ENHANCING THE ANTI-TUMOR IMMUNITY AND THERAPEUTIC POTENTIAL OF ICT01, A BUTYROPHILIN3A-TARGETED, γ9δ2 T CELL-ACTIVATING MONOCLONAL ANTIBODY, WITH LOW DOSE IL-2 IN PATIENTS WITH ADVANCED SOLID TUMORS: THE EVICTION-2 TRIAL

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Background ICT01 is an anti-BTN3A mAb that selectively activates γ9δ2 T cells to orchestrate a robust antitumor immune response of the innate and adaptive immune systems that leads to solid tumor infiltration of activated γ9δ2 T cells, CD8 T cells, and NK cells. (EVICTION trial (NCT04243499); SITC 2021, #503) However, the pharmacodynamic effects of ICT01 are dependent on an adequate population of γ9δ2 T cells, which is lacking in most advanced cancer patients. ICT01 plus low-dose SC (LDSC) IL-2 has been shown to safely and selectively increase the number of γ9δ2 T cells, without Treg expansion, in non-human primates.

Methods EVICTION-2 (NCT05307874) is a phase I/IIa basket trial including Bayesian dose escalation across 8 dose cohorts that is being conducted at 4 clinical sites in the UK, France and Germany. ICT01 is administered IV on day 1 of each Q3W cycle (1, 5, 20 or 75mg) and LDSC IL-2 (1 or 2 MIU/m2) on days 1-5 of the first 3 cycles to patients with colorectal (CRC), ovarian (OV), prostate, or pancreatic cancer. Efficacy evaluable patients are defined as receiving ≥21 cycles with Wk 8 RECIST assessment. Blood samples are collected for immunophenotyping by flow cytometry and cytokine analysis (IFNγ, TNFa, IL-1b/2/4/6/10/12/13) on days 1, 5, 8 and 15 of each cycle. Tumor biopsies (baseline, Day 28) for flow cytometry, IHC, and Nanostring profiling. Patients are monitored during the first 21-day cycle for DLTs and a safety review committee determines if dose escalation can continue.

Results Cohort 1 (n=2) received 1 MIU/m2 IL-2 + 1 mg ICT01 with rapid activation and complete migration of 9δ2 T cells within 30 minutes post ICT01 without any DLTs. This was followed by an absolute increase of γ9δ2 T cells that peaked on day 15 of 52K (CRC pt; 7.5x increase; 12% of total T cells) and 236K (OV pt; 2.2x increase; 43% of total T cells). γ9δ2 T cells returned to baseline in the CRC pt, while the OV patient had ~300K at the time of C2, which was well tolerated. Additionally, rapid activation and migration of CD4 and CD8 T cells, NK cells, and granulocytes were observed on day 1. Cytokine, biopsy and RECIST results will be presented. Dose escalation to 5mg ICT01 + 1 MIU/m2 IL-2 and 1 mg ICT01 +2MIU/m2 IL-2 is ongoing.

Conclusions LDSC IL-2 plus ICT01 safely and significantly increase the number of activated γ9δ2 T cells with broad immune activation.

Trial Registration clinicaltrials.gov NCT05307874

Ethics Approval France Committee for Personal Protection (CPP)

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.