Abstract: P1476

Title: RENI-CEL, THE FIRST ASCAS12A GENE-EDITED CELL THERAPY, SHOWS PROMISING PRELIMINARY RESULTS IN KEY CLINICAL OUTCOMES IN TRANSFUSION-DEPENDENT BETA-THALASSEMIA PATIENTS TREATED IN THE EDITHAL TRIAL

Abstract Type: Poster Presentation

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

Transfusion-dependent β-thalassemia (TDT) is a hereditary blood disorder caused by reduced or absent production of β-globin. Clinical evidence has demonstrated that increased fetal hemoglobin (HbF, α2γ2) can reduce or prevent TDT complications.

Renizgamglogene autogedtemcel (reni-cel; formerly EDIT-301) is an investigational gene-edited autologous hematopoietic stem cell medicine comprised of CD34+ cells edited at the γ-globin gene (*HBG1/2*) promoters. These edits mimic naturally occurring variants of hereditary persistence of HbF in the *HBG1/2* promoters, resulting in reactivation of γ-globin expression and increased HbF production. In preclinical studies, editing of this genomic region in CD34+ cells from patients with TDT led to improved erythropoiesis *in vitro* and erythroid progeny with increased total hemoglobin (Hb) production.

Aims:

The ongoing EdiThal trial (NCT05444894), a Phase I/II, multicenter, open-label, single-arm study is evaluating the safety, tolerability, and efficacy of reni-cel in patients with TDT. Interim clinical data on safety and efficacy are reported. Updated data will be presented.

Methods:

Patients 18–35 years old must have a diagnosis of TDT defined as at least 100 mL/kg/year or 10 U/year of packed red blood cell (RBC) transfusions in the 2 years prior to informed consent. Autologous CD34+ hematopoietic stem and progenitor cells are collected by apheresis after plerixafor + filgrastim mobilization and edited at the *HBG1/2* promoters with the highly efficient and specific, proprietary gene editing nuclease, AsCas12a. After myeloablative conditioning with busulfan, patients received a single infusion of reni-cel (a minimum of 3 × 106 CD34+ cells/kg) and were monitored for engraftment, total Hb, HbF production, percentage of F-cells, transfusion requirement, and adverse events (AEs) for 24 months.

Results:

As of February 9, 2024, 7 patients with TDT had been dosed with reni-cel. Patients were a mean (standard deviation, SD) of 5.8 (2.9) months post-reni-cel infusion (n=7). Neutrophil and platelet engraftment were achieved after a mean (SD) of 24.1 (4.9) and 35.6 (10.4) days (n=7), respectively. Following reni-cel infusion, mean (SD) total Hb remained above the transfusion-independence threshold of 9.0 g/dL, and increased to 12.8 (1.0) g/dL by Month 6 (n=3). The mean (SD) HbF concentration increased early and was 8.9 (2.6) g/dL by Month 3 with pancellular distribution (n=6). After receiving the last RBC transfusion at 0.5–2.2 months post-reni-cel infusion, all 7 patients have been transfusion independent for a range of 1.2–9.9 months. The safety profile of reni-cel was consistent with myeloablative conditioning with busulfan. After reni-cel infusion, no treatment-related AEs were reported through the data cutoff date.

Summary/Conclusion:

These data demonstrate successful engraftment, an increase in Hb and HbF levels with pancellular distribution, and a favorable safety profile of reni-cel in patients with TDT. Additionally, all patients have been transfusion free for up to 9.9 months. These findings support further investigation of reni-cel in the EdiThal clinical trial.

Keywords: Gamma globin, beta thalassemia, Clinical data, Gene therapy