ICT01 PLUS LOW DOSE SC IL-2 PRODUCES A ROBUST ANTI-TUMOR IMMUNE ACTIVATION IN ADVANCED CANCER PATIENTS (EVICTION-2 STUDY)

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Background ICT01 is a first-in-class anti-BTN3A mAb that selectively activates γ9δ2 T cells, leading to remodeling of the tumor microenvironment by activated γ9δ2 T, CD8 T, and NK cells (EVICTION-NCT04243499). However, many cancer patients have very low circulating γ9δ2 T cells that limit their response to ICT01. In the EVICTION-2 trial, a novel regimen of ICT01 plus low dose subcutaneous (LDSCL) IL-2 is being investigated in patients with advanced-stage solid tumors to increase the number of γ9δ2 T cells that generate a more efficacious anti-tumor immune response.

Methods ICT01 (1, 5, 20 or 75 mg, IV Q3W) is given in combination with IL-2 (Proleukin®, 1 or 2 MIU/m², SC) on days 1–5 of the first 3 cycles and will be continued alone thereafter. Per dose combination two patients are enrolled for dose escalation based on the BOIN simulations to identify a dose regimen that safely expands γ9δ2 T cells, which will be expanded to 6 pts for recommended phase 2 dose regimens. The study received ethics approval for all sites involved.

Results Nineteen patients have completed at least one cycle of ICT01 plus IL-2. Treatment-related adverse events were mainly mild to moderate infusion-related reactions, comparable to those observed with ICT01 or IL-2 monotherapy. No dose-limiting toxicities were reported. A 2–11x increase of γ9δ2 T cell counts above baseline was observed for all 3 cycles across all cohorts peaking around day 8 to 15, which appeared greater at low doses where ICT01 was rapidly cleared, while prolonged target occupancy/activation by high doses prevented γ9δ2 T cells from remaining in the circulation. Activation, mobilization, and proliferation of CD8 T cells (2–3x) and NK cells (2–9x) cycles was similarly observed. Elevated levels of IFNγ, TNFα, IL-6 and IL-8 peaked at −4 hours post ICT01/IL-2 dose that returned to baseline despite expansion of γ9δ2 T cells. Increased Tregs by flow cytometry appear to be greater at lower doses of ICT01, which may be similar to effects observed in NHPs. Response data by RECIST1.1 every 8 weeks and IHC of tumor biopsies collected at baseline and on Day 28 will be presented.

Conclusion ICT01 plus LDSCL IL-2 produces a broad anti-tumor immune response that is durable across multiple treatment cycles, which appears different to prior attempts to expand γ9δ2 T cells with bisphosphonates or phosphoantigens.

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