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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Two-Year Follow-up Results of C-CAR066, a Novel Anti-CD20 Chimeric Antigen Receptor Cell Therapy (CAR-T) in Relapsed or Refractory (r/r) Large B-Cell Lymphoma (LBCL) Patients after Failure of CD19 CAR-T Therapy

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Background:
Disease recurrence or progression represents a significant challenge in r/r LBCL treated with CAR-T. In a large analysis of r/r LBCL pts who receive further therapy after CD19 CAR-T treatment failure, the overall response rate (ORR) is 39% (CR 20%; PR 19%) and the median post-treatment-OS and post-treatment-EFS are 8.5 months and 1.9 months respectively. C-CAR066 is a novel 2nd generation CAR-T therapy targeting CD20 antigen. We previously reported that C-CAR066 had shown a favorable safety profile and promising efficacy in pts with r/r LBCL following failure to CD19 CAR-T therapy. At a median follow-up of 4.2 months, the ORR was 100%, with 70.0% (7/10) achieving complete response (CR) (Liang et al. ASCO 2021. #2508). Here we present the updated results to include more pts (n=14) and a longer follow-up period.

Methods:
This first-in-human (FIH) study is an open-label, dose-finding, phase 1 investigator-initiated trial (IIT) to determine the safety and efficacy of C-CAR066 in r/r LBCL (including DLBCL, tFL and PMBCL) after previous CD19 CAR T-cell treatment failure. This study was conducted at two clinical sites in China.
C-CAR066 was administered at doses of 2.0x10 ^{6} CAR-T cells/kg and 3.0x10 ^{6} CAR-T cells/kg after a 3-day conditioning chemotherapy. The primary objective was to assess the safety and tolerability of C-CAR066. 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-CAR066 efficacy and pharmacokinetics (PK). Response was assessed per Lugano 2014 criteria. The study follow-up period was 2 years.

Results:
Between Oct 16, 2019, and Aug 17, 2021, a total of 14 pts received C-CAR066. 11 pts (78.6%) were DLBCL, 3 pts (21.4%) were tFL. The median age was 54.5 years (range, 37-67) with 2 pts (14.3%) ≥65 years. 12 pts (85.7%) were in Ann Arbor Stage III/IV. 7 pts (50.0%) were double-expressor lymphoma. Median number of prior lines of therapy was 5 (range, 2-7). All pts had prior CAR-T therapy, which included CD19 CAR-T (12 pts), CD19/CD22 bispecific CAR-T (1 pts), and CD19/CD79b bispecific CAR-T (1 pts). 12 pts responded to the prior CAR-T therapy (2 CR and 10 PR), and the median duration of response (DOR) was 1.5 months. Median time from prior CAR-T to C-CAR066 infusion were 5.45 months (range, 3.4-14.2). 7 pts (50.0%) received bridging therapy.
As of Jan 15, 2023, 12/14 pts (85.7%) experienced CRS, all were grade 1/2, except for 1 pt dosed at 3.0×10 ^{6} CAR- T cells/kg experienced a grade ≥3 CRS. This pt recovered after receiving corticosteroids and tocilizumab. The median time to CRS onset was 5.5 days (range, 2-15), and the median time to resolution was 4.0 days (range, 1-15). No pts experienced ICANS.

Grade ≥3 neutropenia, anemia, thrombocytopenia, and infection were reported in 92.9%, 50.0%, 21.4% and 14.3% of pts, respectively. No new safety signals were observed in this updated 2-year follow-up.
Investigator assessed ORR was 92.9%, with 57.1% CR. Median time to first response and CR were 1.0 month (range, 0.9-2.8) and 2.5 month (range, 1.0-2.8), respectively. With the median follow-up of 19.5 months, median PFS and DOR were 9.4 months and 8.3 months, respectively. 5 pts remained in CR 12 months after infusion, and 4 of them remained in CR after 24 months. 6 deaths occurred due to progressive disease. Median post-treatment-OS had not been reached at 24 months.
13 of 14 pts had assessable PK and pharmacodynamic data (one pt dropped out before day 28). The median T_{max} was 11 days (range, 10-23), the median C_{max} was 398,996 copies/μg gDNA (range, 51,667-1,286,932), and the median $AUC_{0\text{-}28day}$ of 4,437,474 copies/μg•day (range, 431,534-17,842,217), the median T_{last} was 59 days (21~571). We have observed that C-CAR066 can effectively expand and eliminate CD19+/CD20+ B cells in patients. The median time to B cell depletion was 5.5 days (range, 4-11). B cell recovery was observed in 6 (46.2%) pts from 53 to 366 days after the C-CAR066 infusion, 3 of them remained in CR by the data cutoff date.

Conclusions:

Longer term follow-up demonstrated that C-CAR066 can produce a deep and durable response with a favorable safety profile in pts with r/r LBCL who failed prior CD19 CAR-T therapy.

Disclosures Zhu: *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Huang:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Li:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Zhu:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Zheng:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Yao:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Wan:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company. **Yao:** *Cellular Biomedicine Group Inc:* Current Employment, Current holder of *stock options* in a privately-held company.

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