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INITIAL RESULTS FROM DOSE ESCALATION OF A PHASE 1/2 FIRST-IN-HUMAN, OPEN LABEL STUDY OF AU-007, A MONOCLONAL ANTIBODY THAT BINDS TO IL-2 AND PREVENTS ITS BINDING TO CD25, IN PATIENTS WITH SOLID TUMORS

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Background AU-007 is a computationally designed monoclonal antibody that binds IL-2 on its CD25 binding epitope. AU-007 bound IL-2 (A/IL-2) cannot bind to trimeric (CD25, CD122, CD132) IL-2 receptors (IL-2R) on Tregs and vascular endothelium, but leaving IL-2's binding to dimeric IL-2Rs (CD122, CD132) on T effector and NK cells unhindered. Therefore AU-007 redirects endogenous or exogenous IL-2 (aldesleukin) towards T effector and NK cell activation, while diminishing Treg activation and vascular leak. Unique in the IL-2 field, AU-007 can bind and redirect endogenous IL-2 generated from A/IL-2 driven T cell expansion in vivo, converting a Treg-mediated autoinhibitory loop into an immune-stimulating loop. Additionally, A/IL-2 is expected to substantially prolong the 90-minute T_{1/2} of IL-2, potentially allowing the use of endogenous IL-2 (as A/IL-2) alone to initiate an anti-tumor response. In non-human primates, AU-007 bound IL-2 with a similar affinity to human IL-2 and increased IL-2 serum concentrations in a dose-dependent manner while demonstrating an excellent safety profile.

Methods Phase 1 of this Phase 1/2 study (NCT05267626) consists of 3 dose escalation arms. Each Arm begins with one 1+2 escalation cohort followed by 3+3 escalation cohorts. In Arm 1A, escalating doses of monotherapy AU-007 (Q2W) are evaluated in sequential cohorts. In Arm 1B, AU-007 (Q2W) is evaluated in combination with a single low-dose of aldesleukin with the first AU-007 dose. The AU-007 dose will be fixed with escalating aldesleukin doses in sequential cohorts. In Arm 1C, AU-007 is evaluated in combination with escalating low-doses of aldesleukin, both given Q2W. The AU-007 and aldesleukin dose and schedule for Phase 2 cohort expansion in selected solid tumor types will be based on safety, objective signs of efficacy and PD parameters including increases of IL-2 concentration (as A/IL-2), total lymphocytes, CD8+ T cells, IFN- γ , and soluble CD25.

Results As of July 2022, two patients enrolled into dose escalation Arm 1A, 1 patient on 0.5 mg/kg (First In Human starting dose) and one patient into the second cohort (1.5 mg/kg). AU-007 was well tolerated with no drug related adverse events in the ongoing dose escalation.

Conclusions At this early data cut, AU-007 monotherapy given 0.5 mg/kg Q2W or 1.5 mg/kg Q2W was safe and well tolerated. Data from additional patients are expected to be presented in the poster.

Trial Registration NCT05267626

Ethics Approval HREC: Monash Health Human Research Ethics Committee CT-2021-CTN-03938-1

All of the participants in this study gave informed consent before taking part in the study.

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0775>