A Phase 1 Study of ADI-001: Anti-CD20 CAR-engineered Allogeneic Gamma Delta (γδ) T cells in Adults with B Cell Malignancies.

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Background:

ADI-001 is a first-in-class allogeneic gamma delta (γδ) CAR T cell therapy targeting the B cell antigen CD20. ADI-001 also has both adaptive and innate cytotoxic effector functions to complement CAR targeting, potentially enhancing efficacy and reducing the possibility of tumor escape due to antigen loss. ADI-001 expresses MHC independent γδ T cell receptors, thus lowering the risk of graft versus host disease (GvHD) without the need for gene-editing .

Methods:

This phase 1 trial evaluates ADI-001 in adults with relapsed/refractory advanced B-cell lymphoma. Eligibility criteria included presence of measurable lesions, expression of CD20 and ≥2 prior systemic therapies. All patients received conditioning therapy with fludarabine and cyclophosphamide. ADI-001 is administered at 3 flat dose levels (DL) (DL1:3E7, DL2:1E8, or DL3:3E8 cells) in a 3+3 dose-escalation scheme. Dose-limiting toxicities (DLT) were monitored during the initial 28-days post-treatment. Patients who completed the 28-day DLT period were considered evaluable. Treatment-emergent adverse events were graded by CTCAE v5.0, and immune effector cell toxicity assessment and grading were performed per ASTCT criteria. Objective response rates (ORR) were evaluated by independent radiographic review per Lugano 2014 criteria.

Results:

As of 14 February 2022, eight patients were enrolled and six were evaluable. Of these six patients, 2/6 were female (33%) and the median age was 62 years (range 45-75). The median number of prior therapies was 3.5 (range 2-5) and median IPI score was 3.5 (range 2-4). One patient received prior anti-CD19 CAR T cells therapy with lisocabtagene maraleucel. There were five patients with large B cell lymphoma and one with mantle

cell lymphoma. Among the six evaluable patients, three were treated on DL1 and three on DL2. Most related AEs (78%) were of Grade 1/2. There were three AESI: two CRS (one Grade 1 and one Grade 2) and one Grade 1 ICANS, and the only related SAEs were the Grade 2 CRS and Grade 1 ICANS. There was no reported GvHD and no protocol defined DLT events. At Day-28, the ORR based upon PET/CT was 67% (4/6 patients) and the CR rate was 67% (4/6 patients). Both patients with ≥ 3 months post-treatment follow-up remained in CR. Additional data will be presented at the meeting.

Conclusions: ADI-001 γδ CAR T cells were well tolerated, with a favorable safety profile and encouraging preliminary efficacy. Patients who achieved CR at Day-28 appeared to be disease free during further follow-up at Month-3.

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