(PF1233) AN EXPLORATORY STUDY OF YTS109 CELL THERAPY IN PATIENTS WITH AUTOIMMUNE HEMOLYTIC ANEMIA

Topic: 26. Gene therapy, cellular immunotherapy and vaccination - Clinical

Lele Zhang[1, 2], Ruonan Li[1, 2], Jing Zhang[1, 2], Weiwang Li[1, 2], Jingyu Zhao[1, 2], Xingxin Li[1, 2], Liyun Li[1, 2], Xiao Yu[1, 2], Zhexiang Kuang[1, 2], Yuechen Luo[1, 2], Liwei Fang[1, 2], Neng Nie[1, 2], Meili Ge[1, 2], Yang Li[3], Lei Lei[3], Shasha Zhang[3], Hongli Zheng[3], Xueqiang Zhao[3], Xin Lin[4], Jun Shi*[1, 2]

[1]Institute of Hematology & Blood Diseases Hospital⊠Chinese Academy of Medical Sciences & Peking Union Medical College, National Clinical Research Center for Blood Diseases, Tianjin, China; [2]Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Red Blood Cell Diseases Center & Regenerative Medicine Clinic, Tianjin, China; [3]Bristar Immunotech Limited, beijing, China;[4]Tsinghua University School of Medicine, Department of Basic Medical Sciences, beijing, China;

Background

Autoimmune hemolytic anemia (AIHA) is a rare and heterogeneous autoimmune disorder characterized by the destruction of red blood cells mediated by autoantibodies. Patients with refractory AIHA (rAIHA) who fail multiple lines of therapy have limited treatment options and poor prognosis. Recent studies have demonstrated the potential of autologous CD19-directed CAR-T cell therapy in inducing sustained remission in rAIHA. However, the high cost and complex manufacturing process of autologous CAR-T products limit their widespread application. Allogeneic CAR-T therapies offer a promising alternative by enabling off-the-shelf availability. YTS109 is a novel allogeneic STAR-T product targeting CD19, which has previously demonstrated promising clinical efficacy and a favorable safety profile in patients with severe refractory systemic lupus erythematosus (SLE). Here, we report the first-in-human data of YTS109 in patients with AIHA.

Aims

To evaluate the safety, tolerability, and preliminary efficacy of YTS109 in patients with AIHA who have failed at least three prior lines of therapy.

Methods

This is an investigator-initiated, open-label, dose-escalation study (NCT06770504). Patients with rAIHA received a single infusion of YTS109 following lymphodepletion with fludarabine (25-30 mg/m²) and cyclophosphamide (1000 mg/m²). Three dose levels were explored: 0.5×10^6/kg (n=1), 1×10^6/kg (n=3), and 2×10^6/kg (n=3). Safety assessments included monitoring for cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and infections. Efficacy was evaluated by hemoglobin levels, hemolytic markers, and transfusion independence. Pharmacokinetics included peripheral blood STAR-T copy numbers and B-cell aplasia duration.

Results

As of January 30, 2026, seven patients with rAIHA (median age 45 years, range 24–70 years) had received YTS109 infusion. No dose-limiting toxicities (DLTs) were observed. The safety profile was favorable, with no grade ≥3 CRS or ICANS reported. The most common adverse events were grade 1 CRS (n=3). No severe infections or graft-versus-host disease (GvHD) occurred.
Preliminary efficacy data showed rapid and marked improvement in hemolytic parameters in 6 out of 7 patients. The overall response rate (ORR) was 6/7, with 5 patients achieving complete remission (CR/CRi) and 1 patient achieving partial remission (PR). At data cutoff, the longest responding patient has maintained sustained remission for over 9 months. STAR-T expansion was observed in all patients, with peak levels occurring between Day 4 and Day 7 post-infusion. Nearly all patients achieved B-cell depletion following infusion.

Summary/Conclusion

This first-in-human study of allogeneic STAR-T therapy (YTS109) in refractory AIHA demonstrates a favorable safety profile and promising clinical activity. These early results support the potential of YTS109 as an off-the-shelf immunotherapeutic option for patients with rAIHA. Longer follow-up and expansion cohorts are warranted to confirm durability and optimize dosing.