ical outcomes, the ability to subgroup SA-FPPE samples holds significant prognostic and therapeutic value. We performed the first assessment of MB-DNA methylation patterns in Saudi Arabian SA cohort using archival biopsy materials (FPPE n=49). Of the 41 materials available for methylation assessments, 39 could be classified into the major DNA methylation subgroups (SHH, WNT, G3 and G4). Methylation analysis was able to reclassify tumors that could not be sub-grouped through NGS testing, highlighting its improved accuracy for MB molecular classifications. Independent assessments demonstrate clinical relationships of the subgroups, exemplified by the high survival rates observed for WNT tumors. Surprisingly, the G4 subgroup did not conform to previously identified phenotypes, with a high prevalence in females, high metastatic rates and a large number of tumor-associated deaths. DNA methylation profiling enables the robust sub-classification of four disease sub-groups in SA-MB patients. Moreover, the incorporation of DNA methylation biomarkers can significantly improve current disease-risk stratification schemes, particularly concerning the identification of aggressive G4 tumors. These findings have important implications for future clinical disease management in MB cases across the Arab world.

MBCL-02. ROLE OF PREOPERATIVE CHEMOTHERAPY IN METASTATIC MEDULLOBLASTOMA: A COMPARATIVE STUDY IN 92 CHILDREN

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BACKGROUND: Previous pilot studies have shown the feasibility of preoperative chemotherapy in patients with medulloblastoma, but benefits and risks compared with initial surgery have not been assessed. METHODS: Two therapeutic strategies were retrospectively compared in 92 patients with metastatic medulloblastoma treated at Gustave Roussy, France, between 2002 and 2015: surgery at diagnosis (n=54; group A) and surgery delayed after carboplatin and etoposide-based preoperative therapy (n=38; group B). Treatment strategies were similar in both groups. RESULTS: The rate of complete tumor excision was significantly higher in group B than in group A (93.3% versus 57.4%, p=0.0013). Post-operative complications, chemotherapy-associated side effects and local progressions were not increased in group B. Preoperative chemotherapy led to a decrease in the primary tumor size in all patients, 4/38 patients experiencing meanwhile a distant progression. The histological review of 19 matched tumor pairs (before and after chemotherapy) showed that proliferation was reduced and histological diagnosis feasible and accurate even after preoperative chemotherapy. The 5-year progression-free and overall survival rates were comparable between groups. Comparison of the longitudinal neuropsychological data showed that intellectual outcome tended to be better in group B (the mean predicted intellectual quotient value was 6 points higher throughout the follow-up). CONCLUSION: Preoperative chemotherapy is a safe and efficient strategy for metastatic medulloblastoma. It increases the rate of complete tumor excision and may improve the neuropsychological outcome without jeopardizing survival.

MBCL-03. RESULTS OF HIGH-DOSE THIOTEPA, CARBOPLATIN AND ETOPOSIDE WITH AUTOLOGOUS HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR PATIENTS WITH RECURRENT MEDULLOBLASTOMA

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AIM: Medulloblastoma is a highly lethal disease when it recurs. Very few patients survive with second line conventional treatment after relapse. This study evaluated the use of high-dose thiotepa, carboplatin and etoposide with autologous hematopoietic stem-cell transplantation (HSCT) in patients with recurrent medulloblastoma. METHODS: From 2010 to 2019, 60 patients at the age 4–32 years (median, 12) with recurrent medulloblastoma were received high-dose chemotherapy (HDCT) with auto-HSCT after induction second line chemotherapy. HDCT included thiotepa 150 mg/m^2 #4; carboplatin 500 mg/m^2 #4; etoposide 250 mg/m^2 #4 and +/- etoposide 1 mg intraventricular on days #5 if patient had Ommaya reservoir; followed by HSCT. At the moment of HDCT 24 patients were in complete response (CR), 31 patients were in partial response (PR) and 5 patients had stable disease (SD) after second line conventional chemotherapy. RESULTS: The median follow-up is 65 months (range, 24–227). The median time to engraftment after auto-HSCT was day +11 (range, 8–39). Five-year overall survival (OS) was 58% and disease free survival (DFS) was 46%. DFS was significantly better among patients in CR or PR 50% in compared to children in SD 20% at the moment of HDCT (p=0,002). Transplant related mortality were 12%, there were 7 patients died because of severe complications within 14 days after transplantation. CONCLUSIONS: HDCT with auto-HSCT in pediatric patients with recurrent medulloblastoma may be a feasible option for cases who had CR or PR after induction chemotherapy. It is ineffective as a salvage therapy in refractory patients.

MBCL-04. 5 – AZACYTIDINE IN TREATMENT OF CHILDREN WITH DE NOVO AND RELAPSED METASTATIC MEDULLOBLASTOMA: RESULTS OF INTERCENTER PILOT STUDY

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The aim of this study was to estimate treatment toxicity and event-free survival (EFS) according to therapeutic program, *MYC/MYC-N* gene amplification and MGMT/DNMT (1, 3a, 3b) proteins expression in tumor cells. From 2016 to 2018 twenty four patients were included in trial. Children underwent adjuvant therapy: craniospinal radiation (CSI) or local radiation therapy (RT) to the relapsed site up to 23.4Gy with 5-azacytidine, 2 cycles methotrexate/5-azacytidine/cisplatin/etoposide, 3 cycles 5-azacytidine/temozolomide - for relapsed group (arm A, n = 5); for patients with de novo medulloblastoma: arm B, n = 11 – vincristine/cyclophosphamide/cisplatin/etoposide (OPEC) - based induction, CSI 36Gy + local RT to the tumor bed up to 54Gy with 5-azacytidine, 1 cycle OPEC and 2 cycles thiophosphamide/carboplatin with auto stem cell transplantation (auto-SCT); arm C, n = 8 – cyclophosphamide/cisplatin - based induction, CSI 23.4 Gy followed by 2 cycles 5-azacytidine/thiophosphamide/carboplatin with auto-SCT, local RT with 5-azacytidine. The combination of 5-azacytidine with local RT or temozolomide was safety and tolerability. Arm C was discontinued due to severe gastrointestinal grade 3/4 toxicity, hemorrhagic syndrome after combination of 5-azacytidine with thiophosphamide/carboplatin. EFS was 0% in arm A, 53.0 ± 15.5%, 50.0 ± 17.7% in arms B and C, a median follow-up 8.8 ± 1.1 months (arm A), 18.8 ± 2.5 months (arm B), 25.0 ± 4.4 months (arm C). Addition of 5-azacytidine to RT or chemotherapy did not improve EFS of patients with *MYC/MYC-N* gene amplification positive tumor. There was not determined any prognostic significance of MGMT/DNMT (1, 3a, 3b) proteins expression in this cohort.

MBCL-05. TREATMENT OF CHILDREN WITH MEDULLOBLASTOMA WITHOUT METASTATIC INVOLVEMENT IN THE AGE GROUP OLDER THAN 3 YEARS: RESULTS OF INTERCENTER TRIAL

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The aim of this study was to identify a group of patients aged 3 to 7 years for whom there is the possibility for reducing of craniospinal radiation dose (CSI). From 2008 to 2018 fifty one pediatric patients with primary diagnosed medulloblastoma in the age group 3 - 18 years were included in trial, 38 in standard risk group, 13 in high risk group. Treatment program consisted of surgical removal of the primary tumor site with subsequent radiation therapy (with CSI of 23,4 Gy or 36 Gy, depending on the risk group) and high-dose chemotherapy (with high-dose cyclophosphamide or thiophosphamide). As a result of this study, sufficiently high rates of overall survival and progression/relapse - free survival (PFS) were achieved in standard and high-risk groups patients, which amounted to 76,0 ± 8,8% and 83,3 ± 10,8% with median follow-up 62,9 ± 6,2 months and 52,2 ± 7,8 months, respectively. There was revealed patients group in the age 3 - 7 years with 100% PFS and median follow-up 66,9 ± 8,9 months. Morphological and molecular biological factors of an unfavorable outcome of the