radiographic response to ACT and prolonged progression-free and overall survival. Limited TCR expansion and diversity following ACT was observed in patients with short overall and progression-free survival. CONCLUSIONS: These results emphasize the importance of genetic expression profiling to achieve higher resolution in monitoring immune responses in patients receiving immunotherapeutic treatment. Also, these findings support further study of the use of TCR sequencing to monitor responses to adoptive cellular therapy and suggest that TCR clonal expansion and increasing TCR diversity following treatment may be associated with positive clinical responses.

CTIM-32. FIRST-IN-CHILDREN PHASE 1 TRIAL OF INDOXIMOD-BASED CHEMO-IMMUNOTHERAPY FOR PATIENTS WITH PEDIATRIC BRAIN TUMORS: ANALYSIS OF SAFETY, TOLERABILITY, AND 5-YEAR OUTCOME

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BACKGROUND: Recurrent brain tumors are the leading cause of cancer death in children. We conducted a first-in-children, two-institution, Phase 1 open-label dose-confirmation study using a 3 + 3 design, with expansion cohorts, to determine the recommended pediatric dose of the IDO pathway-inhibitor indoximod (NCT02502708). DESIGN/METHODS: Eligible patients were 3-22 years old with either recurrent malignant brain tumor or newly-diagnosed diffuse intrinsic pontine glioma (DIPG). Palliative radiation, surgery or dexamethasone were allowed as needed for patient management. Indoximod was administered at dose levels escalating in 25 mg/kg/day orally and endosomop 50 mg/m2/day orally for 21 days of each 28-day cycle. RESULTS: Between December 2015 and January 2019, the study enrolled 81 brain tumor patients, including newly-diagnosed DIPG (n = 13) or recurrent and recurrent malignant brain tumor (n = 25; medulloblastoma (n = 13), or other CNS tumors (n = 9). Median follow-up was 52 months (range 39-77 months). No dose-limiting toxicities were observed, and the pediatric indoximod dose was determined (19.2 mg/kg/dose, given twice daily). Indoximod was well tolerated and did not affect the ability to deliver chemotherapy or radiation as planned. Median overall survival was 13.6 months (n = 81). Median overall survival was 34.7 months for the subset of patients who continued indoximod with second-line chemotherapy after progression on indoximod monotherapy (n = 19). CONCLUSIONS: Indoximod was well tolerated and could be combined with a variety of standard treatments for pediatric brain tumors. Preliminary anti-tumor activity and overall survival suggest that indoximod with standard therapy should be further evaluated in pediatric brain tumors, and potentially other pediatric solid tumors.

CTIM-33. SEXUAL DIMORPHISM OF HUMAN IMMUNE SYSTEM PREDICTS CLINICAL OUTCOMES IN GLOBLASTOMA IMMUNOTHERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Biological differences based on sex have been documented throughout scientific literature. Global, but some of the most compelling primary evidence comes from tumor in adults, has a male sex incidence bias, however, no clinical trial data examining differential effects of treatment between sexes currently exist. We analyzed genomic data, as well as clinical trials, to delineate the effect of sex on standard-of-care and glioblastoma-specific immunotherapies. We found that, in general females possess enriched immunological signatures on gene set enrichment analysis, that also stratified patient survival when delineated by sex. Female glioblastoma patients treated with immunotherapies exhibited statistically significant survival advantage at the 1-year mark compared to males (RR = 1.15; p = 0.02). This effect was even more pronounced in vaccine-based immunotherapy, (RR = 1.29; p = 0.0158). Our study shows a meaningful difference in the immunobiology between males and females that also influences overall response rates and outcome following immunotherapy. We study adds to a growing body of literature examining sex differences in male and female immunology. We demonstrate both using large scale omic data sets, as well as clinical trials, that female sexually dimorphic genes are tied to immunological responses, and that females have better outcomes during GBM immunotherapy treatments. This data is critical to better inform treatment practices and further crystallizes the need for balanced trial design and prospective reporting of sex as a variable across all GBM clinical trials.

CTIM-34. PRELIMINARY SAFETY AND EFFICACY DATA ON TWO PATIENTS WITH RELAPSED/REFRACTORY CNS LYMHPHOMA TREATED WITH EMAVUSERTIB (NCT 4948) AND IBBRUTINIB COMBINATION: A SUBSET ANALYSIS OF TAKEAIM LYMPHOMA TRIAL

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BACKGROUND: Emavusertib, an oral interleukin-1 receptor-associated kinase 4 (IRAK4) inhibitor, targets toll-like receptor (TLR) and interleukin-1 receptor (IL-1R) signaling pathway in B-cell proliferation. IRAK4 forms a Myddosome complex with MYD88 adaptor protein and drives overactivation of NF-kB, causing inflammation and tumor growth. Emavusertib has been reported to be well tolerated and active as mono-therapy in heavily pretreated relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL). In a murine PDX model of preclinical NHL (PCNSL), emavusertib crossed the blood-brain barrier, resulting in tumor response and prolonged survival. In combination with Bruton tyrosine kinase (BTK) inhibitors, emavusertib showed in vivo anti-cancer synergy in B-cell NHL. METHODS: This is an ongoing open-label trial (NCT03328078) in patients with R/R NHL. Currently, we are in the dose escalation portion