(PS2335) PD-1AB21-EXPRESSING, ANTI-CD19 CAR T CELLS FOR PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: AN OPEN-LABEL, SINGLE-ARM, PHASE 1 STUDY

Topic: 26. Gene therapy, cellular immunotherapy and vaccination - Clinical

Bo Peng*[1], Liping Dou[2], Dai-Hong Liu[2]

[1]Senior Department of Hematology, Chinese PLA General Hospital, Beijing, China;[2]The Fifth Medical Center of Chinese PLA General Hospital, Chief Department of Hematology, Beijing, China;

Background

While CD19-directed chimeric antigen receptor (CAR) T-cell therapy has improved outcomes for relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL), primary resistance, relapse, and limited response durability remain significant challenges. Strategies to overcome these limitations, including combination with PD-1 blockade, often face issues with systemic toxicity and variable efficacy.

Aims

We aimed to assess the safety, feasibility, and preliminary efficacy of a novel CD19-directed CAR T-cell product engineered to express a bifunctional fusion protein targeting PD-1 and interleukin-21 (PD-1Ab21-CD19 CAR-T) in patients with R/R DLBCL.

Methods

In this open-label, single-arm, phase I trial, patients (aged 14–75 years) with CD19-positive R/R DLBCL received lymphodepletion with fludarabine/cyclophosphamide, followed by a single infusion of PD-1Ab21-CD19 CAR-T cells at doses of 0.3, 1, 3, or 9×10^6 cells/kg. The primary endpoint was the safety and feasibility of PD-1Ab21-CD19 CAR-T cell. Secondary endpoints included efficacy, CAR-T persistence, progression-free survival (PFS), and overall survival (OS).

Results

Between November 2022 and October 2024, 14 patients received PD-1Ab21-CD19 CAR-T cell infusion. Cytokine release syndrome (CRS) occurred in 11 patients (78.6%; grade 3: 7.1%), with a median onset of 10 days. Immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 1 patient (grade 3, 7.1%). No treatment-related mortality or unexpected immune-related adverse events were observed. The overall response rate was 71.4%, with 57.1% achieving complete metabolic remission. At a median follow-up of 22.2 months, the 6-month PFS and OS rates were 64.3% and 71.4%, respectively(Figure 1).
Figure 1. Response of R/R DLBCL patients treated with PD-1Ab21-CD19CAR-T. a. Individual patient swimmer plots and their response to PD-1Ab21-CD19CAR-T over time. b. PET/CT scans of patient 3 before and 1 month after PD-1Ab21-CD19CAR-T infusion, demonstrating CMR. c. Overall survival in patients treated with PD-1Ab21-CD19CAR-T. d. Progression-free survival in patients treated with PD-1Ab21-CD19CAR-T.

Summary/Conclusion

PD-1Ab21-CD19 CAR-T therapy demonstrated a manageable safety profile and promising antitumor activity in patients with heavily pretreated R/R DLBCL. The localized delivery of PD-1 blockade and IL-21 via engineered CAR-T cells may mitigate systemic toxicity while enhancing efficacy. These findings warrant further in