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A FIRST-IN-HUMAN TRIAL OF HSTC810 (ANTI-BTN1A1 AB), A NOVEL IMMUNE CHECKPOINT WITH A MUTUALLY EXCLUSIVE EXPRESSION WITH PD-1/PD-L1, IN PATIENTS WITH RELAPSED/REFRACTORY SOLID TUMORS

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Background Butyrophilin 1A1 (BTN1A1) is a novel immune checkpoint with a mutually exclusive expression with PD-1/PD-L1 and may offer a promising therapeutic target for tumors that are anti-PD-1/PD-L1 antibody refractory. BTN1A1 was identified as a potential stress-inducible candidate immune checkpoint using the STCube *in vivo* immune checkpoint target discovery platform. Murine studies demonstrated that the anti-BTN1A1 antibody exhibited antitumor activity as a single agent as well as when combined with anti-PD-1/PD-L1 or radiation therapy. A humanized anti-BTN1A1 antibody, hSTC810, was developed and evaluated in immunologically cold A549 tumors that are unresponsive to anti-PD-L1 treatment. hSTC810-treated mice exhibited significantly reduced tumor volumes relative to hlgG4-treated control animals without any treatment-related toxicity. Humanized STC810 is currently being evaluated in a first in human study to identify hSTC810's maximally tolerated dose (MTD) and initial safety profile for patients with advanced solid tumors.

Methods A Phase I clinical study using a standard 3 + 3 escalation design to explore safety, tolerability, dose-limiting toxicities (DLTs), pharmacokinetics, define a recommended phase II dose (RP2D) and to evaluate preliminary efficacy in patients with advanced solid tumors is currently enrolling (NCT05231746). The study is a multi-site, non-randomized, open-label study with subjects ages >18 to be enrolled with various advanced solid tumors. Eligible patients receive hSTC810 intravenously (0.3mg/kg-15 mg/kg) once every 2-weeks as a single agent until disease progression or lack of tolerability. Dose expansion cohorts are planned at RP2D to further assess safety, pharmacokinetics (PK), pharmacodynamics and immunohistochemistry in pre-and post-treatment tumor tissue samples.

Results To date, 13 patients have been enrolled, and 2 dose levels have been completed. No DLTs have been observed and enrollment continues. Subject enrollment in the dose escalation cohorts is expected to be completed in the fourth quarter of 2022.

Conclusions Interim clinical data, including safety and tolerability and initial anti-tumor activity, from the ongoing Phase 1 dose-escalation study of STCube's hSTC810 in advanced solid tumors will be presented at the conference.

Trial Registration NCT05231746

Ethics Approval The study obtained ethics approval from Korea University Anam Hospital (2022AN008) and the other all participating institutions and a statement that participants gave informed consent before taking part.

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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