ALT+DCV following HDC + ASCR (group A) or NMAC (group B) in pts with (n=2) or without (n=1) disease 33-42 months following treatment. TCR sequencing demonstrates massive clonal expansion of T cells following ALT+DCV and positive correlation with clinical outcomes. Persistence of tumor-reactive (IFN-gamma secreting) T cell clones in the peripheral blood was observed 4 months after treatment in a patient with long-term disease control. CONCLUSIONS: ALT+DCV is feasible, safe, and shows signs of biologic and clinical activity in some pts with r-PNET.

IMMU-26. PEPTIDE VACCINE IMMUNOTHERAPY BIOMARKERS AND RESPONSE PATTERN IN PEDIATRIC GLIOMAS

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Atypical teratoid/rhabdoid tumors (AT/RTs) are commonly regarded as immunologically anastomosing. Here, we report on the trend of T-cell response to two exclusive targets in pediatric glioma (pleomorphic xanthoastrocytoma, PXA) xenografts, D-645 PXA, and the human melanoma cell line, A375. Two peptide-based therapies were tested: T-cell receptor (TCR) therapy and peptide vaccines. The results showed that TCRs can target specific epitopes and that antigen-specific vaccine-induced CD8+ T cells can recognize tumor-specific neoantigens and kill tumor cells in vitro. These findings support the use of TCR-based and vaccine strategies for the treatment of AT/RTs.

IMMU-27. RE-MATCH PROTOCOL: PHASE I STUDY OF AUTOLOGOUS TUMOR SPECIFIC LYMPHOCYTE TRANSFER (ALT) + DC VACCINE (DCV) DURING RECOVERY FROM MYELOABLATIVE CHEMOTHERAPY (MAC) AND AUTOLOGOUS STEM CELL RESCUE (HDC + ASCR) OR CHEMOTHERAPY (NMAC) IN PATIENTS WITH RECURRENT CENTRAL PNETS (R-PNET)

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We performed a phase I study to assess feasibility, safety, and efficacy of ALT+DCV following HDC + ASCR (group A) or NMAC (group B) in pts with r-PNET. METHODS: Eligible pts underwent surgery to confirm diagnosis and obtain tumor tissue for vaccine preparation. Pts with (local) group A or metastatic (group B) recurrence received 4 cycles of cytoreductive chemotherapy prior to either MAC (carboplatin + thiotepa + etoposide) (group A) or NMAC (cyclophosphamide + Fludarabine) (group B). Two dose levels of ALT were evaluated (3 x 1011 cells/kg with concomitant immunosuppression generated by tumors. An ongoing phase-I/IIa study (NCT025502708) using indoximod in combination with temozolomide and/or re-irradiation for children with relapsed/refractory pediatric brain tumors has established the recommended phase-2 dose (RPD) of indoximod for this purpose and has shown this approach to be well-tolerated and feasible in these highly complex and fragile patients. Diffuse Intrinsically Pontine Glioma (DIPG) is an FDA-designated orphan disease, with no curative treatment options and dismal prognosis. The primary hypothesis is that addition of indoximod-based immunotherapy to standard-of-care radiation, followed by immunotherapy-chemotherapy with indoximod plus temozolomide will improve objective response rates, 12-month event-free survival, and median overall survival. DESIGN/METHODS: Newly-diagnosed DIPG patients age 3 to 21 years are treated with indoximod (RPD2) in combination with conformal radiation therapy (54 Gy), followed by cyclic immune-chemotherapy using indoximod (RPD2=38.4 mg/kg/day divided BID throughout each cycle) combined with temozolomide (200 mg/m2/day, days 1-5 of each 28-day cycle). Up to 10 additional cycles may be enrolled for NMAC. The trial is ongoing. At this time, we have enrolled the first 6 newly-diagnosed DIPG patients. At the end of the indoximod plus radiation block, the first two patients had objective tumor response without any significant adverse events to date. Interim outcome and safety data for the first 8 months of accrual will be presented.

LOW GRADE GLIOMA

LLG-01. EVALUATION OF COBIMETINIB, A MEK INHIBITOR, IN LOW GRADE PEDIATRIC BRAIN TUMOR CELL LINES

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Cobimetinib is an orally bioavailable small-molecule that specifically binds to and inhibits the catalytic activity of MEK, resulting in inhibition of ERK phosphorylation and activation and decreased tumor cell proliferation. Cobimetinib is used in the treatment of patients with a previously untreated metastatic melanoma, and preclinical studies have demonstrated that cobimetinib is effective in inhibiting the growth of cells from other tumor types bearing an activating BRAF mutation. Two low-grade pediatric glioma (pleomorphic xanthoastrocytoma, PXA) xenograft xenografts, D-645 PXA, which carries the BRAF V600E mutation, and D-2836 PXA were grown...