ELSEVIER

Blood 142 (2023) 3484–3485

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Efficacy and Safety of TLR2 Co-Stimulated CAR T Cells in CD19-Positive Lymphoid Malignancies with Central Nervous System Involvement

Bailin He, PhD[1], Hongsheng Zhou, MD[1], Ren Lin[2], Zhixiang Wang[3], Na Xu[1], Qiang Wang, MD[1], Jing Sun, Mphil, BEng[4], Xiaoli Liu[1], Peng Li, PhD[5], Qifa Liu, MD[2]

[1] Department of Hematology, Nanfang Hospital, Southern Medical University, Guangzhou, China
[2] Nanfang Hospital, Southern Medical University, Guangzhou, China
[3] Nanfang Hospital, Southern Medical University, Guangzhou, CHN
[4] Nanfang hospital of southern medical university, guangzhou, China
[5] Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China

Background
CD19 chimeric antigen receptor (CAR) T cell therapy showed remarkable remission rates in patients with refractory or relapsed (R/R) non-Hodgkin's lymphoma (NHL) and acute lymphoblastic leukemia (ALL). However, data on outcomes of CAR T cell therapy for patients with central nervous system (CNS) involvement are limited, as most of them have been excluded from most pivotal CAR-T studies because of concerns about treatment-related neurotoxicity. Here, we show results of a third generation of CD19 CAR T cells for patients with R/R B cell cancers with CNS involvement in a single-center cohort study.

Methods
A total of 21 patients with R/R B cell malignancies (including ALL and NHL) with CNS involvement were included in this study. Patients derived peripheral lymphocytes were collected through apheresis and lentivirally transduced with a 3 rd generation CAR containing CD28 and TLR2 co-stimulatory domains. The cells were expanded ex vivo and administered in a single infusion (1×10^6 or 2×10^6 CAR T cells per kilogram of body weight) after a conditioning regimen of cyclophosphamide and fludarabine.

Results
Of the 21 patients with CNS involvement, 11 patients with ALL and 10 with NHL were included in this study, with a data cutoff of July 2023. All 11 patients with ALL had both bone marrow (BM) and cerebrospinal fluid (CSF) involvement. Of the 10 patients with NHL, 5 of the 10 lymphoma patients had parenchyma involvement, 6 patients (6/10) had CSF infiltration and 1 had oculus sinister involvement; the majority of patients (8/10) were diagnosed with secondary CNS lymphoma, whereas 2 patient was primary CNS lymphoma. Of the 21 patients who were treated, the overall response rate (ORR) was 71% (15/21), with 73% (8/11) in ALL and 70% (7/10) in NHL. 67% of patients with ALL (7/11) had a complete remission in both BM and CSF, while 40% of NHL patients (4/10) had a complete response and 30% (3/10) received a partial response. The median overall survival (OS) of ALL was 14.3 months, with a median follow-up of 20.3 months, while the median OS of NHL was not reached with a median follow-up of 14.2 months. Median progression-free survival (PFS) of ALL and NHL were 11.1 months (95% CI, 0.7-29.9 months) and 4.8 months (95% CI, 1.0-15.3 months), respectively ($P = 0.84$). In the total CNS cohort, cytokine release syndrome (CRS) of any grade was seen in 20 patients (95%), grade 3 in 3 patients (14%). ICANS occurred in 9 patients (42.8%, including 5 ALL and 4 NHL patients), grade 3 in 5 patients (23.8%), and there was no grade 4 event. Median time to ICANS was 5 days (range, 2-10 days) after CAR-T infusion. All the CRS or ICANS were manageable. No significant difference in occurrence of and time to ICANS was seen between ALL and NHL patients ($P = 0.22$ and 0.96). CAR T cells were identified in CSF of patients following infusion, and the median time to peak CAR T cells in CSF of ALL and NHL were 6.5 days and 10 days post-infusion, respectively ($P = 0.141$). Median time to last documented follow-up of all patients (alive or dead) was 18.1 months (range 1.0-31.2 months). At the end point of observation, 5 of the 11 ALL patients and 5 of 10 NHL patients were still alive with sustained CR of CNS disease and systemic disease (Figure 1).

Conclusion
TLR2-costimulated CAR T cell therapy for patients with R/R B cell malignancies with CNS involvement is safe, feasible, and results in high response rates and durable remission in both ALL and NHL patients with CNS disease. The clinical trial was registered at www.clinicaltrials.gov as # NCT04605666.

Disclosures Li: *Wellington Zhaotai Therapies Limited:* Current equity holder in private company; *Guangdong Zhaotai Biomedicine Ltd:* Current equity holder in private company, Patents & Royalties.

https://doi.org/10.1182/blood-2023-184492