Abstract: P1168

Title: *DURABLE REMISSION AFTER SEQUENTIAL CD19/20 CAR T-CELL "CAKE-ICING" THERAPY OCCURRED IN REFRACTORY/RELAPSED DLBCL*

Abstract Type: Poster Presentation

Session Title: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

The prognosis for patients with refractory/relapsed (R/R) diffuse large B-cell lymphoma (DLBCL) is poor. CD19 chimeric antigen receptor (CAR) T cell therapy has dramatically improved objective response rate, however, up to 70% eventually develop progression after treatment with CD19CAR T-cell therapy, usually within 1 year. Antigen escape and short duration of CART cell persistence in vivo are important determinants of recurrence. CD20 is an important target for the treatment of lymphoma, and CD20 monoclonal antibody has dramatically changed the treatment landscape for B cell lymphoma, to which sequential different targeting of CD19 and CD20 has been proposed as a potential solution.

Aims:

The study was conducted to explore the effectiveness and safety of sequential CD19/20 CAR T cell therapy in advanced R/R DLBCL.

Methods:

From March 2019 to January 2022 in Beijing Boren hospital, we conducted a pilot study (Clinical Trials Number: ChiCTR1900020980) in 21 patients who had advanced R/R DLBCL. All patients received lymphodepleting chemotherapy before CD19CAR T cells infusion (cycle-CD19CART), and CD20CAR T-cells were subsequently infused (cycle-CD20CART) when CD19 CAR T cells undetectable by FCM in peripheral blood or before the possibility of relapse (named cake-icing therapy).

Results:

1. Enrolled in this trial were 21 patients. Among them, 7 (33.3%) were older than 60 years, and 14(66.7%) had high IPI scores (≥3). A higher disease burden (bulky ≥5cm) was observed in 10(47.6%). All patients received ≥3 lines of treatment.2. All 21 patients (100%) had a response to CD19CART including 8CRs and 13PRs. Before CD20CAR T-cell infusion, all patients had remained in CR and PR. After CD20CART treatment, 8 patients who had a CR at month 3 maintained their responses, and 10 of 13 patients who had a PR within 3 months continued to have a CR. With a median follow-up of 24.7 months (range, 11.64-45.86), 15 patients remained in CR, and 6 developed progressives one of whom was dead. The median progressive-free survival (PFS) and median overall survival (OS) were not reached. The 3-year PFS rate and the 3-year OS rate were 74.2% and 95.2%, respectively. Notably, there were no significant differences in PFS(p=0.395) or OS (p=0.433) when compared to patients who achieved PR in cycle-CD19CART with patients who achieved CR in cycle-CD19CART.3. The median infusion dose of CD19CAR T-cells was 1.9×10^6/kg(range,0.04-10), and that of CD20CAR T-cells was 1.56×10^6/kg(range,0.06-5.64). There was no significant difference between the two types of CART-cell dose(p=0.35). While the median amplification peak of CD20CART was not as high as that of CD19 CART (3.61×10^6/L vs 60×10^6/L, p<0.0001), and the median time of duration of CD20CART was not as long as that of CD19 CART (21 days vs 30 days, p=0.009). The median interval between the 2 cycles of infusion was 3.72 months（range,2.56-9）.4. Cytokine release syndrome（CRS） occurred in 17 of 21 patients in cycle-CD19CART and was severity (≥grade 3) in 2 patients; immune effector cell-associated neurologic toxicity（ICANS） was observed in one patient, and no serious ICANS occurred. While in cycle-CD20CART， 17 patients experienced CRS and all had mild or moderate（grade 1-2）; no ICANS occurred.

Summary/Conclusion: Sequential CD19/20 CAR T cell "cake-icing" therapy can induce a durable response without serious side effects. CD20-a different targeting CART as consolidation therapy after CD19 CART may

extend CAR T-cell persistence and improve long-term outcomes.

Keywords: CAR-T, Lymphoma therapy, Diffuse large cell lymphoma