

of HLA class I suggests that pediatric brain tumors have developed immune evasion strategies to prevent recognition by conventional T cells.

#### IMMU-07. IMMUNE EFFECTOR CELL ASSOCIATED NEUROTOXICITY (ICANS) AMONG PEDIATRIC AND AYA PATIENTS: MD ANDERSON CANCER CENTER EXPERIENCE

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**INTRODUCTION:** Immune effector cell associated neurotoxicity (ICANS) and cytokine release syndrome (CRS) are potentially life-threatening complications associated with immune effector cell (IEC) therapies. We characterize ICANS in pediatric and adult young adolescent (AYA) patients receiving IEC therapy at our institution. **METHODS:** We reviewed clinical characteristics and severity (based on ASTCT Consensus Criteria) in pediatric and AYA patients with IEC products from 2018–2019 at MDACC. **RESULTS:** Nine patients, median age 15.5 (range: 3–25) years received chimeric antigen receptor (CAR-T) IEC therapy. Four (44%) developed ICANS within median of 8 (range: 3–27) days of CAR T cell infusion and median 6 (range: 2–7) days after CRS. Primary diagnoses were pre-B cell acute lymphoblastic leukemia (8) and mediastinal large B-cell lymphoma (1). Median CRS and ICANS severity grade was 2 (range 1–4). Symptoms included altered mental status (AMS) (5), seizure (1), aphasia (2), impaired ability to write a standard sentence (4). Neuroimaging did not correlate to ICANS symptoms or severity. EEG was performed in 3 and 1 had background slowing correlating with aphasia. CSF was obtained in two revealing lymphocytosis. All received prophylactic anti-epileptic medication and tocilizumab for concomitant CRS. Three received steroids. **CONCLUSION:** ICANS may present in almost half of pediatric patients within one week of receiving CAR-T products associated with CRS. CAR-T trafficking into the CSF may explain pleocytosis in the CSF. Prospective studies may clarify. Impaired ability to write a standard sentence and the Cornell Assessment of Pediatric Delirium (CAPD) may be early indicators of ICANS in pediatric/AYA patients.

#### IMMU-08. REMATCH PROTOCOL: PHASE II STUDY OF EX-VIVO EXPANDED AUTOLOGOUS TUMOR SPECIFIC LYMPHOCYTE TRANSFER (X-ALT) + TOTAL TUMOR RNA DC VACCINE (TT-RNA DC) DURING RECOVERY FROM MYELOABLATIVE CHEMOTHERAPY (MAC) AND PERIPHERAL BLOOD STEM CELL (PBSC) RESCUE OR NON-MYELOABLATIVE CHEMOTHERAPY (NMAC) AND PBSC IN PATIENTS (PTS) WITH RECURRENT PNET (R-PNET)

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A phase II study was performed to assess vaccine-related toxicities and efficacy of x-ALT+tt-RNA DC following MAC +PBSC (group A) or NMAC +PBSC (group B) in pts with r-PNET. **METHODS:** Eligible pts underwent biopsy to confirm r-PNET and obtain tumor for vaccine preparation. Pts with local (group A) or metastatic (group B) disease received cytoreductive induction chemotherapy prior to either MAC (carboplatin+ thiotepa+ etoposide) or NMAC (cyclophosphamide + fludarabine) respectively and then received one dose of x-ALT ( $3 \times 10^7$  cells/kg), PBSC, and 3 doses of bi-weekly intradermal tt-RNA DCs ( $10^7$  cells each). Patients were followed for survival and vaccine-related toxicities. Correlative studies included TCR RNA sequencing and measurement of serum cytokines **RESULTS:** 20 evaluable pts (75% males) [Medulloblastoma 17, PNET 3; unifocal 40%] were treated on protocol (group A 7, group B 13). There were no significant vaccine-related toxicities. At a median follow-up of 8.5 months, 5 patients (all with medulloblastoma) are alive following vaccine therapy; 2 pts with SD (3.5+ and 6.5+ months) and 3 pts with PD that stabilized with salvage therapies (26+, 31+, and 46+ months respectively). One patient with medulloblastoma and bone marrow involvement who had PD despite MAC, had an almost complete response one month following x-ALT + tt-RNA DCs and TCR RNA sequencing demonstrated massive clonal expansion of T cells. Correlative studies are ongoing **CONCLUSIONS:** x-ALT+tt-RNA DC following either MAC or NMAC is safe and shows signs of biologic and possible clinical activity in some pts with r-PNET.

#### IMMU-09. NIVOLUMAB THERAPY FOR A PEDIATRIC-ONSET PRIMARY INTRACRANIAL MELANOMA

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Primary intracranial malignant melanoma (PIMM) is an uncommon cancer in childhood, that accounts for approximately 1% of melanoma, and 0.07% of brain tumors even in all age group. Because extracranial malignant melanoma usually occurs as a cutaneous lesion, affected patients have a chance to receive the early diagnosis and curable resection of the isolated tumor. However, unresectable metastatic cases have a poor prognosis with a median overall survival of 8 months. We report a 12-year-old girl with PIMM who received nivolumab therapy after an administration of dacarbazine. The tumor harbored no *BRAF* mutation. After the intravenous administration of nivolumab, cerebrospinal fluid 5-S-cysteinyldopa levels declined and circulating CD8<sup>+</sup>HLA-DR<sup>+</sup>T cells increased, indicating the initial effect of nivolumab on PIMM. However, multiple lesions progressed for two month-immunotherapy, during which cerebrospinal fluid nivolumab concentrations attained to 1.2% of serum ones. The present case demonstrated the safety and modest effect of nivolumab for CNS melanoma. Nivolumab is a tolerable first-line therapy for diffuse PIMM, but pediatric patients need a more intensified CNS-specific immunotherapy.

#### IMMU-10. INTERIM ANALYSIS OF THE HIT-HGG REZ IMMUNOVAC STUDY - DENDRITIC CELL VACCINATION WITH PARTIAL TREG DEPLETION IN CHILDREN, ADOLESCENTS, AND ADULTS WITH RELAPSED HIGH-GRADE GLIOMAS

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Efficacy of therapeutic dendritic cell vaccines (DCV) can be limited by immunosuppressive mechanisms in the microenvironment of high-grade gliomas. In the HIT-HGG-Rez Immunovac trial (Eudra-CT 2013-000419-26), we investigate whether a reduction of Treg with metronomic cyclophosphamide (metrCyc) might be a feasible option to improve vaccine efficacy. 10 pediatric (mean age 11.4±4.2y) and 5 adult patients (mean age 39.5±19.9y) with relapsed glioblastoma were treated according to the HIT-HGG-Rez Immunovac protocol so far. 2 children were treated within the trial, the other 13 in the pilot phase. Patients received upfront oral metrCyc for 2–4 weeks. After reoperation and monocyte-apheresis, patients received 4 weekly intradermal doses of autologous, TNFα/IL-1β matured DCs pulsed with tumor lysate in imiquimod-prepared skin. Thereafter, tumor lysate boosts were given. All patients received at least 5 vaccines (4xDCs, 1xlysate boosts). MetrCyc was well tolerated and led to a reduction in Treg-frequency of 35.6±17.8% followed by a rebound after cessation of metrCyc. Importantly, 13/14 analyzed patients showed a positive IFNγ-T-cell response against autologous tumor lysate with a tendency to decrease over time. 6-month overall survival was 100%, compared to 65% in a historical control. Mean PFS and OS were 5.7 and 21.1 months with no difference between adults and children. We conclude that DCV in combination with partial Treg depletion is feasible, safe, and related with a high rate of tumor-specific IFNγ-responses. As the clinically and immunologically beneficial effects seem to diminish over time, we aim to combine our approach with checkpoint inhibition in the next amendment.

#### IMMU-11. LOCOREGIONAL DELIVERY OF TRANSIENT GD2 CAR T CELLS FOR SAFE AND EFFECTIVE TREATMENT OF DIPG

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Diffuse intrinsic pontine glioma (DIPG) is a universally fatal pediatric brain tumor with a median survival of one year. Recently Mount et al (Nat Med 2018) discovered the disialoganglioside GD2 is present at high levels on the surface of DIPG and can be targeted using GD2-directed CAR T cells. However, permanently expressed CAR T cells created by lentiviral transduction resulted in a significant number of deaths from tumor swelling with uncontrolled T cell proliferation. We hypothesized that using mRNA to create transient GD2-directed CAR T cells delivered locally with repeated dosing would result in a safer yet equally effective way to treat DIPG using CAR T cell therapy. In vitro studies using mRNA GD2-directed CAR T cells resulted in robust tumor cytotoxicity and T cell degranulation across a panel of six DIPG cell lines. Using an orthotopic murine model of SU-DIPGXIIIIP\*, an extremely aggres-