Abstract: P1438

Title: INATICABTAGENE AUTOLEUCEL(CNCT19) IN RELAPSED OR REFRACTORY B-CELL LYMPHOMA: RESULTS OF A PHASE I CLINICAL TRIAL

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

CAR-T cell therapies have exhibited efficacy in patients with relapsed or refractory B-cell malignancies. We have developed a unique autologous CD19-specific second-generation chimeric antigen receptor (CAR) T-cell product, inaticabtagene autoleucel (CNCT19), featuring a patent-protected CD19 scFv derived from clone HI19α (distinct from the commonly used FMC63) and a 4-1BB/CD3-ζ costimulatory domain. In November 2023, CNCT19 received approval in China for the treatment of adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia. Here, we report the results of a phase I clinical trial of CNCT19 in patients with relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (R/R B-NHL).

Aims:

The primary objective was to assess the safety profile, dose-limiting toxicities (DLTs), and the recommended phase II dose (RP2D) of CNCT19. Secondary objectives included preliminary antitumor activity, and pharmacokinetics (PK).

Methods:

This phase I, single-arm, open-label study (NCT04232826) with a dose-escalation design was conducted at two centers in China. Enrolled patients were R/R B-NHL patients who had previously received at least two lines of therapy or relapsed after autologous stem-cell transplantation (ASCT). A single dose of CNCT19 was administered 2 to 5 days after lymphodepleting chemotherapy containing fludarabine (30mg/m^2/day for 3 days) and cyclophosphamide (500mg/m^2/day for 2 days). The trial employed a “3+3” design for dose escalation across three dose level (DL) cohorts: DL1 (1×10^8), DL2 (2×10^8), and DL3 (4×10^8) CAR+ T cells.

Results:

Between January 15, 2020, and November 1, 2022, 14 patients underwent screening, with 9 proceeding to leukapheresis and subsequently receiving CNCN19 treatment. Among the 9 patients, 5 had diffuse large B-cell lymphoma, and 4 had transformed follicular lymphoma. The median age was 50 years (range, 36 to 65), with the majority (77.8%) presenting with advanced stage III/IV disease. The median line of prior systemic therapies was two (range, 2 to 4). Five (55.6%) patients were refractory to the last line of therapy, and 2 had undergone prior ASCT. More than half (55.5%) of the patients suffered a large tumor burden with SPD≥5000mm^2. Three patients were treated at DL1, and six at DL2. No DLTs were observed at the two dose levels. DL3 wasn’t performed as it met the efficacy target according to investigators’ assessment, and DL2 was determined as the RP2D after DSMB evaluation. The most common adverse events (AEs) were laboratory abnormalities and cytokine release syndrome (CRS)(Figure 1). Six (66.7%) patients experienced CRS, all of which were grade 1 or 2, and no cases of immune effector cell-associated neurotoxicity syndrome were reported. As of November 1, 2022, the median follow-up since CNCT19 infusion was 24.1 months (range, 3.9 to 27.3). The overall response rate was 66.7%, with 55.6% achieving complete response (CR). The median duration of response was not reached (95% CI, 1.18 months to Not Available. Median overall survival (OS) was not reached (95% CI, 3.94 months to NA), with 2-year progression-free survival and OS rates of 33.3% and 66.7%, respectively. CNCT19 peaked at a median of 14 days (range, 9 to 59) post-infusion and remained detectable in two of three (66.7%) ongoing CR patients at 2 years.

Summary/Conclusion:

Inaticabtagene autoleucel demonstrated favorable safety and promising efficacy in patients with R/R B-NHL. A phase II multicenter clinical trial (NCT04586478) evaluating the administration of CNCT19 at a target dose of 2×10^8 (±20%) CAR+T cells in R/R large B-cell lymphoma is currently underway.

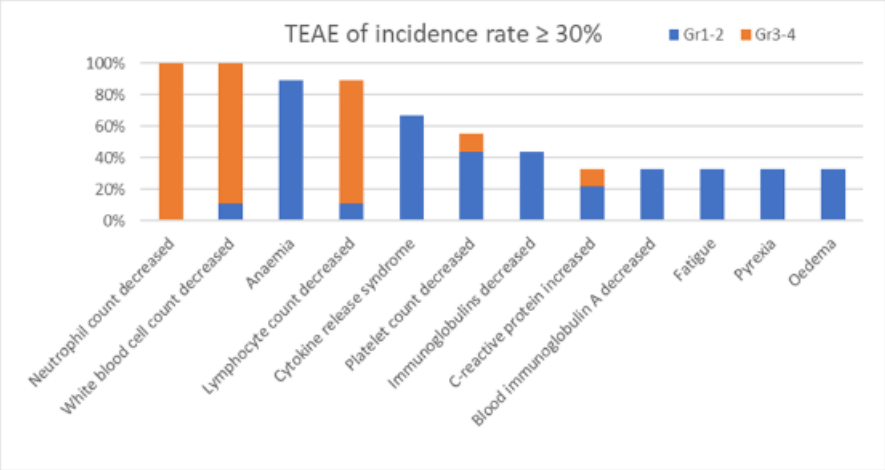

Figure.1 All Grade treatment-emergent adverse event (TEAE) ≥30% Incidence in 9 patients.

Keywords: B cell lymphoma, CD19, CAR-T