ATIM-11. PHASE 2 TRIAL OF SL-701, A NOVEL IMMUNOTHERAPY COMPRISED OF SYNTHETIC SHORT PEPTIDES AGAINST GBM TARGETS IL-13Rα2, EphA2, AND SURVIVIN, IN ADULTS WITH SECOND-LINE RECURRENT GBM: INTERIM RESULTS

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BACKGROUND: SL-701 is a novel immunotherapy comprised of synthetic short peptides designed to elicit an immune response against three overexpressed GBM targets: interleukin-13 receptor alpha-2 (IL-13Rα2), EphrinA2 (EphA2), and Survivin. We report preliminary data from an ongoing multicenter, 2-stage Phase 2 clinical trial of SL-701 in HLA-A2 positive adults with first recurrence of GBM. METHODS: Patients had to have evidence of progression (KPS > 60, absence of standard RTT/MX) in Stage 1 and SL-701 with adjudicated GM-CSF and imiquimod is administered biweekly for 6 months, then every 28 days thereafter. In Stage 2, SL-701 with the adjuvant poly-ICLC is administered biweekly with bevacizumab (10mg/kg). Primary objectives: 1) safety and tolerability; 2) investigator assessed objective response rate (iORR) using RANO criteria and 3) survival rate at 12 months. RESULTS: As of S/17/16, 58 patients (46 in Stage 1 and 12 in Stage 2) received SL-701. Accrual for Stage 1 is complete. Stage 2 accrual is ongoing. Median age is 55 years (range: 23-74), median KPS is 90, and 67% are male. Patients received a median of 4 doses. The most frequent grade 3-4 treatment-related adverse events (TRAEs) were fatigue (n = 1; 1.7%) and altered mental status (n = 1; 1.7%). Among 30 evaluable patients in Stage 1, there was 1 partial response (PR) (35+ weeks duration, ongoing) and 15 stable diseases (SD) (median duration: 8 weeks; range: 8-42+ weeks, ongoing). Of the 4 evaluable patients in Stage 2 to date, there has been 1 PR (8+ weeks duration, ongoing) and 3 SD (median duration: 8 weeks; range: 5-8+ weeks, ongoing). CONCLUSIONS: SL-701 plus adjuvants GM-CSF/ imiquimod or poly-ICLC and bevacizumab is well-tolerated. Persisting CAR T cells were detected in the tumor cyst fluid or cerebral spinal fluid for a minimum of 7 days for patients with surviving CAR T cell populations. T cell responses have been observed in a subset of patients, including decreased IL13Rα2 tumor antigen expression post-treatment. One patient of particular interest with recurrent multifocal GBM that included metastatic sites in the spine, was first treated with six weekly infusions of IL13BEC1, into the resection cavity of the largest tumor, followed by ten weekly intraventricular infusions. In the absence of any other therapeutic interventions, this patient experienced a dramatic antitumor response with all intracranial and spinal tumors regressing >79%-97% by maximum area. This response was sustained for more than 7-months post-initiation of CAR T cell treatment. These early clinical findings suggest that intracranial delivery of second-generation IL13Rα2-targeted CAR T cells is safe and well-tolerated, and that CAR T cells are capable of eliciting potent antitumor responses against recurrent glioblastoma.

ATIM-14. FIRST KOREAN EXPERIENCE OF DENDRITE CELL-BASED IMMUNOTHERAPY IN PATIENTS WITH PRIMARY GliOBLASTOMA

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OBJECTIVE: Dendritic cells are antigen presenting cells that recognize antigens and trigger an immune response in human immune system. Dendritic cell-based immunotherapy (DCI) has the potential to target and eliminate GBM cells. We evaluated the safety and efficacy of DCI in patients with primary glioblastoma. MATERIALS AND METHODS: The dendritic cells with self-tumor lysate, WT1 and KLH are intradermal injected on the upper dermis of DCI T cell treatment. These cells were weekly and twice at intervals of two weeks after the 4weeks of rest period. We followed up patients two years. Treatment response was evaluated with CT and MRI, and immune response was evaluated with T cell proliferation assay and ELISPOT test. The control group was set up to histological reference (newly diagnosed, standard treatment completed 24 patients).

RESULTS: Thirteen patients received this immunotherapy. The total 83 related adverse events occurred. The eighty-two (Grade 1) and one (Grade 2) event were not serious adverse events. Kim et al. (2017) had confirmed the effective density gradient. A clinically-relevant finding that emerged from the multiparametric analysis of antigen coexpression in gliomas was the partial co-expression of IL13Rα2 and Ki67; many Ki67+ (proliferating) cells did not express IL13Rα2 (i.e., IL13Rα2-Ki67-) and many IL13Rα2+ cells did not express Ki67 (i.e., IL13Rα2+Ki67-). This observation is consistent with the failure of several clinical trials that had targeted toxins to gliomas via IL13Rα2. CONCLUSIONS: FCM can be used to classify astrocytoma cells within single-cell dissociated brain lesions. The developed method represents a first step towards a quantitative, user-independent means for multiparametric classification and study of solid tumors.

ATIM-13. PHASE 1 STUDY OF CHIMERIC ANTIGEN RECEPTOR-ENGINEERED T CELLS TARGETING IL13Ra2 FOR THE TREATMENT OF GliOBLASTOMA

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T cell immunotherapy is emerging as a powerful strategy to treat cancer, and may offer opportunities to improve outcomes for patients with glioblastoma (GBM). We have optimized a chimeric antigen receptor (CAR) T cell therapy targeting the GBM-associated antigen IL13Ra2 that utilizes CD62L-enriched central memory T cells (Tcm) engineered by lentiviral transduction to express a second-generation 4-1BB-containing CAR (IL13BB). We report here initial findings from our first-in-human clinical trials in GBM. The aims of this trial include: (1) exploration of the safety and feasibility of targeting IL13Rα2; and (2) comparison of intracranial delivery through intratumoral (with and without tumor resection) and intraventricular routes. To date, we have treated 10 patients and completed the first low-dose cohort of three resection patients. Local Cell Biol / Beckman Res Inst / City of Hope, Duarte, CA, USA, 1Department of Neurosurgery, City of Hope Comprehensive Cancer Center, Duarte, CA, USA.