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ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE CLINICAL TRIALS AND TOXICITIES

CD19 CAR T-Cell Therapy in Refractory Autoimmune Hemolytic Anemia

Ruonan Li[1,2,3], *Lele Zhang*[3,2,2], *Hong Pan*[4,3,3], *Weiwang Li*[5,3,2], *Jiaxiu Ma*[3,1], *Linzhu Tian*[1,3,2], *Yucan Shen*[3,2,1], *Zhen Gao*[1,2,3], *Jingyu Zhao, MSc*[2,3,1], *Ke Huang*[3,2,1], *Liyun Li*[3,2,1], *Xiao Yu*[2,1,3], *Zhexiang Kuang*[6,2,3], *Meili Ge*[3,7,8], *Liwei Fang*[1,3,2], *Lijun Liu*[1,3], *Weiping Yuan*[9,3], *Shuo Chen*[1,3], *Lulu Lv, PhD*[10], *Junhong Song*[10], *Yi Feng*[10], *Haiqing Xiong*[1,3], *Jun Shi*[2,3,1]

[1] State Key Laboratory of Experimental Hematology National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[2] Red Blood Cell Diseases Center & Regenerative Medicine Clinic, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[3] Tianjin Institutes of Health Science, Tianjin, China
[4] Red Blood Cell Diseases Center & Regenerative Medicine Clinic, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[5] State Key Laboratory of Experimental Hematology,National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[6] State Key Laboratory of Experimental Hematology National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[7] State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China
[8] State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[9] State Key Laboratory of Experimental Hematology, Institute of Hematology & Blood Diseases Hospital, National Clinical Research Center for Blood Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[10] Juventas Cell Therapy Ltd, Tianjin, China

CD19 chimeric antigen receptor (CAR) T-cell therapy emerged as a novel treatment in autoimmune diseases. Refractory autoimmune hemolytic anemia (rAIHA) is characterized by life-threatening hemolysis, and traditional B-cell-targeting treatments often fail to halt the disease. We hypothesize that resetting aberrant autoimmunity through deep depletion of B cells by CD19 CAR T-cell could be a potential strategy for rAIHA to achieve sustained drug-free remission (DFR).

Refractory AIHA patients who had failed at least three lines of therapies were enrolled in a compassionate-use CD19 CAR T-cell program (n = 5) and phase I clinical trial (NCT06231368) (n = 3) to evaluate the safety and efficacy. Patients received a single dose infusion of autologous CD19 CAR T-cell 1×10^6 cells/kg (compassionate use) and 0.5×10^6 cells/kg (phase I clinical trial, dose 1) respectively after preconditioning with fludarabine (25 mg/m²/day on days -5 to -3) and cyclophosphamide (1.0 g/m²/day on day -3). Safety assessments included cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), hematologic and non-hematologic toxicities were assessed according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Efficacy was evaluated based on hemoglobin levels and biochemical markers of hemolysis. Single-cell RNA sequencing (scRNA-seq) and single-cell V(D)J sequencing were performed to monitor the process of B cell reconstitution in bone marrow (BM) and peripheral blood (PB) at baseline, 12 weeks (W12), and month 6 (M6) after CD19 CAR T-cell infusion.

As of July 31, 2024, the median follow-up time for the 8 patients were 6.8 months (range, 0.8-10.5 months). The safety profile in these 8 patients was satisfactory: 5 patients experienced grade 1 CRS, and two patients experienced grade 2 CRS. One

patient each had grade 1 CRS and grade 1 ICANS. No hospitalization due to severe infections occurred during the follow-up period. Among the 7 patients currently evaluable for efficacy, all achieved complete remission (CR), yielding a CR rate of 100%. One relapse was observed in compassionate-use UPN2 of at 6.8 months, maintaining DFR for 6.3 months. The median duration of sustained DFR was 6.3 months (range, 1.3-9.7 months). The median time to partial remission (PR) was 15 days (range, 11-27 days) and to CR was 57 days (range, 26-118 days). CAR T-cell levels rapidly expanded after infusion, reaching peak concentrations at a median time of 10 days (range, 7-11 days). At the peak of expansion, the median number of circulating CAR T-cell was 118.8 cells/ul (range, 44.9 to 244.6 cells/ul). B-cell aplasia lasted a median of 85 days (range, 57-91 days) in 6 patients who have undergone immune B cells reconstitution. scRNA-seq and single-cell V(D)J sequencing data showed that B-cell lineage and plasmablasts were reset in both BM and PB.
CD19 CAR T-cell therapy induce rapid remission, unprecedented DFR, and favorable safety profile in rAIHA patients. These exciting data support CAR T-cell as a novel strategy for autoimmune hemolytic anemia, and provide rationale for further clinical trials.

Disclosures No relevant conflicts of interest to declare.

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