Abstract: P1475

Title: C-CAR039, A NOVEL ANTI-CD20/CD19 BI-SPECIFIC CAR T-CELL THERAPY SHOWS DEEP AND DURABLE CLINICAL BENEFITS IN PATIENTS WITH RELAPSED OR REFRACTORY B-CELL NON-HODGKIN LYMPHOMA IN LONG TERM FOLLOW UP

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

Despite of the impressive anti-CD19 CAR T-cell therapies outcomes, relapse with CD19− disease remains a challenge. Targeting two different antigens may reduce the risk. C-CAR039, an autologous anti-CD20/CD19 bispecific CAR-T, previously demonstrated a favorable safety profile and promising efficacy among 28 patients (pts) with relapsed or refractory B-cell Non-Hodgkin lymphoma (r/r B-NHL), with 92.6% ORR and 85.2% CR. Here, we present the updated results.

Aims:

To evaluate safety and efficacy profile of C-CAR039 for r/r B-NHL patients.

Methods:

This investigator-initiated trial is an open-label, dose escalation and expansion study of C-CAR039. Pts with r/r diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL) were enrolled and received a single C-CAR039 infusion at a dose of 1.0-5.0x106 CAR-T cells/kg. The primary objective was to assess the safety and tolerability. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded according to ASTCT 2019 criteria. The secondary objectives were to evaluate C-CAR039 efficacy and pharmacokinetics. Response was assessed per Lugano 2014 criteria.

Results:

Between Nov 5, 2019, and Jan 11, 2022, 48 pts received C-CAR039 manufactured using Miltenyi Biotec CliniMACS Prodigy® System. Of the 48 pts, 44 pts had large B-Cell Lymphoma (LBCL) (DLBCL, n = 37; transformed FL, n=4; PMBCL, n = 3), 3 pts had FL and 1 had MCL. The median age was 55 years (range, 25-71), and 11 (22.9%) pts were ≥ 65 years. Thirty-six (75%) pts were in Ann Arbor Stage III/IV with a median of 3 prior lines of therapy. All pts received anti-CD20 antibody and alkylating agents. Eight (16.7%) pts had prior ASCT, and 22 (45.8%) pts never achieved CR to their prior therapies. Prior to C-CAR039 infusion, 12 (25%) pts received bridging therapy.

As of Sep 25, 2023, 45 out of 48 pts (93.8%) experienced CRS, and only 1 (2.1%) was grade 3. The median time to CRS onset was 3 days (range, 1-12), with a median duration of 5 days (range, 2-78). Three pts at the dose of 5.0x106 CAR-T cells/kg had ICANS, of which 2 were grade 1 and 1 was grade 2. The median time to onset of ICANS was 6 days (range, 5-29), with a median duration of 12 days (range, 3-53). All CRS and ICANS were resolved. Grade 3 or higher cytopenias not resolved by Day 30 following C-CAR039 infusion included neutropenia (54.2%), anemia (20.8%) and thrombocytopenia (20.8%). Grade 3 or higher infections were observed in 12 (25.0%) pts. Second primary malignancy after C-CAR039 infusion were observed in 3 pts and none were related to C-CAR039. Fifteen deaths occurred, where 11 were due to disease progression, 2 were due to AE of AML, and 1 was due to an unknown cause.

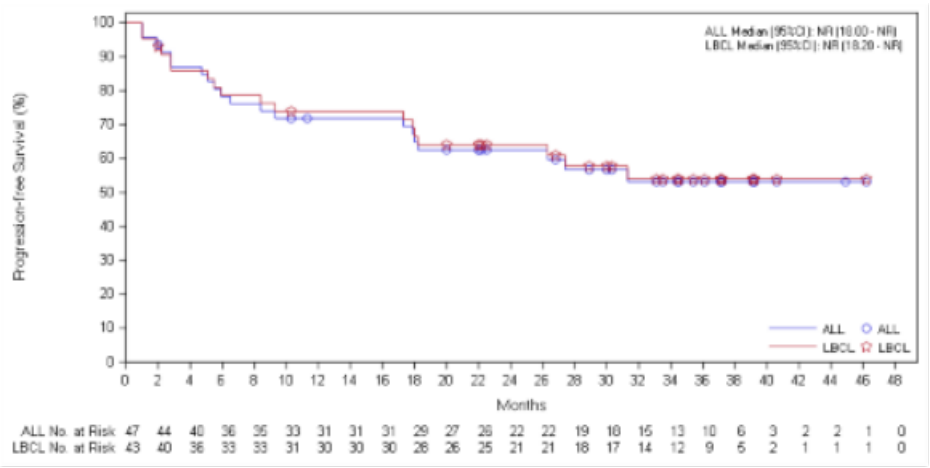
Of the 48 pts, 47 were evaluable for efficacy (1 patient had no measurable disease at baseline). The ORR and CR rate were 91.5% and 85.1%, respectively. The median time to the first response and to CR were 1.0 and 1.2 month, respectively. Among the 43 LBCL pts, they showed 90.7% ORR and 86.0% CR rate. Median DOR, PFS

and OS were all not reached. The KM estimation of PFS and OS rate for all pts at 24 months were 62.6% and 76.5%, respectively.

The pharmacokinetic profile showed C-CAR039 has a robust expansion and long-term persistence, with median Tmax and Tlast of 11.5 days and 216 days, respectively.

Summary/Conclusion:

With median follow-up of 30.0 months, C-CAR039 demonstrated a favorable safety profile with deep and durable response in pts with r/r B-NHL, especially in LBCL pts.



Keywords: CAR-T, CD20, CD19, B cell lymphoma