High Durable CR Rates and Preliminary Safety Profile for JCAR017 in R/R Aggressive B-NHL (TRANSCEND NHL 001 Study): A Defined Composition CD19-Directed CAR T Cell Product with Potential for Outpatient Administration

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**Background:** JCAR017 is a CD19-directed 4-1BB CAR T cell product administered in a defined composition at a precise dose of CD8 and CD4 CAR T cells in a seamless design Phase 1 pivotal trial of relapsed/refractory (R/R) B-cell NHL (TRANSCEND NHL 001; NCT02631044). Patients with R/R DLBCL NOS (de novo or transformed from indolent lymphoma), PMBCl, FL grade 3B, or MCL and adequate organ function are eligible. No minimum ALC required; patients with failed prior allo-SCT, secondary CNS involvement, and ECOG 2 are eligible. The FULL dataset includes patients with DLBCL, PMBCl and FL grade 3B. The CORE dataset includes only patients meeting inclusion for a planned pivotal cohort (DLBCL NOS [de novo or transformed from FLJ], ECOG 0-1, no prior allo-SCT).

**Methods:** Patients with R/R DLBCL NOS (de novo or transformed from indolent lymphoma), PMBCl, FL grade 3B, or MCL and adequate organ function are eligible. No minimum ALC required; patients with failed prior allo-SCT, secondary CNS involvement, and ECOG 2 are eligible. The FULL dataset includes patients with DLBCL, PMBCl and FL grade 3B. The CORE dataset includes only patients meeting inclusion for a planned pivotal cohort (DLBCL NOS [de novo or transformed from FLJ], ECOG 0-1, no prior allo-SCT).

**Results:** As of July 7, 2017, 69 patients were treated in the DLBCL cohort and evaluable for safety, including 67 DLBCL NOS, 1 FL grade 3B, 1 PMBCl, 46% (67/225) were chemorefractory and 32% (46%) had any prior transplant. Thirty-eight patients were treated at dose level 1 (DL1, 5 x 10⁸ CAR T cells), 25 at dose level 2 (DL2, 1 x 10⁹ CAR T cells), and 6 at DL1 2-dose schedule. In the FULL dataset, 21 patients (30%) had CRs, with 1 serious CRS event (1%; Gr 4). Neurotoxicity (NT) at any grade was 32% (21/69), with 53% (21/40) of patients experiencing NT. Three patients (4%) had any grade 3 CRS or NT event. No serious infusional toxicity occurred, and the majority of patients, 64% (44/69), had no CRS or NT, suggesting outpatient delivery of JCAR017 may be feasible.

In the DLBCL cohort, 68 patients were evaluable for efficacy (FULL dataset); best overall response, 3-month, and 6-month response rates were 75% (51/68), 49% (27/55), and 40% (14/35), respectively. The best overall, 3-month, 6-month CR rates were 56% (38/68), 40% (22/55), and 37% (13/35), respectively. Among 16 double/triple hit patients, best ORR was 81%, and 3-month CR rate was 60%. A trend toward improved response rate at 3 months was observed in patients treated at DL2 compared with DL1.

Analysis of the planned pivotal population (CORE dataset; n = 49) shows similar rates of CRS and NT. Best overall, 3-month, and 6-month response rates were 84% (41/49), 65% (26/40), and 57% (13/23), respectively. The best overall, 3-month, and 6-month CR rates were 61% (30/49), 53% (21/40), and 52% (12/23), respectively. A similar trend in improved durable ORR and CR at 3 months at higher doses was again observed: 80% (12/15; 95% CI 52, 96) and 73% (11/15; 95% CI 45, 92) at DL2 compared to 52% (11/21; 95% CI 30, 74) and 33% (7/21; 95% CI 15, 57) in DL1 with P = .159 and P = .0409 respectively.

**Conclusions:** JCAR017 produces high overall and complete response rates in chemorefractory aggressive B-cell lymphomas, many of which appear durable. Rates of severe CRS and neurotoxicity were low and manageable, and support evaluation of outpatient administration. Updated efficacy and safety data will be presented.

Chimeric Antigen Receptor T-Cell (CAR-T) Therapy Can Render Patients with ALL Into PCR-Negative Remission and Can be an Effective Bridge to Transplant (HCT)

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**Background:** CAR-T therapy, while effective, may not be durable for all, and antigen negative escape is a growing problem. HCT, in relapsed/refractory ALL, can be curative, particularly for those in an MRD negative remission. We demonstrated that CAR-T therapy effectively rendered patients into MRD negative remissions (by flow cytometry (FC)) and the leukemia free survival post-HCT was high (Lee, ASH 2016, abstract 218). In this analysis, we further analyze the depth of remission, CAR-T persistence, and post-transplant toxicities to better understand the role of CAR-T in the peri-HCT setting.

**Design:** Children and young adults with relapsed/refractory CD19+ or CD22+ ALL treated on our phase I anti-CD19 (NCT01593696) or anti-CD22 CAR-T protocols (NCT02315612) were analyzed. The anti-CD19 CAR-T construct utilized a CD28 costimulatory domain; while the anti–CD22 CAR-T incorporated 41BB. MRD was assessed by flow cytometry (FC) in all. PCR based MRD analysis with IgH or TCR based testing was assessed in select patients on the anti-CD22 CAR-T trial. HCTs were performed at each patient’s local institution based on standard of care and included varying conditioning regimens, donor types, stem cell source, and GVHD prophylaxis.

**Results:** On our CD19 and CD22 CAR trials, 52 and 33 patients were treated, respectively. 51 patients attained a CR, of whom were MRD negative by FC (28 on CD19 CAR; 15 on CD22 CAR) of whom 25 went to transplant. The median time to HCT was 57 days (range: 44-126 days) post-CAR-T, which was a first HCT in 19, and a 2nd or greater HCT in 6. Using a competing risks analysis (risk of relapse vs transplant related mortality (TRM)), the 24-month cumulative incidence of post-HCT relapse of all HCT patients and limited to first HCT only was 13.5% (95% CI: 3.2-32.1%) and 11.3% (95% CI: 1.7-31.1%), respectively (Figure). 10 of 25 (40%) developed acute GVHD, which was grade 3-4 in 3 (12%). Six died from TRM, in 2, this was following a second HCT. PCR based MRD analysis available in 8 patients on the CD22 protocol demonstrated that all patients achieved PCR based negativity. In 6, this was simultaneous with the 1 month MRD negative FC, and in 2, PCR negativity was achieved over time (FC remained negative). Regarding CAR persistence, 10