(PS1483) PHASE I CLINICAL TRIAL OF CD19 CAR -T CELLS SECRETING PD-1-TARGETING IL-21 IN RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Topic: 02. Acute lymphoblastic leukemia - Clinical

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Background

Patients with relapsed or refractory B-cell acute lymphoblastic leukemia (R/R B-ALL) have an extremely poor prognosis. Although CD19-targeted CAR-T cell therapy can induce high initial response rates, T cell exhaustion often leads to relapse, with the PD-1/PD-L1 axis being a key mechanism.

Aims

This study aimed to evaluate the safety and efficacy of a novel bispecific armored CAR-T cell therapy (PZ04) for R/R B-ALL. These engineered cells constitutively secrete a PD-1Ab21 fusion entity, designed to locally block the immune checkpoint and enhance T-cell function.

Methods

This single-center, Phase I study (ChiCTR2300072572) enrolled 17 patients with R/R B-ALL. Patients received PZ04 cell infusion following lymphodepleting chemotherapy with an FC regimen (fludarabine/cytarabine). Primary endpoint was safety and the second endpoint was complete remission (CR) rate.

Results

The results demonstrated a CR rate of 81.3% (13/16), with all responders achieving minimal residual disease (MRD)-negative status. The 1-year overall survival (OS) rate was 53.0%. Among six patients with baseline central nervous system involvement, four (83.3%) achieved complete remission. Regarding safety, the incidence of grade ≥3 cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) was 18.8% each (3/16 for each). No severe adverse events related to systemic immune checkpoint inhibitors were observed. Further analysis indicated a trend toward superior long-term survival in patients (n=6) who underwent consolidative allogeneic hematopoietic stem cell transplantation (allo-HSCT) following CAR-T therapy (1-year event-free survival 53.3% vs. 21.8%, P=0.075).

Summary/Conclusion

Conclusion: The bispecific CD19-targeted CAR-T cells secreting the PD-1Ab21 fusion entity (PZ04) demonstrate a high response rate and a manageable safety profile in patients with R/R B-ALL. Its innovative design provides a novel strategy to counteract T-cell exhaustion and shows potential as an effective bridge to transplantation. Larger studies are warranted to validate its long-term efficacy.