TPS6581 **Poster Session**

First-in-human study of autologous chimeric engulfment receptor T-cell CER-1236 targeting TIM-4-l in acute myeloid leukemia (CertainT-1).

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Background: Acute myeloid leukemia (AML) is the most common adult acute leukemia. Patients with relapsed or refractory (R/R) disease have dismal outcomes with complete remission (CR) rates of 5%- 15% and median overall survival of 3 to 6 months with best available therapies. In addition, patients in remission with measurable residual disease (MRD) have poor outcomes with no approved therapies. CER-1236 is an autologous chimeric engulfment receptor T cell (CER-T) which fuses external domain of TIM-4 with intracellular domains from T cells and innate immune cells including Toll-like receptor 2 (TLR2), CD28 and CD3ζ. This receptor binds TIM-4-ligand (phosphatidylserine) on tumor cells leading to phagocytosis and lysis of target cells followed by tumor antigen processing and cross-presentation to induce an adaptive immune response. CER-1236 was shown to eliminate AML cell in vitro, and in vivo in a xenograft model. TIM-4 is the key receptor which binds to TIM-4-L and leads to target cell engulfment. TIM-4-L is expressed in 88% of primary patient AML samples, across TP53 mutated and other mutational subgroups, with significantly higher expression than bone marrow from healthy donors. **Methods:** This is an open label phase I study to evaluate the safety and preliminary activity of CER-1236 in patients with R/R AML. We will evaluate 3 doses levels from 1 to 5 x10^6/kg CER+ T cells using a BOIN dose escalation design. Subsequently we will evaluate patients in 3 expansion cohorts including R/R AML, TP53 mutated AML, and AML in composite CR (cCR), i.e., CR/CRi/CRh with positive MRD. For the dose escalation study we will enroll adults with R/R AML or myelodysplastic syndrome (MDS)/AML per ICC 2022 criteria who have exhausted standard therapeutic options and patients with treated secondary AML who have progressed to AML after receiving AML directed therapy for antecedent hematological disorder, e.g, MDS. Patients will need an ECOG performance status of 0 to 1 and adequate end organ function. We will exclude patients with t(15;17), proliferative disease or active infections. For the MRD dose expansion cohorts we will enroll patients with cCR with MRD $\geq$0.1% by validated multiparametric flow cytometry. Study treatment: Patients will receive lymphodepleting chemotherapy (LDC) with fludarabine 30 mg/m^2/d and cyclophosphamide 400 mg/m^2/d for 3 days followed by a single infusion of CER-1236 2 days later. Patients may receive standard treatments as bridging therapy after apheresis and prior to LDC. The primary objective of the study is the safety of CER-1236 in terms of dose-limiting toxicities, cytokine release syndrome, and Immune effector cell-associated neurotoxicity syndrome. Secondary objectives are to measure objective response rate per the ELN 2022 criteria including CR+CRh+CRi+MLFS, cCR, MRD negativity by flow cytometry, and PK/PD profile and biomarkers of response. Research Sponsor: None.