Abstracts

**MEDULLOBLASTOMA TREATED BY UPFRONT RADIOTHERAPY – TIME TO RADIOTHERAPY IMPACTS SURVIVAL**

**METHODS**: Patients 15–39 years old with MB who was sent for upfront craniospinal irradiation (CSI) followed by maintenance chemotherapy were included. Kaplan-Meier statistics were used to estimate the local recurrence-free survival (LRFS) and overall survival (OS). The rest of the patients were received RT alone, all were M0. The median craniospinal RT-doses would be reduced compared to sandwich strategies.

**RESULTS**: Patients with desmoplastic medulloblastoma (DMB) or medulloblastoma with extensive nodularity (MBEN) (n=42) had 93% 3-year PFS, 100% 5-year OS and 95% 3-year CSS-free survival. Patients with CMR/LCA (n=1) had 37% 5-year PFS, 37% 5-year OS and 35% 3-year CSS-free survival. Local radiotherapy did not improve survival in CMR/LCA patients. All DMB/MBEN assessed by DNA methylation profiling belonged to the SHH-Inf subgroup. Group 3 patients (5y-PFS 36% [n=14]) relapsed more frequently than Group 2 (5y-PFS 93% [n=20]) or the SHH-Inf (n=6), p<0.001. SHH-INF split into iSHH-I and iSHH-II subtypes in HIT-2000-BIS4 and the validation cohort, without diagnostic impact (5y-PFS: iSHH-I 73% vs iSHH-II 83%, p=0.25, n=99). Mean IQ was 90 (radiotherapy-free survivors) vs. 74 (patients that received CSI) [p=0.012]. CONCLUSION: Systemic chemotherapy and intraventricular methotrexate led to favorable survival in both iSHH-subtypes of SHH-activated DMB/MBEN patients with acceptable neurotoxicity. Survival in non-WNT/non-SHH CMR/LCA patients was not improved by local radiotherapy; Survival was more favorable in patients with Group 4 than in patients with Group 3 medulloblastoma.

**MBC-08. INTEGRATIVE MOLECULAR ANALYSIS OF PATIENT-MATCHED DIAGNOSTIC AND RELAPSED MEDULLOBLASTOMAS**

**INTRODUCTION**: The next generation of clinical trials for relapsed medulloblastoma demands a thorough understanding of the clinical behavior of relapsed tumors as well as the molecular relationship to their diagnostic counterparts. METHODS: A multi-institutional molecular cohort of patient-matched (n=126 patients) diagnostic MBs and relapses/subsequent malignancies was profiled by DNA methylation array. Entity, subgroup classification, and copy-number wide-copy-number change analysis of parallel whole-genome exome sequencing was performed to detect somatic driver mutations. RESULTS: Comprised of WNT (2%), SHH (41%), Group 3 (18%), Group 4 (39%), primary tumors retained subgroup affiliation at relapse with the notable exception of 10% of cases. The majority (8/13) of discrepant classifications were determined to be secondary glioblastomas. Additionally, rare (n=5) subgroup-switching events of Group 4 primary tumors to Group 3 relapses were identified coincident with MYC/MYCN pathway alterations. Among truly discordant analyses, multiple gene mutations were shared between primary MBs and their respective relapses with Group 3 (35% of alterations shared) and Group 4 tumors (63% alterations shared) sharing a larger proportion of cytogenetic alterations compared to SHH tumors (42% alterations shared) and Group 1 tumors (i.e., p-value < 0.001). Study and gene-specific patterns of conservation and divergence amongst putative driver genes were also observed. CONCLUSION: Integrated molecular analysis of relapsed MB discloses potential mechanisms underlying treatment failure and disease recurrence while motivating rational implementation of relapse-specific therapies. The degree of genetic divergence between primary and relapsed MBs varied by subgroup but suggested considerably higher conservation than prior estimates.

**MBC-09. ISOLATED M1 METASTASES IN PEDIATRIC MEDULLOBLASTOMA: IS POSTOPERATIVE RADIOTHERAPY FOLLOWED BY MAINTENANCE CHEMOTHERAPY SUPERIOR TO POSTOPERATIVE SANDWICH CHEMOTHERAPY AND RADIOTHERAPY?**

**OBJECTIVE**: The aim of this study is to evaluate the local recurrence-free survival (LRFS) and overall survival (OS) of MB in AYA patients at our institute. METHOD: Patients 15–39 years old with MB who was sent for post-operative radiation therapy (RT) in 2007–2017 at our institute were included. Kaplan-Meier statistics were used to estimate the LRFS and OS. RESULTS: Seven patients were included. The median age at RT was 18.3 years (16.7–28.6 years). Male was more common than female, 5 males vs 2 females. NTR or GTR was achieved in 71.4% (5 in 7 patients). Only one patient had metastatic disease (M1) and received combined chemotherapy-RT. The rest 6 patients were received RT alone, all were M0. The median craniospinal irradiation (CSI) dose and total RT dose were 36Gy (23.4–46.6Gy) and 54Gy (54–65Gy), respectively. Five patients had available follow-up MRI brain. The local recurrence (LR) was found in one patient at 4.3 years after finished RT. Her initial treatment was subtotal resection (STR) followed by RT alone; CSI 36 Gy and posterior fossa boost to 35.6Gy. The 2-years and 5-years LRFS were 100% and 66.7%, respectively. Both 2 years and 5 years OS were 54.4% (79%). Patients with upfront CSI had more favourable outcomes (5y-PFS 66.1% vs. 55.8% [p=0.119]; 5y-OS 90.6 vs 64.5% [p=0.035]). The trend towards improved survival in patients with postoperative CSI was retained when only non-contraindicated patients were considered (p=0.176). Conclusions were derived only from patients with postoperative CT. CONCLUSION: Isolated M1-MB is rare. Patients without contraindication for CSI appear to benefit from treatment by upfront CSI followed by maintenance CT, while cumulative CT-doses were reduced compared to sandwich strategies.
Integrating neuroimaging, clinical, and molecular data to improve patient care

**Abstracts**

**NEURO-ONCOLOGY • December 2020**

iii390

ASIAN MEDULLOBLASTOMA PATIENT SURVIVAL INFILTRATING IMMUNOLOGICAL CELLS ASSOCIATED WITH MBCL-12. MOLECULAR SIGNATURES AND TUMOR risk-stratified therapy, outcome for non-metastatic medulloblastoma treated with surgery and post-resection radiotherapy plus chemotherapy as the major type of treatment currently. METHODS: A cohort of 52 medulloblastoma patients were treated in Taipei Medical University Hospital and the Veterans General Hospital, Taipei, Taiwan. The average age at presentation is 7.21 ± 4.15. Genome-wide RNA profiling were performed on fresh-frozen surgical samples. Tumor infiltrating immune cell percentages were inferred by the cibersort immune deconvolution algorithm. RESULTS: A total of 97 key gene families, including DTL1, AM2C, SLC2A17, TRPM3, PRPS2P5 and KCNCl3, were found to be significantly associated with overall survival (A P < 0.001). A risk score was constructed, which is indicative of overall survival (Hazard Ratio [HR] = 2.720, 95% confidence interval [CI] = 1.798 – 4.112, P = 0.001) and recurrence-free survival (HR = 1.645, CI = 1.337 – 2.026, P < 0.001). After adjustment of clinical factors, the score remained significantly associated with overall survival (HR = 2.781, CI = 1.762 – 4.390, P < 0.001) and recurrence-free survival (HR = 1.604, CI = 1.292 – 1.992, P < 0.001). The percentage of Natural Killer and T follicular helper (Tfh) cells were higher in patients with better overall survival (P = 0.046 and 0.001, respectively). Furthermore, the Tfh percentage is also positively associated with mutation burdens in the expressed exonic regions (P < 0.001). CONCLUSION: Higher mutation burdens are indicative of better post-surgery prognosis.

**MBCL-13. CORRELATION OF HISTOPATHOLOGY, CHROMOSOMAL MICROARRAY, AND NANOSTRING BASED 22-GENE ASSAY FOR MEDULLOBLASTOMA SUBGROUP ASSIGNMENT ON “HEAD START” 4 CLINICAL TRIAL**

Candida Blu1, Parth Patel1, Maxwell Mochizuki1, Isabel Almiraz-Suarez2, Eugene Hwang3, Christopher Persson2, Daniel Bouse2, and Jonathan Finlay3.

1University of Alabama at Birmingham, Birmingham, AL, USA, 2Nationwide Children's Hospital, Columbus, OH, USA, 3Children's National Medical Center, Washington DC, USA.

“Head Start” 4 (HS 4) is a prospective randomized clinical trial that tailors treatment to patients based on medulloblastoma molecular subgroups at diagnosis. The goals of this study are to determine the utility of the 22-gene assay and chromosomal microarray analysis (CMA) in classifying medulloblastoma samples into SHH, WNT, or non-WNT/non-SHH subgroups at the time of diagnosis. NanoString based 22-gene assay is retrospectively performed to test concordance. We compared pathology, CMA, and NanoString data on 26 infans and young children with medulloblastoma enrolled on HS 4. Pathology/CMA was able to assign all samples to SHH, WNT or non-WNT/non-SHH subgroups, which were then compared to NanoString based 22-gene assay. In all cases: one case was classified as Group 1, and the second as SHH by both CMA and NanoString. CMA was indeterminate in six cases of which, pathology/CMA was able to assign all six samples to SHH, WNT or non-WNT/non-SHH subgroups. NanoString was indeterminate in two cases: one case was classified as SHH and the other as WNT. In all cases, the score remained significantly associated with overall survival (Hazard Ratio [HR] = 2.720, 95% CI = 1.762 – 4.390, P < 0.001) and recurrence-free survival (HR = 1.604, CI = 1.292 – 1.992, P < 0.001). The percentage of Natural Killer and T follicular helper (Tfh) cells were higher in patients with better overall survival (P = 0.046 and 0.001, respectively). Furthermore, the Tfh percentage is also positively associated with mutation burdens in the expressed exonic regions (P < 0.001). CONCLUSION: Higher mutation burdens are indicative of better post-surgery prognosis.

**MBCL-14. A STUDY OF LOW-DOSE CRANIOSPINAL RADIATION THERAPY IN PATIENTS WITH NEWLY DIAGNOSED AVERAGE-RISK MEDULLOBLASTOMA**

Aaron Mochizuki1, Anna Janss1, Sonia Partap2, Paul Fisher1, Yimei Li1, Michael Anderson1, and Jane McCormick1.

1Department of Pediatric Neurosurgery, University of California, Stanford University, Palo Alto, CA, USA, 2Children’s Healthcare of Atlanta, Atlanta, GA, USA, 3Children’s Hospital of Philadelphia, Philadelphia, PA, USA.

INTRODUCTION: Medulloblastoma is one of the most common malignant brain tumors in children. To date, the treatment of average-risk (non-metastatic, completely resected) medulloblastoma includes craniospinal radiation therapy and adjuvant chemotherapy. Modern treatment modalities and now risk stratification of subgroups have extended the survival of these patients, exposing the long-term morbidities associated with radiation therapy. METHODS: We performed a single-arm, multi-institution study, seeking to reduce the late effects of treatment in patients with average-risk medulloblastoma prior to advances in molecular subgrouping. To do so, we...