A Phase 1 Study of ADI-001: Anti-CD20 CAR-Engineered Allogeneic Gamma Delta1 (γδ) T Cells in Adults with B-Cell Malignancies

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Introduction: ADI-001 is a first-in-class allogeneic gamma delta (γδ) CAR T cell therapy targeting the B-cell antigen CD20. ADI-001 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 multicenter phase 1 clinical trial is evaluating ADI-001 in adults with relapsed / refractory B-cell lymphoma. Eligibility criteria included the presence of measurable lesions, expression of CD20 on tumor cells and ≥ 2 prior systemic therapies. All patients received conditioning therapy with fludarabine and cyclophosphamide. ADI-001 can be administered at four

dose levels (DL) (DL1:3E7, DL2:1E8, DL3:3E8 and DL4:1E9 CAR+ cells) in a 3+3 dose-escalation scheme. Patients who completed the 28-day DLT period were considered evaluable. In DL3, patients could receive a second course of conditioning therapy and be re-dosed with ADI-001 if there was no DLT during the first 28 days, no progressive disease on PET/CT assessment on Day 28, and have recovered from cytopenias. Treatment-emergent adverse events were graded by CTCAE v5.0, and Immune Effector Cell Associated Neurologic Syndrome (ICANS) and Cytokine Release Syndrome (CRS) assessments were performed per ASTCT criteria. Objective response rates (ORR) were evaluated by independent radiographic review per Lugano 2014 criteria.

Results: As of 15 July 2022, 11 patients were enrolled and nine were evaluable. Of these nine patients, six (67%) were male and the median age was 62 years (range 45-75). Eight patients had large B-cell lymphoma (LBCL) and one had mantle cell lymphoma (MCL). Of the eight patients with LBCL, five had diffuse-large B-cell lymphoma (DLBCL), two had high-grade B-cell lymphoma (HGBCL) with double/triple hit, and one had HGBCL not otherwise specified. At baseline, the median IPI score was four (range 2-4); the median tumor burden was 2,974 (150-7,919) mm^2, and 89% (8/9) had stage III/IV disease. The median number of prior therapies was four (range 2-5). Four patients had prior anti-CD19 CAR T cell therapy (two Liso-cel and two Axi-cel). Among nine evaluable patients, three patients were treated at each of DL1, DL2, and DL3. Two patients at DL3 were re-dosed with a second course of ADI-001.

Two patients developed CRS: one Grade 1 and one Grade 2. One patient developed a Grade 1 ICANS which resolved within 24 hours. There were no ≥ Grade 3 CRS or ICANS. The only related SAEs were Grade 2 CRS, Grade 1 ICANS and Grade 3 adenoviraemia. There was no reported GvHD or protocol-defined DLT events. The best ORR was 78% (7/9), and the complete response (CR) rate was 78% (7/9). For the four patients who had prior CD19 CAR T therapies, the ORR was 100% (4/4) and CR rate was also 100%. As of the data cut-off date, of the seven patients who had achieved CR, two patients progressed, one died while in complete remission and four were still in CR and in active follow-up, with a range of follow-up time between 1.2 and 8.8 months. CAR+ γδ T cell kinetics improved in a dose-dependent manner with peak cell expansion occurring between Days 7 and 10 at DL3 based on flow cytometry.

Conclusions: ADI-001 γδ CAR T cells maintained a favorable safety profile. Preliminary efficacy showed encouraging CR rate and sustained durability in

patients, including those previously exposed to CAR T therapy. Additional data will be presented at the meeting.

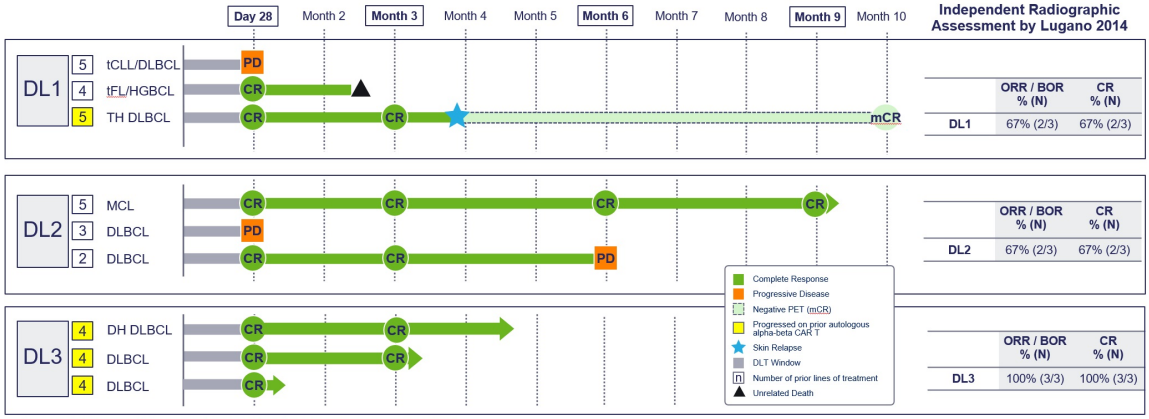

Figure 2. Preliminary Efficacy and Durability Results. Data cut-off date: 15 Jul 2022

TH=triple hit; DH=double hit; DLBCL=diffuse large B-cell lymphoma; tCLL=transformed chronic lymphocytic leukemia; HGBCL=high grade B-cell lymphoma; MCL=mantle cell lymphoma

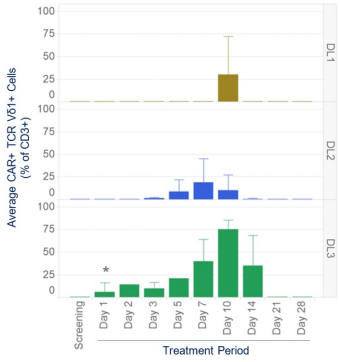

Figure 2. ADI-001 expansion in the peripheral blood based on flow cytometry analysis

CAR+ Vδ1 γδ T cells are gated on CD3+CAR+TCRαβ-TCRγδ+ cells. N=3 subjects per dose level (DL). Asterisk represents a sample was collected post-infusion of ADI-001 instead of pre-infusion.