

CORRELATION OF BASELINE CIRCULATING VG9VD2 T CELL COUNTS AND PHARMACODYNAMIC ACTIVITY OF ICT01 IN CANCER PATIENTS: PRELIMINARY RESULTS FROM EVICTION AND A NOVEL PATIENT ENRICHMENT STRATEGY

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Background ICT01, a novel, anti-BTN3A immunotherapeutic mAb for activating g9d2T cells, is currently evaluated in a Phase 1/2a clinical trial in patients with advanced-stage, relapsed/refractory cancer (NCT04243499, EVICTION). ICT01 indirectly activates g9d2 T cells that secrete inflammatory cytokines and migrate into tumors to coordinate antitumor immune responses. Therefore, the baseline number of g9d2 T effector cells constitutes a biomarker of interest and a potential selection criterion for target patients.

Methods Full immunophenotyping (cell counts and activation state) was performed by flow cytometry on fresh blood collected pre- and on-treatment. Serum cytokines were monitored at baseline and post-treatment. Tumor biopsies were harvested at baseline and on Day 28, and multiplex IHC coupled with digital pathology was used to quantify g9d2T cell, CD8 T cell, NK cell, and T reg infiltration and activation state

Results Baseline circulating g9d2 T cell count was highly variable in solid tumor patients enrolled in the monotherapy arm of EVICTION (median 6918 cell/mL, n=26). Melanoma and colorectal patients displayed respectively the highest (median 42277 cell/mL, n=3) and the lowest (median 3040 cell/mL, n=9) baseline number. During the dose escalation phase, g9d2 T cell activation (CD69+) and migration from the blood was observed 30 min post-ICT01 administration. Serum cytokine levels showed variability within ICT01 dose cohorts. IFN γ , TNF α , IL-6 and IL-8 levels post-ICT01 dosing were ICT01 dose dependent and clearly related to baseline number of circulating g9d2 T cells. Activation of peripheral blood NK cells, granulocytes and CD8 T cells was observed post-dosing at ICT01 doses \geq 7 mg, which was significantly correlated with baseline g9d2 T cell counts, but not with other immune subsets (Spearman $r=0.51$, 0.47 and 0.65 for CD69+NK, CD69+CD8 and PD-L1+granulocytes respectively, $p<0.05$, $n=19$). Baseline circulating g9d2 T cell count was positively correlated with gdTCR+ T cell density in baseline tumor biopsies (Spearman $r=0.76$, $p=0.0086$, $n=11$). Finally, a trend was observed between baseline g9d2 T cell counts and overall tumor immune cell infiltration and activation post-ICT01 treatment, with 4 patients (out of 13 with available biopsy pairs) with g9d2 T cell counts above the median displaying the highest tumor immune cell infiltration and activation.

Conclusions These results suggest the utility of measuring baseline g9d2 T cells as part of the patient selection process for ICT01 clinical trials. Patient enrichment based on this biomarker will be tested in EVICTION expansion arms where a minimum baseline threshold of g9d2 T cells counts will be one of the eligibility criteria.

Trial Registration NCT04243499

Ethics Approval The study has obtained Competent Authority and Ethics Committee approvals. Informed consent forms were obtained from all enrolled patients.

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