+4 and 73%+3, respectively. Isotretinoin randomization was closed due to futility. 5-year EFS was 66 + 5 with carboplatin versus 59 + 5 without (p=0.11), with effect exclusively observed in Group 3 subtype: 73%+8 with carboplatin versus 54%+9 without (p<0.05). Overall survival differed by molecular subgroup (p=0.006): WNT 100%, SHH 54%+11, Group 3 74%+6, Group 4 77%+5 at 5 years. *MYC* amplification or isochromosome 17 were unfavorable in Group 3 (p=0.029). Chromosome 11 loss or chromosome 17 gain were favorable in group 4 (p<0.001). No survival difference was observed with *TP53* mutation in SHH subtype in this high-risk cohort. CONCLUSIONS: Therapy intensification with carboplatin improved survival for high-risk group 3 medulloblastoma. These findings further support an integrated clinical and molecular risk stratification for medulloblastoma.

MBCL-17. METASTATIC MEDULLOBLASTOMA CAN BE CURED WITHOUT EXCISION OF THE PRIMARY TUMOR: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Metastatic medulloblastoma is a challenging disease The current clinical approach advocates removal of the primary tumor in the posterior fossa despite evidence of metastatic disease and administer oncologic treatment within several weeks: Infants of 3–4 years are treated by tandem high dose chemotherapy with stem cell support (ACNS0334 protocol), while older children are given radiotherapy and tandem high dose chemotherapy with stem cell support (SJMB03 protocol). We postulate that a resection of the primary tumor is not obligatory, and a biopsy may suffice in order to enable prompt oncological treatment without affecting the long-term survival. PATIENTS AND METHODS: Between 2010-2019 7 patients with metastatic medulloblastoma (median age 4.5, age 1–10) were treated with biopsy only, five spinal and two from the primary tumor. Six children had a concurrent VP shunt. Four presented with cord compression, and two with neurological deterioration. Four needed emergency radiotherapy. Two infants received protocol ACNS0334, five patients received protocol SJMB03. RESULTS: Six patients (85%) survived; .3 patients are long term survivors (> 5 years), 2 patients are in remission for 2–3 years, one patient is on active therapy. Only 1 patient died after a late (4 years) metastatic relapse not in the posterior fossa. CONCLUSIONS: Metastatic medulloblastoma can be cured without excision of the primary tumor and without mutilating surgery. Long term prognosis is probably more attributable to disease subtype and prompt oncologic treatment. This approach merits further studies and may have implications on treatment of non-metastatic tumors.

MBCL-18. ANALYSIS OF DNA METHYLATION PROFILES OF PEDIATRIC MEDULLOBLASTOMAS: EXPERIENCE AT THE BAMBINO GESÙ CHILDREN'S HOSPITAL

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BACKGROUND: Medulloblastoma is the most frequent malignant brain tumor in children, still resulting fatal in about one third of affected patients. An accurate diagnosis is essential for correct therapeutic stratification. The DNA methylation profile (DMP) is a combination of changes in DNA methylation and genetic features that reflect the cell of tumor origin. DMP contributed to classify Medulloblastoma into four subgroups: WNT, SHH, Group 3/4 (the latter recently further subdivided into 8 subclasses). Each Methylation is associated with different genetic, demographic and clinical characteristics. We report our experience on Medulloblastoma molecular classification based on DMP. MATERIALS AND METHODS: 54 Medulloblastoma patients (28 males, 26 females) were selected. The DMP analysis was carried out via IlluminaEPICarrays. The results were obtained using the brain tumor classifier (Capper, 2018). RESULTS: In all cases the DMP allowed to classify the neoplasm, with an optimal score, in a defined methylation class. 10 WNTs, 15 SHHs, 10 Group 3, 19 Group 4 were found. Groups 3/4 were further re-