503 **CLINICAL ACTIVITY OF ICT01, AN ANTI-BTN3A-TARGETED, γ9δ2-ACTIVATING MAB, ALONE AND IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED/REFRACTORY SOLID TUMORS: EVICTION TRIAL**

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Background We presented EVICTION Trial data from patients with solid tumors that showed microgram doses of ICT01 rapidly activate γ9δ2 T cells that release inflammatory cytokines (e.g., IFNγ) and traffic from the circulation (Abstract #316, SITC 2020). Confirming tumor infiltration of activated γ9δ2 T cells and the subsequent clinical benefit are the next steps in characterizing the therapeutic potential of ICT01.

Methods EVICTION is an ongoing Phase 1/2a, EU and US trial assessing ICT01 monotherapy (IV Q3W) in advanced/refractory solid and hematologic cancers, and ICT01 in combination with pembrolizumab (200mg IV Q3W) in solid tumor patients who failed ≥1 CPI. Pharmacodynamic activity was monitored by immunophenotyping and cytokine level analysis. Tumor biopsies (baseline, Day 28) were used for immunohistochemistry of BTN3A and tumor-infiltrating lymphocytes, and gene expression profiling. Efficacy evaluations were conducted every 8 weeks.

Results ICT01 monotherapy dose escalation (20μg to 200mg IV ICT01 Q3W) in solid tumor patients (Group A, n=32) has been completed, and 3 dose cohorts of ICT01 (700μg, 2 and 7 mg) plus Pembro (Group C, n=12) were completed; both without any DLTs. First-dose fever and chills (Grade 1/2) were the most common AEs that increased in frequency but not severity with dose and did not recur.ICT01 induced trafficking of >95% of circulating γ9δ2 T cells within 30 min post ICT01 (≥2mg), which was sustained for 21 days at doses ≥75mg. Transient, dose-dependent increases in serum cytokines at 30 min (TNFα) or 4h (IFNγ) post-dose were correlated with baseline γ9δ2 T cell counts and with activation and migration of NK and CD8 T cells out of the blood at doses ≥7mg. Higher baseline circulating γ9δ2 T cells and lower TILs were associated with more robust intra-tumoral increases in total γδ(3–34x increase), CD3 (3–55x increase) and CD8 T cells (1.3–66x increase), which demonstrated the potential to transform an immune desert tumor phenotype. Disease control by ITT analysis of RECIST1.1 data was observed in 6/32 (SD) and 4/7 patients (3 SD (bladder, melanoma, NSCLC), 1 PR (bladder)) in Groups A and C, respectively, with 5/6 patients at 7mg in Group C not yet evaluable.

Conclusions These results show a broad antitumor immune response in the blood and tumors comprising γ9δ2, CD8 T cell, and NK cell activation and tumor-infiltration following ICT01 alone and in combination with pembrolizumab. Preliminary efficacy data suggest low-dose ICT01 plus pembrolizumab may be more effective than ICT01 monotherapy for advanced/refractory solid tumors, which requires confirmation.

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Trial Registration www.clinicaltrials.gov NCT04243499; EudraCT Number: 2019-003847-31

Ethics Approval This study was approved by the following Ethics Committees: COMITE DE PROTECTION DES PERSONNES, Sud-Méditerranée V (Gustave Roussy, IPC, Nantes), Comité d'Ethique Institut Jules Bordet, COMITÉ DE ÉTICA DE INVESTIGACIÓN CLÍNICA CON MEDICAMENTOS del Hospital Universitari Vall d'Hebron, Ethikkommission an der TU Dresden, HRA London-Surrey Borders Research Ethics Committee.

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.

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