HLA-A2 dextramer along with a panel of T-cell and myeloid markers. RESULTS: Among all 29 patients enrolled, we analyzed samples from all 19 DIPG and 9 of 10 non-brainstem DMG cases, of which 18 had longitudinal samples available (range: 2–5). Utilizing a novel CyTOF-based immuno-monitoring platform, the expansion of H3.3K27M-reactive CD8+T-cells, defined as a 25% increase at any time-point relative to baseline, was observed in 7 of these 18 patients. Survival analyses indicated that the expansion of H3.3K27M-reactive CD8+T-cells, particularly the effector-memory phenotype, positively correlated with longer overall survival (OS) (median: 16.1 vs 9.7 months, p=0.03), whereas an abundance of early and monocytic myeloid-derived suppressor cells at baseline correlated with shorter OS among DIPG patients (9.5 vs 14.3 months, p=0.002). CONCLUSION: Our novel immuno-monitoring approach offers insight into how vaccine-induced immune responses impact clinical outcomes.

IMMU-26. DISEASE CONTROL IN A PEDIATRIC PATIENT WITH NEWLY DIAGNOSED GLIOBLASTOMA MULTIFORME (GBM) AND SOMATIC HIGH MICROSATELLITE INSTABILITY (MSI-H) WITH PD-1 INHIBITOR NIVOLUMAB (NIVO) ONLY AND NO FOCAL RADIOTHERAPY (RT)

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Immune checkpoint inhibitors that target programmed death receptor-1 (PD-1) have recently been shown to be a promising option for the management of recurrent mismatch repair (MMR) deficient GBM following radiotherapy. We report a case of a 9-year-old boy who presented with a 6 week history of frontal headaches and was found to have a left frontal lobe mass. Pathology obtained from a gross total resection (GTR) was consistent with classic GBM, WHO Grade IV. Neuroimaging four weeks following initial resection was remarkable for local recurrence. The patient underwent another GTR of the tumor at our center. While pathology again confirmed GBM, GlioSequencing of tumor tissue from second resection showed MSI-H, NF2 mutation p.R338H, NF1 mutations p.R2450* and pI193Yfs*11, TP53 mutations p.R213* and p.R273C, EGFR mutation, and multiple variants of uncertain significance. Germline testing was negative for MMR deficiency or other deleterious mutations. Parents opted to defer radiotherapy and consented to monotherapy treatment with Nivolumab (Opdivo, BMS pharmaceuticals, USA), a PD-1 inhibitor, at a dose of 3 mg/kg administered every two weeks. Our patient is now 22 months post-second resection and continues to receive Nivolumab without evidence of recurrent disease or adverse autoimmune effects from PD-1 blockade. He has remained in school with good academic performance and has exhibited no regression of functional status during the entirety of his treatment course. This case provides evidence of possible efficacy of PD-1 blockade without focal radiotherapy in this child with GBM and somatic MSI instability.

IMMU-27. ANALYSIS OF IMMUNE SIGNATURES IN PEDIATRIC GLIOBLASTOMAS FOR PATIENT STRATIFICATION TO IMMUNOTHERAPY

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BACKGROUND: Pediatric glioblastoma (pGBM), despite being relatively rare (incidence rate: 0.5/100,000), are a leading cause of cancer deaths in children with a median overall survival of 9–15 months. In recent years, immunotherapy has emerged as one of the more promising advances in oncology, with impressive response rates reported in several malignancies. Effective application of immunotherapy in brain tumors depends upon a better understanding of the immune cell phenotype and mechanisms of immunosuppression in these tumors. This understanding will allow for the selection of patient population who are most likely to benefit from immunotherapeutic approaches. MATERIAL AND METHODS: In order to determine the frequency, distribution, and phenotype of tumor-infiltrating immune cells in pGBMs, we undertook an immunohistochemical survey on 19 recurrent pGBMs for CD3, CD8, CD4, CD163, PD-1, PD-L1, and FoxP3; RNA-Seq was also performed on a subset of 9 cases. Distribution of lymphocytes (LYMPHS) was recorded as intratumoral (IT) or perivascular (PV). RESULTS: The analysis indicates intratumoral CD3+ LYMPHS are commonly <5% of tumor cell mass; however, approximately half (10/19) of these recurrent pGBM have infiltrates that range from 5 to 30% CD3+ LYMPHS. Of these, 4/10 CD3+ tumors exhibit brisk CD8+ infiltrates that are associated with PD-L1+ tumor cells. These tumors with brisk CD3+/CD8+ LYMPHS and PD-L1+ tumor cells were associated with longer survivals. The data

were confirmed by RNA-seq analysis. CONCLUSION: PD-L1+ pGBMs associated with CD3+/CD8+ LYMPH infiltrates deserve further investigation as candidates for immunotherapy.

IMMU-28. IMMUNOGENOMIC ANALYSIS REVEALS LGALS1 CONTRIBUTES TO THE IMMUNE HETEROGENEITY AND IMMUNOSUPPRESSION IN GLIOMA

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Mutualistic and dynamic communication between tumour cells and the surrounding microenvironment accelerates the initiation, progression, chemoresistance and immune evasion of glioblastoma (GBM). However, the immunosuppressive mechanisms of GBM has not been thoroughly elucidated to date. We enrolled six microenvironmental signatures to identify glioma microenvironmental genes. The functional enrichment analysis such as ssGSEA, ESTIMATE algorithm, Gene Ontology, Pathway analysis is conducted to discover the potential function of microenvironmental genes. In vivo and in vitro experiments are used to verify the immunologic function of LGALS1 in GBM. We screen eight glioma microenvironmental genes from glioma databases, and discover a key immunosuppressive gene (LGALS1 encoding Galectin-1) exhibiting obviously prognostic significance among glioma microenvironmental genes. Gliomas with different LGALS1 expression have specific genomic variation spectrums. Immunosuppression is a predominate characteristic in GBMs with high expression of LGALS1. Knockdown of LGALS1 remodels the GBM immunosuppressive microenvironment by down regulating M2 macrophages and myeloid-derived suppressor cells (MDSCs), and inhibiting immunosuppressive cytokines. Our results thus implied an important role of microenvironmental regulation in glioma malignancy and provided evidences of LGALS1 contributing to immunosuppressive environment in glioma and that targeting LGALS1 could remodel immunosuppressive microenvironment of glioma.

IMMU-29. AIF1 IS A PROGNOSTIC BIOMARKER AND CORRELATED WITH IMMUNE INFILTRATES IN GLIOMAS

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Gliomas remain highly variable clinical behaviors, leading to emerging studies to identify prognostic factors. AIF1 (Allograft Inflammatory Factor 1) is critical for promoting both macrophage- and dendritic cells (DCs)-mediated inflammatory response and growth of vascular smooth muscle cells and T-lymphocytes. Through comparative analyses of primary LGG patients from The Cancer Genome Atlas (TCGA) dataset and Chinese Glioma Genome Atlas(CGGA) dataset, we reported that the expression level and methylation level of AIF1 gene vary among glioma patients and AIF1 expression or gene body methylation is significantly associated with glioma patient survival. Cox regression results confirmed that AIF1 played an independent predictor of survival in lower-grade glioma(LGG), with a cox coefficient of 0.251 indicating a worse prognosis. Moreover, AIF1 expression was positively correlated with infiltrating levels of CD4+ T and B cells, macrophages, neutrophils, and DCs in LGG and glioblastoma(GBM). AIF1 expression also showed strong correlations with specific immune cell markers in LGG and GBM. In addition, AIF1 expression potentially contributed to the regulation of glioma-associated macrophages and microglia. In conclusion, our findings suggested that AIF1 was correlated with prognosis and immune infiltrating levels, and it can be used as a prognostic factor in gliomas.

IMMU-30. UPREGULATED T CELL AND INTERFERON-Γ-RELATED GENE EXPRESSION IS ASSOCIATED WITH INCREASED SURVIVAL IN RECURRENT PEDIATRIC HIGH-GRADE GLIOMA

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