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ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Dasatinib and CAR-T Cell Therapy for Newly Diagnosed Ph-Positive Acute Lymphoblastic Leukemia in Adults

Mingming Zhang[1,2,3,4], *Yongxian Hu*[4,2,3,1], *Guoqing Wei*[5,2,3,4], *Shan Fu*[1], *Jingjing Feng*[1], *Ruimin Hong*[1], *Alex H. Chang*[6], *He Huang*[7,5,8,3]

[1] Bone Marrow Transplantation Center, the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China
[2] Institute of Hematology, Zhejiang University, Hangzhou, China
[3] Zhejiang Province Engineering Laboratory for Stem Cell and Immunity Therapy, Hangzhou, China
[4] Liangzhu Laboratory, Zhejiang University Medical Center, Hangzhou, China
[5] Bone Marrow Transplantation Center, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China
[6] Shanghai YaKe Biotechnology Ltd, Shanghai, China
[7] Liangzhu Laboratory, Zhejiang University Medical Center, Hangzhou, China
[8] Institute of Hematology, Zhejiang University, Hangzhou, China

Introduction
The use of tyrosine kinase inhibitors has improved outcomes of Ph-positive Acute lymphoblastic leukemia (ALL), but combinations with other agents are needed to achieve molecular response. CAR-T cell therapy has made a breakthrough in refractory or relapsed ALL, but has not yet been applied in newly diagnosed patients.
Methods
We conducted a phase 2 single-group trial of first-line therapy in adults with newly diagnosed Ph-positive ALL. Dasatinib in combination with a two-week vincristine and glucocorticoids regimen were administered, followed by sequential infusions of CD19 and CD22 CAR-T cells. All patients received single-agent dasatinib maintenance after CAR-T cell therapy. The primary endpoint was complete molecular response (defined as undetectable *BCR/ABL1* transcript with a sensitivity of 0.001%) in the bone marrow after this treatment. Here we report initial results from this study.
Results
At the cut-off date of 31 May 2023, 18 patients have received CD19 CAR-T cell infusions, and 14 of these patients have received subsequent CD22 CAR-T cell infusions. At the end of induction therapy, the complete hematologic remission rate was 100%, and 27.8% (5/18) of the patients had a complete molecular response. The percentage of complete molecular response increased to 72.2% (13/18) after CD19 CAR-T cell therapy, and increased further to 76.9% (10/13) after CD22 CAR-T cell therapy (1 patient has not been evaluated). Notably, of the 5 patients who did not achieve complete molecular response after CD19 CAR-T cell therapy, 4 have received CD22 CAR-T cell therapy, of which 1 eventually achieved complete molecular response and 2 experienced relapses. One patient had a CD19+ CD22+ relapse accompanied by mutations in *BCR/ABL1* (F317L and Y253H) and the other patient had a CD19dim CD22+ relapse. After a median follow-up of 13.5 months, 16 patients remained in complete hematologic remission, and 14 patients remained in sustained complete molecular response. No patient received allogeneic stem cell transplantation. No grade 3 or higher cytokine release syndrome or Immune effector cell-associated neurotoxicity syndrome was observed during CAR-T cell therapies.
Conclusions
Dasatinib in combination with CAR-T cell therapy has enabled chemotherapy-free treatment in newly diagnosed Ph-positive ALL. This treatment is characterized by high complete molecular response, high long-term survival, low toxicity and short treatment cycles.

Disclosures No relevant conflicts of interest to declare.

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