Abstract: P1517

Title: INTERIM RESULTS OF GENE THERAPY USING OPTIMIZED LENTIHBBT87Q VECTOR IN FIVE CHINESE PATIENTS WITH TRANSFUSION DEPENDENT B-THALASSEMIA

Abstract Type: Poster Presentation

Topic: Thalassemias

Background:

Gene therapy is increasingly being acknowledged as a potentially cure for transfusion-dependent β-thalassemia (TDT). The sustained and durable expression of exogenous functioning β-globin, encoded by lentiviral vector, provides clinical benefits to TDT patients by the reducing or eliminating the requirements for transfusions. A significant challenge in lentiviral gene therapy for β-thalassemia is finding a balance between maintaining low vector copy numbers to avoid genotoxicity and ensuring uniform efficacy for all genotypes. Previous clinical studies have shown delayed platelet engraftment and reported in the literature for patients with TDT undergoing autologous hematopoietic stem cell transplantation (auto-HSCT). Various populations of patients with thalassemia exhibit a combination of common and geographically clustered rare mutations. This is the first pilot study, focusing on five Chinese pediatric patients carrying either β+ or β0 mutations, including the common mutations β+ IVS-II-654 and βe. As a result, a** lentiviral vector named LentiHBBT87Q was developed and the transduction procedure optimized for the treatment of Chinese patients with TDT, yielding a promising result in our preclinical study.

Aims:

The safety and efficacy of gene therapy based on LentiHBBT87Q were assessed among Chinese pediatric patients with TDT.

Methods:

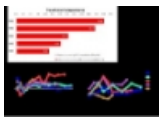
In an ongoing pilot phase 1/2 trial (NCT05745532, SZ-101), all subjects with TDT (age of 8 to 16 years) enrolled and signed informed consent form before screening stage. Patients undergo HSC mobilization using granulocyte colony-stimulating factor (G-CSF) and plerixafor. CD34+ cells obtained through apheresis are transduced with the LentiHBBT87Q. Subsequently, patients receive myeloablative conditioning with pharmacokinetic-adjusted busulfan over a period of 4 days, followed by infusion of HGI-001 Injection. Then, 24-month following-up visits are conducted to assess the safety and efficacy of HGI-001 injection. Summary statistics presented as median (min-max).

Results:

As of 31st January 2024, a total of 5 subjects were treated in SZ-101 with a median follow-up period of 21.1 (13.2 to 35.8) months. Hospitalization from initiation of conditioning to discharge from transplant unit ranged from 27 to 33 days. The rapid bone marrow successfully happened after administration of HGI-001 Injection, with neutrophil and platelet engraftment 19 days (17-22) and 18 days (13-21), respectively. The last blood transfusion occurred between Day 13 and Day 17 post-infusion HGI-001 Injection. All subjects followed ≥12 months stopped red-cell transfusions for ≥12 months,2/5 subjects followed ≥24 months achieved independent transfusion for ≥24 months. HbAT87Q levels at Months 3 (n=5), 6 (n=5), 12 (n=5), 18 (n=3) and 24 (n=2) were 7.2 (5.8-10.9), 7.5 (7.4-10.4), 7.2(6.1-13.0), 7.3(6.6-13.0) and 7.1(7.0-7.3) g/dL, respectively, which contributed to median total hemoglobin (Hb) of 10.5 (9.8-13.6), 10.5 (10.3-11.4), 10.4 (9.4-14.4), 10.6 (8.8-14.2) and 10.0 (9.8-10.1) g/dL at these time points, respectively. Total Hb at last visit varied between 9.8-14.3 g/dL and HbAT87Q was 6.1-13.0 g/dL, with a range of 0.81 to 2.82 PBMC VCN. No clone dominance related to vector integration nor RCL has been observed.

Summary/Conclusion:

Gene therapy with optimized LentiHBBT87Q vector assist five Chinese TDT patients become transfusion-independent without special concerned serious adverse events related to gene therapy.



Keywords: Gene therapy, Autologous hematopoietic stem cell transplantation, beta thalassemia