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Recurrent pediatric high-grade glioma (pHGG) is the leading cause of cancer-related mortality in children. Immunotherapy is a successful treatment approach for a growing number of cancers and is being investigated as a treatment strategy for pHGG. Immunotherapy has shown the most benefit in tumors with increased infiltrating T cells at baseline. Our recently published results revealed that neoadjuvant checkpoint inhibition in recurrent adult glioblastoma was associated with upregulation of a T cell and interferon-γ-related gene expression signature (Tcell-IFNγGES) and was correlated with a significantly extended overall survival (OS). In this study, we examined the immune landscape in recurrent pHGG and the association of Tcell-IFNγGES in the tumor with survival. We analyzed tumor RNAseq data collected at time of recurrence from a historical cohort of 42 pHGG patients from the Children's Brain Tumor Tissue Consortium. We found a significant transcriptional enrichment of Tcell-IFNγGES in 54% of the tumors. The survival of patients with high Tcell-IFNγGES was observed to be significantly higher than patients with low Tcell-IFNγGES, (log-rank p=0.05). The 3-year OS for patients with low *versus* high Tcell-IFNγGE was 28.5% (95%, CI:13.7%-59.5%) compared to 50.2% (95%, CI:33.1%-76.1%). When patients were stratified by age, gender and race, low Tcell-IFNγGES was found to be a poor OS prognostic factor (hazard ratio=2.4 (1.14–5.14), p=0.02). This indicates a strong relationship of decreased Tcell-IFNγGES and increased risk of death. Future investigations are necessary to validate these findings, and to explore the value of Tcell-IFNγGES as a predictive biomarker for response to immunotherapy in pHGG.

IMMU-31. PNOC007: H3.3K27M SPECIFIC PEPTIDE VACCINE COMBINED WITH POLY-ICLC FOR THE TREATMENT OF NEWLY DIAGNOSED HLA-A2+ H3.3K27M DIFFUSE MIDLINE GLIOMAS (DMG)

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OBJECTIVE: To assess safety and efficacy within a multi-center trial the H3.3K27M specific peptide vaccine with poly-ICLC in HLA-A02.01$^+$ patients diagnosed with H3.3K27M$^+$ DMGs. METHODS: After focal radiation therapy, participants 3–21 years of age were enrolled into two strata. Stratum A: newly diagnosed diffuse intrinsic pontine glioma (DIPG); Stratum B: other DMGs. H3.3K27M vaccine was administered with poly-ICLC IM every 3 weeks for 8 doses followed by every 6 weeks for a total of 96 weeks. Immuno-monitoring of peripheral blood mononuclear cell (PBMC) and imaging occurred every 3 months. Modified iRANO criteria were applied. PBMC samples were evaluated by mass cytometry. RESULTS: From November 2016 until March 2019, 19 eligible patients (median age 11, range 5–17 yrs; 53 % female) were enrolled in Stratum A and 10 eligible patients (median age 13, range 7–18 yrs; 60 % female) in Stratum B. Treatment was well tolerated (7 grade 3; 0 grade 4 related toxicities). Median number of vaccines per participant was 6 (range 1–11). Overall survival at 12 months was 40% (95% CI 22–73%) for Stratum A and 39% (95% CI 16–93%) for Stratum B. Among the 19 subjects with longitudinal immune cell assessments, 7 exhibited an expansion of K27M-reactive CD8+ effector memory T-cells correlating with prolonged survival (p=0.028). CONCLUSION: H3.3K27M specific vaccine in combination with poly-ICLC is well tolerated. CyTOF-based immune monitoring of PBMCs facilitates sensitive high-throughput analysis. Further investigation is warranted to determine if this may be predictive of clinical outcomes.

LOW GRADE GLIOMA

LGG-01. CLINICAL MANAGEMENT AND GENOMIC PROFILING OF PEDIATRIC LOW-GRADE GLIOMAS IN SAUDI ARABIA

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Pediatric Low Grade Gliomas (PLGGs) display heterogeneity regarding morphology, genomic drivers and clinical outcomes. The treatment modality dictates the outcome and optimizing patient management can be challenging. In this study, we profiled a targeted panel of cancer-related genes in 37 Saudi Arabian patients with pLGGs to identify genetic abnormalities that can inform prognostic and therapeutic decision-making. We detected genetic alterations (GAs) in 97% (36/37) of cases, averaging 2.51 single nucleotide variations (SNVs) and 0.91 gene fusions per patient. The *KIAA1549-BRAF* fusion was the most common alteration (21/37 patients) followed by *AFAP1-NTRK2* (2/37) and *TBLXR-PI3KCA* (2/37) fusions that were observed at much lower frequencies. The most frequently mutated) genes were NOTCH*1 3* (7/37), *ATM* (4/37), *RAD51C* (3/37), *RNF43* (3/37), *SLX4* (3/37) and *NF1* (3/37). BRAF V600E mutations were observed in only 2/37 patients, while H3F3A (K27M) histone mutations were not detected. Interestingly, we identified a GOPC-*ROS1* fusion in an 8-year-old patient whose tumor lacked *BRAF* alterations and histologically classified as low grade glioma. The patient underwent gross total resection (GTR) currently he is disease free. To our knowledge this is the first report of *GOPC-ROS1* fusion in PLGG which may represent a genomically-distinct subgroup of pLGGs that could be targeted with oral target therapy crizotinib. Taken together, we reveal the genetic characteristics of pLGG Saudi patients can enhance diagnostics and therapeutic decisions. In addition, we identified a GOPC-*ROS1* fusion that may be a biomarker for pLGG. Our study proves the possibility of using genetic profiling to guide optimal treatment strategies for pLGG in Saudi population

LGG-02. A BRAIN TUMOR DIAGNOSED AFTER TRANSITION TO THE DEPARTMENT OF ADULT NEUROSURGERY FROM THE DEPARTMENT OF PEDIATRICS

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The patient was a 17-year-old boy with a history of 4 non-febrile convulsions at 15 and 16 years of age. He visited the Department of Pediatrics at a pediatric hospital. An electroencephalogram showed right frontal spike discharge. MRI was performed and judged to show no abnormality. The pediatric doctor diagnosed him with epilepsy. At 17 years old, he was referred to our Department of Adult Neurosurgery for transition. Physical and neurological examinations showed no abnormalities. Brain MRI showed right frontal cortical small tumor, with T1 low, T2 high, diffusion-weighted imaging low, and partial contrast enhancement. We diagnosed him with a brain tumor and symptomatic epilepsy. We surgically removed a right frontal cortical tumor. A pathological examination finalized the diagnosis of dysembryoplastic neuroepithelial tumor. MRI confirmed the total removal of the tumor. Anticonvulsant was started before surgery. No epileptic seizure was observed, so the anticonvulsant medication was gradually tapered and stopped at two years after the surgery. No epilepsy nor recurrence has been observed thus far. The problem with the initial management of this case at the Department of Pediatrics in the pediatric hospital was that the brain tumor was missed despite an MRI examination. Had the transition not happened, this brain tumor might not have been diagnosed. A brain tumor is a rare disease, and epilepsy is a common disease. However, in cases of non-febrile convulsion, a brain tumor should be considered. Collaboration within a single department, hospital and local area should be established.

LGG-03. INCIDENCE AND OUTCOME OF PEDIATRIC IDH-MUTANT GLIOMA

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INTRODUCTION: The incidence of *IDH* mutations in pediatric glioma is unclear. Recent publications suggest rates ranging between 0–20%.

Therapy poses challenges as it is unclear if the biology and prognosis of pediatric *IDH*-mutant gliomas are identical to adults. METHODS: We performed an IRB approved, systematic retrospective search for *IDH*-mutant gliomas in the Dana-Farber Cancer Institute/Boston Children's Hospital database between 2009–2018, analyzing incidence, demographics, histology, co-occurring genetic alterations and outcome. RESULTS: We identified 575 patients with glioma, ages 0–21 years. Of these, 394 underwent biopsy/resection (0–9 years:n=204; 10–21 years:n=190), with 294 genetic testing. Fifteen of 294 tumors (5%) were *IDH1*-mutant. Among patients 0–9 years and 10–21 years, 1/156 (0.6%) and 14/138 (10%) had *IDH1*-mutant tumors, respectively. Among patients 10–21 year old, 13/115 low-grade gliomas were *IDH1*-mutant (11%). High-grade gliomas accounted for the remaining 23, with one *IDH1*-mutant glioma (4%). Most common co-occurring genetic alterations for diffuse astrocytoma (n=12) were *TP53* (n=9) and *ATRX* (n=2). Three patients with *IDH1*-mutant oligodendrogliomas had 1p/19q deletion. Eleven *IDH1*-mutant patients were evaluable for outcomes with median follow-up of five years. Five-year radiation-free, progression-free and overall survival for patients with low-grade histology were 76% and 100%, respectively. One patient with high-grade glioma recurred 1.2 years after upfront chemo-radiation and died soon after recurrence. CONCLUSION: *IDH*-mutant gliomas comprise a small proportion of pediatric gliomas. Incidence rate is higher in the second decade of life. Comparative analyses between pediatric *IDH*-mutant gliomas and adult historical cohorts are currently underway, evaluating outcomes, radiation therapy and frequency of malignant transformation.

LGG-04. A PHASE II RE-TREATMENT STUDY OF SELUMETINIB FOR RECURRENT OR PROGRESSIVE PEDIATRIC LOW-GRADE GLIOMA (PLGG): A PEDIATRIC BRAIN TUMOR CONSORTIUM (PBTC) STUDY

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The PBTC conducted a re-treatment study (NCT01089101) evaluating selumetinib (AZD6244, ARRY-142886), a MEK I/II inhibitor, in children with recurrent/progressive pLGG. Eligible patients must have previously enrolled on PBTC-029 or PBTC-029B and progressed after coming off treatment with selumetinib. Patients must have maintained stable disease (SD) for ≥12 courses or had a sustained radiographic response (partial or complete) during their first exposure to selumetinib. Thirty-five eligible patients (median age: 13.11 years [range 7.96–25.33]) were enrolled, 57% of whom had optic pathway or hypothalamic target lesions. At the time of submission, median duration of treatment was 18 courses (range 2–48) and 21 subjects remained on therapy. Best responses reported to date are 6/35 (17%) partial response, 22/35 (63%) SD and 7/35 (20%) progressive disease with a 2-year progression-free survival of 75.7 + 8.3%, which met the design parameters for success. The most common attributable toxicities were grade 1 diarrhea, elevated AST, hypoalbuminemia, elevated CPK, maculo-papular rash, fatigue, paronychia, ALT elevation, acneiform rash and grade 2 CPK elevation. Rare grade 3 toxicities included CPK elevation (3), lymphopenia (2), paronychia (2) and ALT elevation (2). There was only one grade 4 CPK elevation. Five patients (14%) required dose reductions due to toxicity. There does not appear to be a notable difference in toxicities observed during initial selumetinib therapy versus re-treatment. In pLGG that has recurred/progressed following treatment with selumetinib, re-treatment with selumetinib appears to be effective with 80% of patients again achieving response or prolonged stable disease. Long-term follow-up is ongoing.

LGG-05. MOLECULAR GUIDED THERAPY FOR A PEDIATRIC LOW GRADE GLIOMA: A CASE REPORT

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Low grade gliomas are the most common type of central nervous system tumors among children. Despite the fact that they are not typically life threatening, low grade gliomas remain a significant clinical challenge. Case Study: Patient is a 4-year-old male who presented at 20 months of age with several weeks of ataxia, emesis, and head tilt. Imaging revealed a right temporal lobe lesion; he was subsequently taken to surgery, where a gross total resection was achieved. Imaging 9 months post resection revealed recurrent disease within the right temporal region with leptomeningeal involvement. Four months later imaging revealed progression of multifocal disease and new growth within the sella. At this time the patient started standard treatment, Carboplatin and Vincristine, per CCG 9952A. Persistent slow progression was observed despite receiving standard therapy. The patient developed a grade 3 reaction to carboplatin, worsening with each subsequent dose. At this time, he was referred to our Precision Genomics Neuro Oncology program for tumor molecular characterization. Somatic tumor testing revealed an ETV6-NTRK3 fusion, at which time standard treatment was stopped, and patient began targeted therapy, Larotrectinib. Imaging was preformed 2 months post start of targeted therapy and revealed interval decrease in size of previously enhancing nodular lesions; findings consistent with treatment response. Disease burden continues to decrease with therapy. This case illustrates a clear benefit of using molecular guided therapy in low grade gliomas.

LGG-06. LONG-TERM OUTCOME OF NEWLY DIAGNOSED LOW GRADE GLIOMA

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INTRODUCTION: Low grade glioma (LGG) is the most common central nervous system (CNS) tumor in children accounted for 30–50%. Regarding benign characteristic of disease, surgical management remains the mainstay of treatment. However, surgical approach is limited in some conditions such as location at brainstem or infiltrative tumor. Chemotherapy and radiation treatments have been included in order to control tumor progression. The 5-years survival rate is approach 90% especially in patients who receive complete resection. However, the outcome of children with LGG in low to middle income is limited. Therefore, the aim of the study was to determine long-term outcome of children with newly diagnosed LGG. METHODS: A retrospective study enrolled children aged <18 years who were newly diagnosed LGG during January 2006- December 2019. Diagnosis of LGG was confirmed by histological findings of grade I and II according to WHO criteria. RESULTS: A total of 40 patients, female to male ratio was 1:1.35 and mean (SD) for age was 6.7 (4.0) years. The most common location was optic chiasmatic pathway (42.5%), followed by suprasellar region (25.0%). Sixty percent of patients received at least partial tumor removal. Chemotherapy and radiation had been used in 70% and 10.0% respectively. The 10-year progression free survival was 74.1±11.4% and overall survival was 96.2±3.8%. SUMMARY: Treatment of Pediatric LGG mainly required surgical management, however, chemotherapy and radiation had been used in progressive disease. The outcome was excellent.

LGG-09. CORRELATING GENETIC SIGNATURE OF PILOMYXOID ASTROCYTOMAS AND PILOCYTIC ASTROCYTOMAS WITH QUALITATIVE AND QUANTITATIVE MR IMAGING CHARACTERISTICS

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PURPOSE: Pilomyxoid astrocytomas are predominantly located in supra-chiasmatic region and are more clinically aggressive than pilocytic astrocytomas, although recent WHO 2016 classification placed them into the grade I/II category. In our study, we describe imaging correlation of PMA to their genetic signature. MATERIALS AND METHODS: We identified 12 pediatric patients with pathologically proven PMA, PA, and PA with myxoid features in an IRB approved study. Three of the tumors had whole exome somatic and germline sequencing. Qualitative MRI characteristics of location, size, enhancement, edema, T2 and T1 intensity, and multifocality were assessed. RESULTS: Among the PMA, 3 cases were found to have *KIAA1549-BRAF* fusion, 1 case *BRAF* V600E mutation, and 2 cases had wildtype *BRAF*. The *BRAF* wildtype tumors had atypical imaging features with intraventricular extension of tumor, involvement of frontal lobe parenchyma and one tumor demonstrating increase in size and development of enhancement at 5 years. Whole exome sequencing of *BRAF* wildtype tumors identified somatic truncation mutations in *NF1* R1534X and R1513X with wildtype germline *NF1* and missense mutations in KMT2C and GLTSCR1. Among PAM, one was *BRAF* wildtype with mutations i *PTCH1* M956V and *PTPN1* (A72V) and demonstrated atypical features of intratumoral hemorrhage on presentation. Among PA, one was positive for *KIAA1549-BRAF*, one was *BRAF* wildtype. CONCLUSIONS: *BRAF* wildtype PMA and PA demonstrate atypical tumor localization and are associated with atypical genetic mutations on whole exome sequencing. On the contrary, presence