

Administration of risto-cel

ICD-10 Coordination and Maintenance Committee Update

Beam Therapeutics
Fall 2026

Ristoglogene autogetemcel (risto-cel)

Risto-cel is an investigational therapy that has not been approved by any regulatory authority. The safety and effectiveness of risto-cel has not yet been established.

Risto-cel Treatment Regimen, Documentation, and Code Request

Code Request

- Current ICD-10-PCS codes do not adequately describe and identify the intravenous administration of risto-cel, which is necessary to track utilization, outcomes, and resources associated with this product.

Risto-cel Administration Summary

- For patients receiving risto-cel includes cell mobilization and apheresis to collect the patient's own stem cells, editing of the cells at a manufacturing facility, shipping the edited cells to the authorized treatment center (e.g., hospital), myeloablative conditioning, and single intravenous infusion of risto-cel into a vein
- The myeloablative conditioning and risto-cel infusion occur in the inpatient setting

Expected Documentation

- The comprehensive process by which risto-cel is administered will likely be described in the medical record and traceable via use of a deidentified patient number on physician orders, cellular laboratory order, pharmacy notes, and treatment summary

Sickle Cell Disease (SCD) is a multi-system disorder of varying severity, with a high prevalence in specific populations

SCD is the **most common** genetic disease in the USA¹

~100,000

people are estimated to be affected by SCD nationwide²



1 in 356

Black or African-American people have SCD²



Prevalence of SCD is high among **Sub-Saharan African, Indian, South Asian, Middle Eastern, and Mediterranean** ethnicities³



1 in 12

African Americans carry the **autosomal recessive** (non-symptomatic) mutation^{1,3}

Multi-organ damage can lead to a decreased life expectancy for individuals with SCD

Individuals with SCD experience lifelong, debilitating, multi-system organ damage, resulting in high morbidity and mortality¹⁻³



Simultaneous complications in the kidneys, lung, and heart are common and often lead to **premature death**^{3,4}



Developing **any** end-organ damage significantly **increases the risk of mortality** in individuals with SCD⁴
The **number of organs affected** is also significantly associated with mortality³



Median survival for individuals with SCD is **≥20 years shorter** than the average life expectancy in the USA^{5,6}

Vaso-Occlusive Crises (VOCs) may lead to repeat hospitalization impacting ability to work

VOCs are **recurrent, severe pain episodes** caused by sickle-shaped RBC aggregates that disrupt blood flow and lead to **complications** that **negatively affect** patients' lives^{1–3}

Recurrent VOCs may require **repeat ER visits and hospitalizations**^{2,4,5}

- Severe VOCs last **1+ week**, with an average hospital stay of **~9–11 days**⁶



VOCs are associated with significant **lifetime healthcare utilization**^{2,4,5}

- **Nearly four times higher** than no VOCs³



VOCs, chronic pain, and organ dysfunction can **limit work ability and employment options**³

- Of individuals with SCD:
 - Less than **one-third** are employed
 - **44%** are unable to work³
- SCD symptoms result in:
 - An average of **36.8 missed workdays**



ER, emergency room; RBC, red blood cell; SCD, sickle cell disease; VOC, vaso-occlusive crisis

1. Kato GJ, et al. Nat Rev Dis Primers 2018;4:18010; 2. Shah NR, et al. J Med Econ 2020;23:1345–1355; 3. Holdford D, et al. Value Health 2021;24:1095–1101; 4. Udeze C, et al. HemaSphere 2022;6(Suppl. 3): 1585–1586 (Poster P1704); 5. Shah N, et al. J Health Econ Outcomes Res 2020;7:52–60; 6. Ballas SK, et al. Blood 2012;120:3647–3656

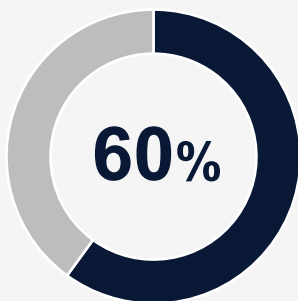
For Medical Affairs scientific exchange only.
Not for promotional use

SCD negatively impacts quality of life and emotional wellbeing

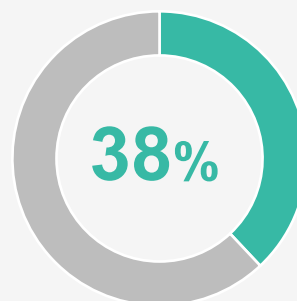
The significant burden of the physical symptoms and stigmas associated with SCD **negatively impacts an individual's quality of life and emotional wellbeing**¹⁻⁴

In the **SWAY survey (N=2145)**,* individuals with SCD reported that SCD causes:³

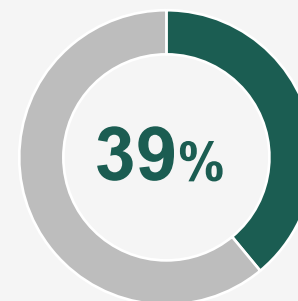
A 'high negative impact' on emotions



Anxiety



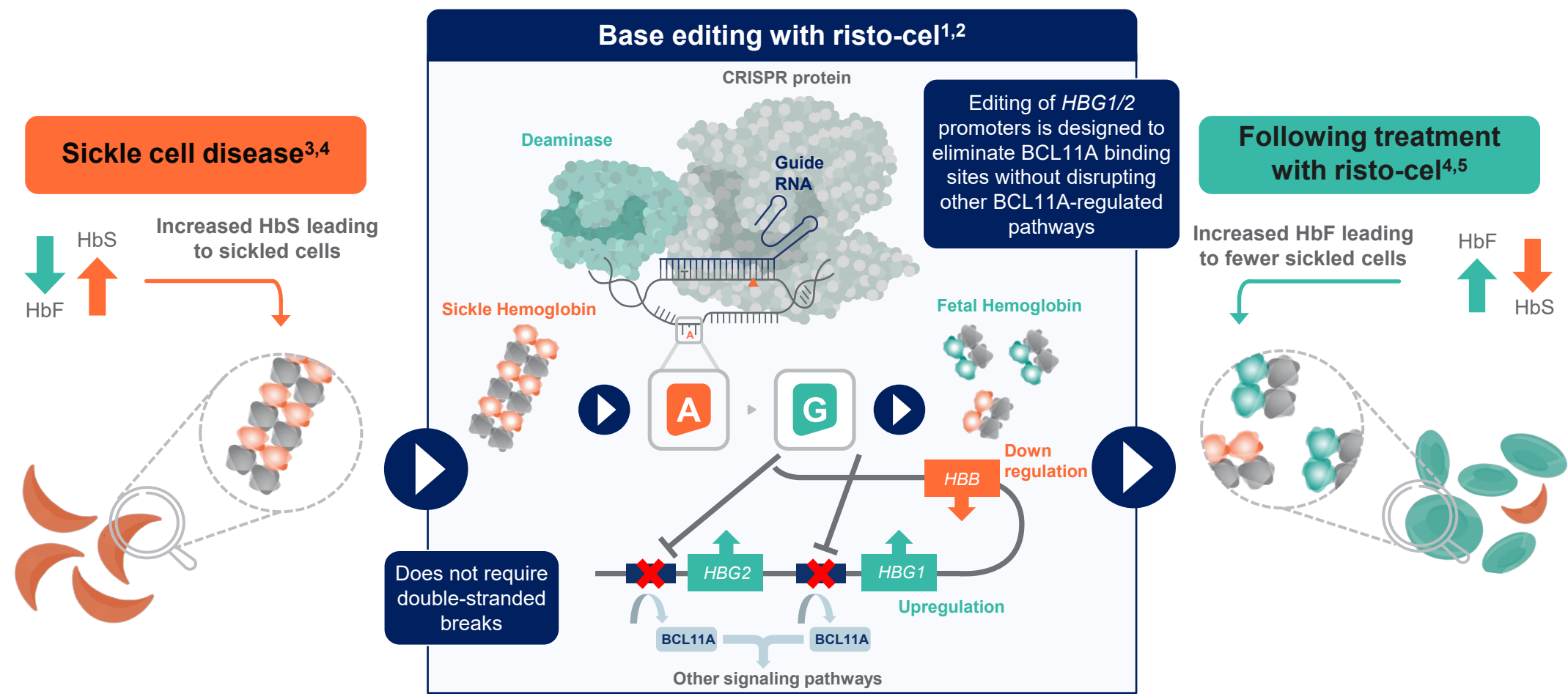
Depression



Acute anemia, a complication due to SCD, can lead to cognitive impairments such as issues with working memory, attention, and verbal learning⁴

*SWAY was a multi-country, cross-sectional survey, which assessed the impact of SCD in 2145 participants across six geographical regions between April 3, 2019, and October 4, 2019
 SCD, sickle cell disease; SWAY, Sickle Cell World Assessment Survey
 1. Kato GJ, et al. Nat Rev Dis Primers 2018;4:18010; 2. Jenerette CM, Brewer C. J Natl Med Assoc 2010;102:1050-1055; 3. Osunkwo I, et al. Am J Hematol 2021;96:404-417; 4. Sahu T, et al. Ann Neurosci 2022;29:255-268

Risto-cel uses precise base editing to increase levels of HbF^{1,2}



1. Beam Therapeutics Inc. Protocol BTX-AUT-001; 2. Beam Therapeutics Inc. Investigator's brochure; 3. Eaton WA, Bunn HF. Blood 2017;129:2719–2726; 4. Akinsheye I, et al. Blood 2011;118:19–27; 5. Steinberg MH, et al. Blood 2014;123:481–485.

A, adenine; BCL11A, transcription factor B-cell lymphoma/leukemia 11A; CRISPR, clustered regularly interspaced short palindromic repeats; G, guanine; HBB, hemoglobin subunit beta; HBG, hemoglobin subunit gamma; HbF, fetal hemoglobin; HbS, sickle hemoglobin; RNA, ribonucleic acid

BEACON is a Phase 1/2 study evaluating the safety and efficacy of Risto-cel in patients with SCD and sVOCs¹



Key eligibility criteria

- ▶ Age ≥ 12 to ≤ 35 years
- ▶ SCD with β^S/β^S , β^S/β^0 , or β^S/β^+ genotypes
- ▶ ≥ 4 sVOCs in 24 months prior to screening
- ▶ No available matched sibling donor
- ▶ No history of overt stroke

Key safety endpoints

- ▶ Proportion of patients with successful neutrophil engraftment
- ▶ Time to neutrophil engraftment
- ▶ Time to platelet engraftment

Key efficacy endpoints

- ▶ Proportion of patients sVOC-free for 12 consecutive months*
- ▶ Total Hb levels
- ▶ HbF and HbS levels
- ▶ Hemolysis parameters
- ▶ RBC function and organ damage

Adult and adolescent enrollment completed; 31 patients dosed as of August 2025²

Phase 1/2, non-randomized, open-label, single-arm, multicenter, safety and efficacy study of the administration of BEAM-101 to patients with SCD (NCT05456880).

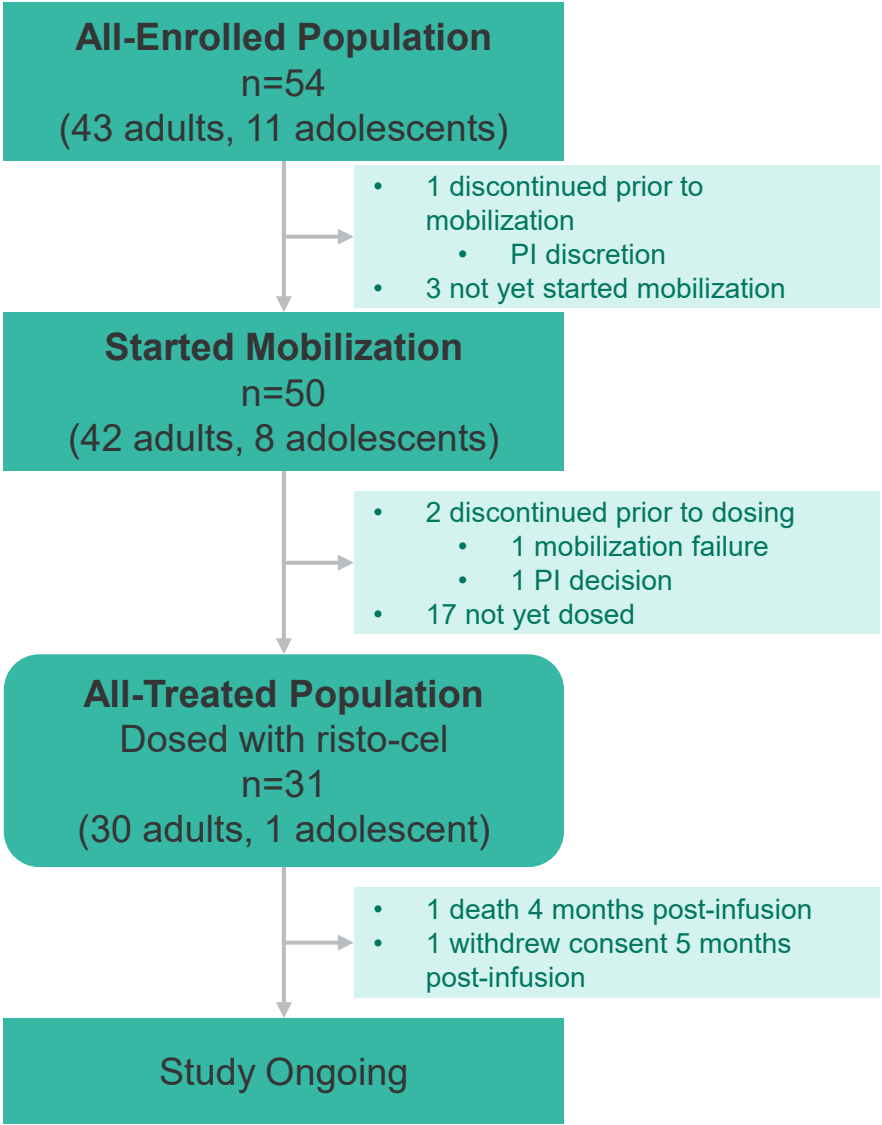
To qualify as a sVOC, the event must consist of acute episodes of pain, with no medically determined cause other than a VOC that required at least 24 hours of management in a hospital or observation unit; or a visit to an emergency department, urgent care, or outpatient facility involving therapy with an opioid or IV or IM NSAID; or ACS, as defined by the acute onset of pneumonia-like symptoms (e.g., cough, fever, shortness of breath) along with new pulmonary infiltrates; or splenic sequestration crisis, as defined by left upper quadrant pain, splenic enlargement, and a decrease in Hb of ≥ 2 g/dL; or priapism episode, defined as a sustained, unwanted, painful erection requiring evaluation and treatment at a medical facility. *From 60 days after last RBC transfusion.

ACS, acute chest syndrome; b, hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin; IM, intramuscular; IV, intravenous; NSAID, non-steroidal anti-inflammatory drug; RBC, red blood cell; SCD, sickle cell disease; sVOC, severe vaso-occlusive crisis

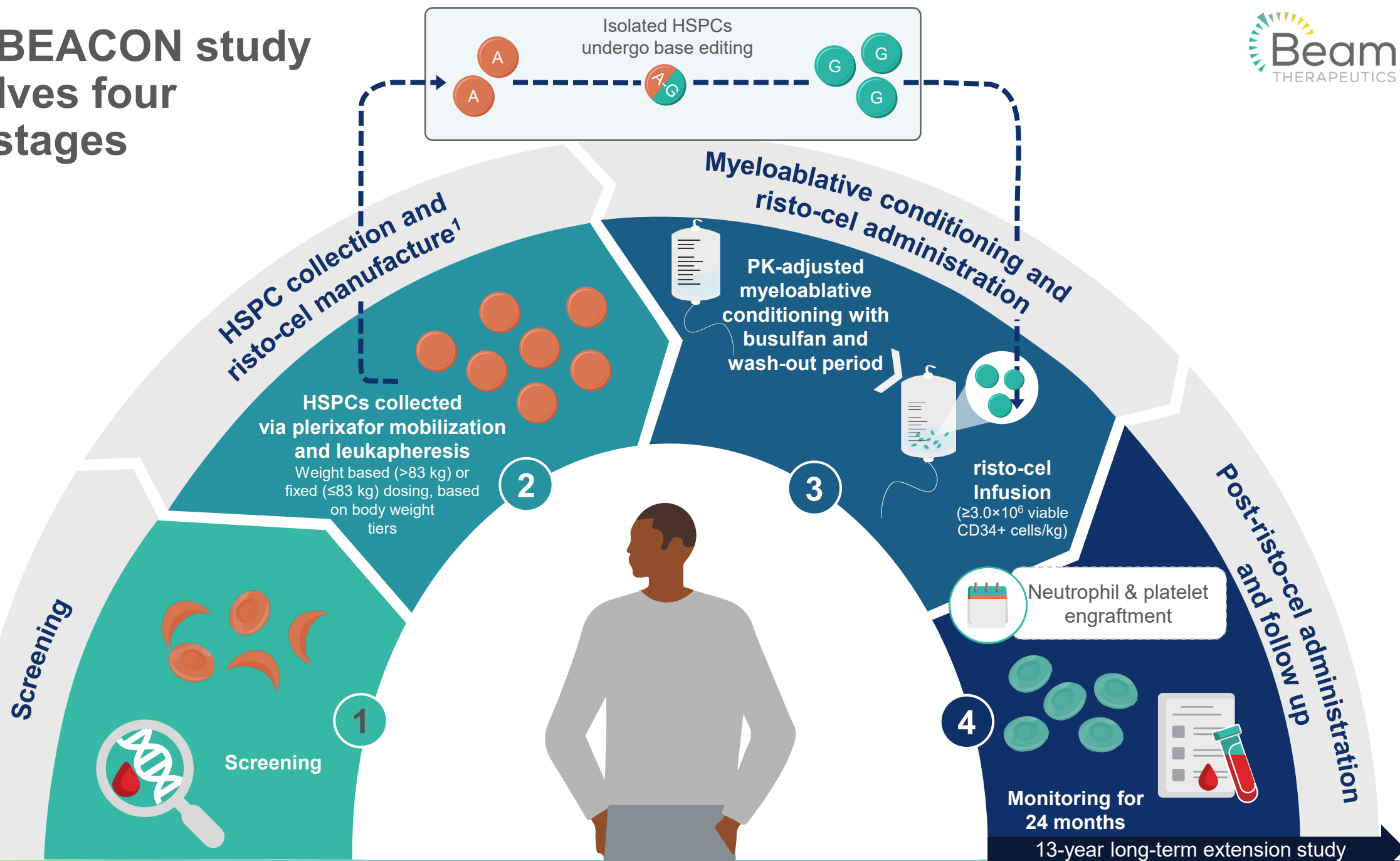
1. Beam Therapeutics Inc. Protocol BTX-AUT-001; 2. Gupta P, et al. Poster presented at ASH 2025

Baseline demographics and characteristics of patients treated with risto-cel

Baseline characteristics	N=31
Age (years), mean (range)	22.8 (16–34)
Sex, n (%)	
Male	16 (51.6)
Female	15 (48.4)
Genotype, n (%)	
β^S/β^S	28 (90.3)
β^S/β^0	1 (3.2)
β^S/β^+	2 (6.5)
Race, n (%)	
Black or African American	25 (80.6)
White	1 (3.2)
Not reported	4 (12.9)
Other	1 (3.2)
Previous hydroxyurea use, n (%)	31 (100)
Investigator-reported sVOCs in the 2 years prior to start of study, median (range)	7 (4–60)

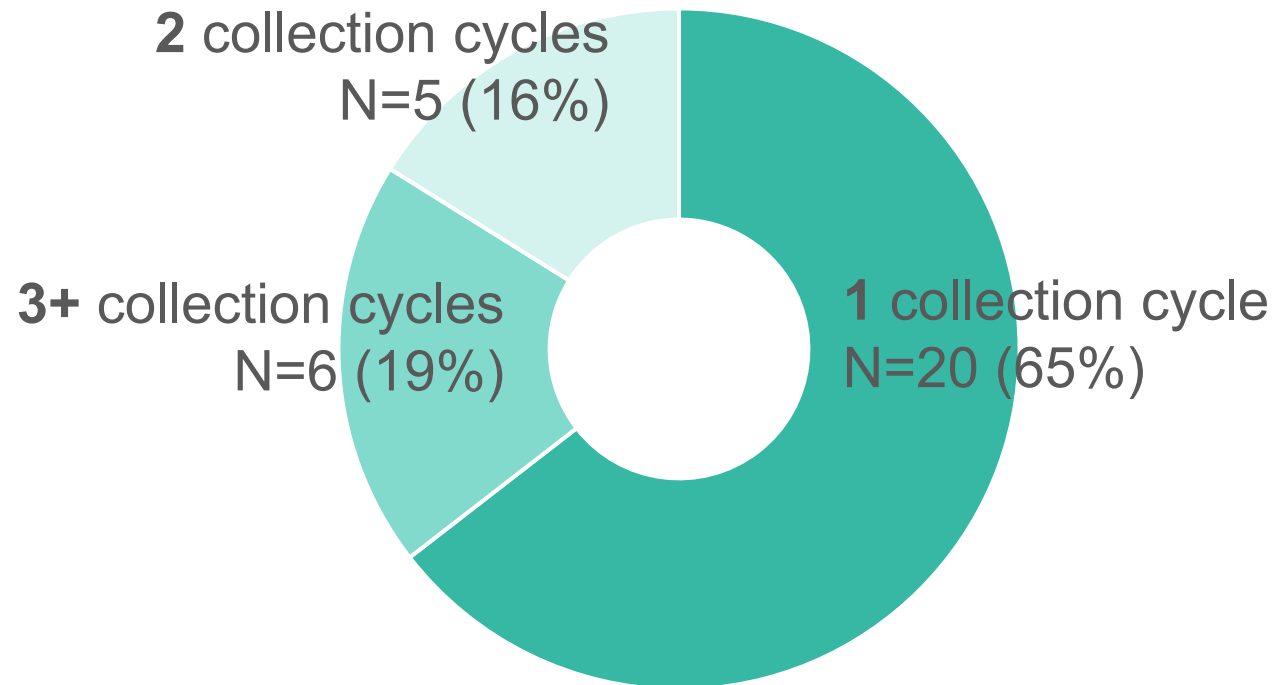


The BEACON study involves four key stages



1. Kopesky P, et al. Poster presented at EHA; Jun 2024; Madrid, Spain DMT, disease-modifying therapy; HSPC, hematopoietic stem and progenitor cell; PK, pharmacokinetic

Patients required a low number of stem cell collection cycles to manufacture risto-cel



risto-cel's efficient manufacturing process resulted in patients requiring few stem cell collection cycles and total collection days to manufacture risto-cel

- Patients required a median of **1 (1–5) stem collection cycle**
- A median of **3 (1–13) total collection days** was required for risto-cel manufacture, and store back-up/rescue cells at site

risto-cel treatment and engraftment characteristics

Treatment	N=31
Estimated average AUC of busulfan for entire conditioning ($\mu\text{g}\cdot\text{h}/\text{mL}$), mean (range)	71 (61.0–86.1)
risto-cel dose infused ($\times 10^6$ CD34+ cells/kg), mean (range)	6.2 (3.2–23.4)
Duration (months) of follow up after risto-cel dosing, median (range)	6.6 (0.3–20.4)
Day of last RBC transfusion, median (range)	14 (1–26)*
Neutrophil engraftment	N=28[†]
Time to neutrophil engraftment (days), median (range)	17.5 (12–30)
Duration of severe neutropenia (ANC <500 cells/ μL) (days), median (range)	7 (1–17)
Platelet engraftment	N=27[§]
Time to platelet engraftment (days), median (range)	19 (11–53)
Did not require a platelet transfusion, n (%)	9 (29)
Platelet count remained $\geq 50,000/\mu\text{L}$, no.	6/9

Patients achieved rapid and robust bone marrow reconstitution with few neutropenic days; some patients did not require platelet transfusions

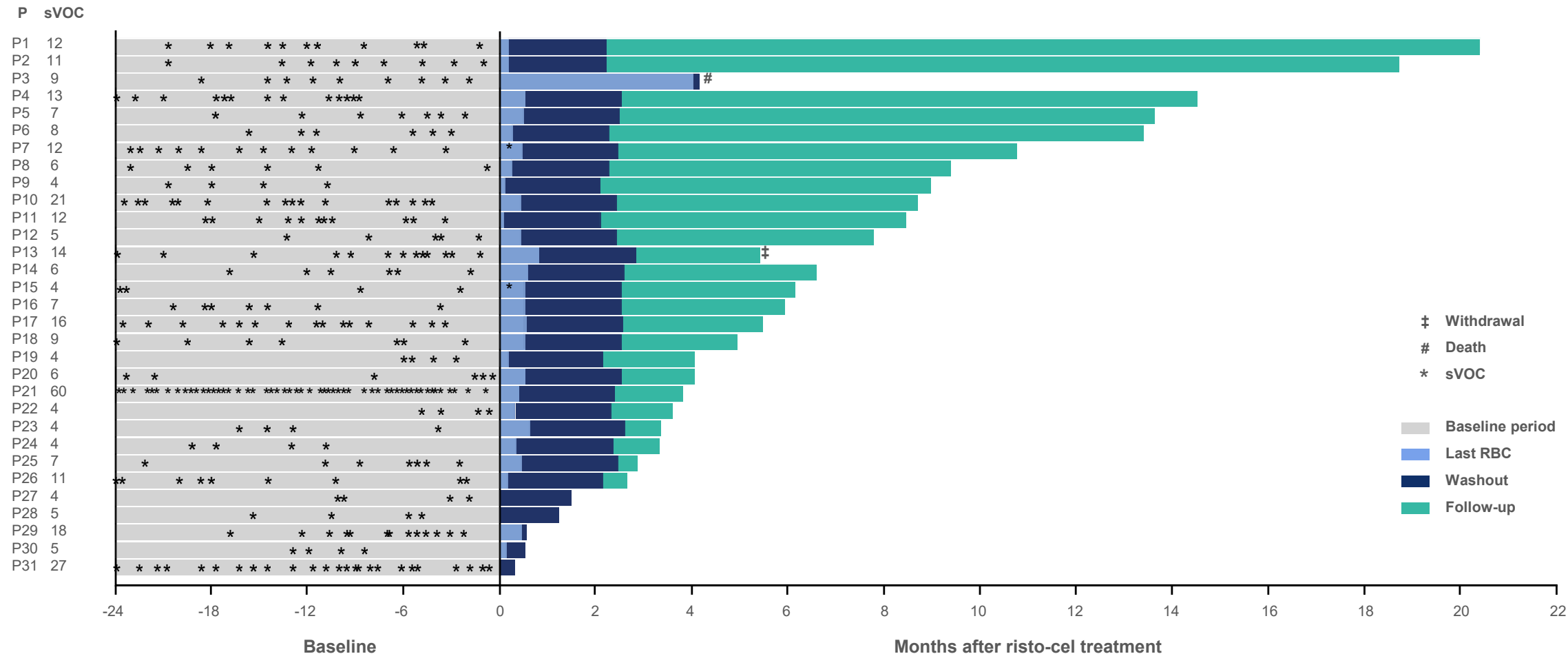
Data cutoff Aug 6, 2025

*One patient was excluded who required several RBC transfusions up to 122 days due to acute illness that ultimately resulted in death at 4 months post-infusion. [†]Three patients achieved neutrophil engraftment after the data cutoff date at 17, 17, and 21 days post-risto-cel infusion. [§]Four patients achieved platelet engraftment after the data cutoff date at 24, 24, 26, and 52 days post-risto-cel infusion.
ANC, absolute neutrophil count; AUC, area under curve; RBC, red blood cell

No patients experienced any investigator-reported sVOCs post-engraftment



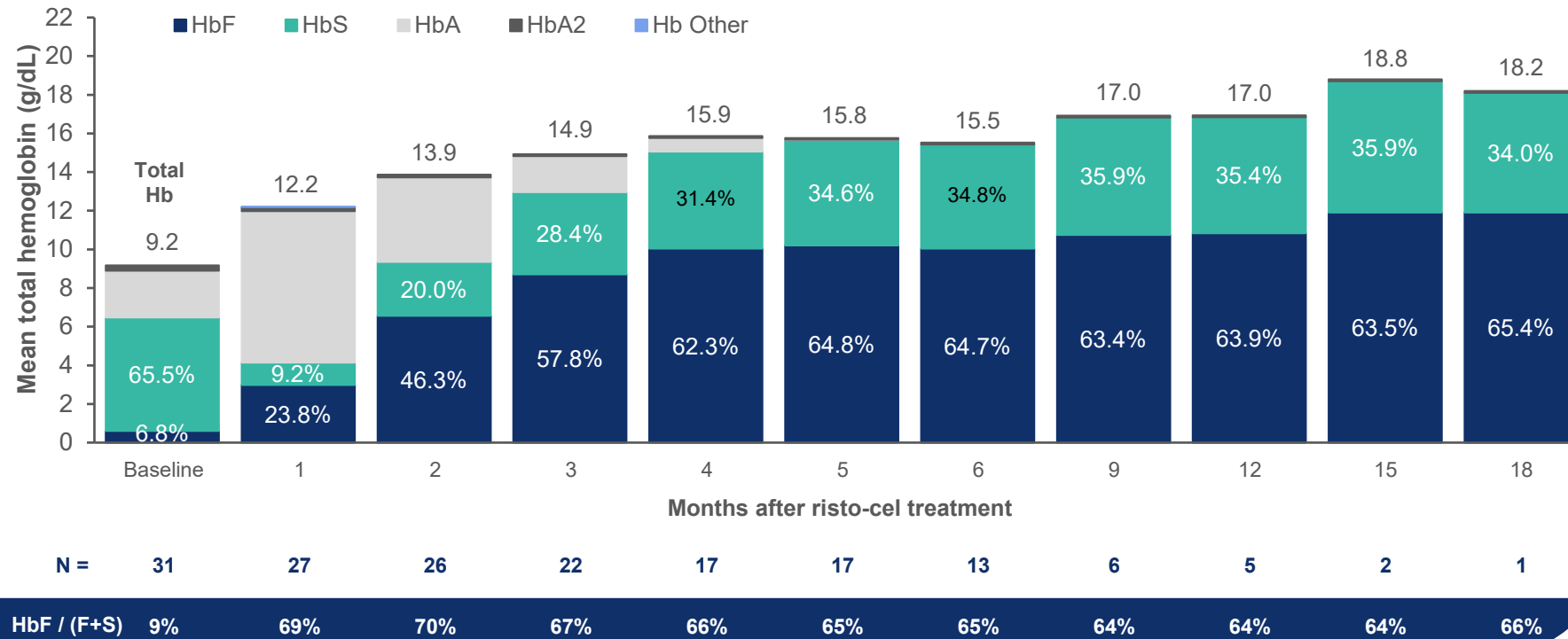
Investigator-reported sVOCs following treatment with risto-cel



Data cutoff Aug 6, 2025
Investigator-reported VOCs reported in this figure have not been formally adjudicated
P, patient; RBC, red blood cell; sVOC, severe vaso-occlusive crisis

Patients achieved rapid and robust HbF induction with corresponding HbS reduction

Patients achieved endogenous HbF >60% and HbS <40% by 1 month after risto-cel treatment and sustained through follow-up, suggesting resolution of anemia



► Elevated total Hb levels above the upper limit of normal were observed in 4 patients beyond Month 6 without any associated clinical manifestations or therapeutic interventions needed

Data cutoff Aug 6, 2025

HbF % is calculated as a % of untransfused blood (HbF/HbF+HbS)

Hb, hemoglobin; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin

The safety profile of risto-cel's treatment regimen is consistent with busulfan conditioning, autologous HSCT, and underlying SCD

Patients with, n (%)	N=31
Any TEAEs	31 (100)
Related to risto-cel	3 (9.7)*
Any TEAEs ≥Grade 3	27 (87.1)
Related to risto-cel	1 (3.2)†
Serious TEAEs	12 (38.7)
Related to risto-cel	0
Death	1 (4)‡
Related to risto-cel	0

Most common TEAEs , n (%)	N=31
Stomatitis	24 (77.4)
Febrile neutropenia	22 (71.0)
Decreased appetite	10 (32.3)
Hypokalemia	10 (32.3)
Skin hyperpigmentation	10 (32.3)
Platelet count decreased	8 (25.8)
Anemia	7 (22.6)
Hypomagnesemia	7 (22.6)
Constipation	6 (19.4)
Hypertension	6 (19.4)
Nausea	6 (19.4)
Anxiety	5 (16.1)
Headache	5 (16.1)
Peripheral edema	5 (16.1)
Pruritus	5 (16.1)
Pyrexia	5 (16.1)

Data cutoff Aug 6, 2025

*Included cough, vomiting, dyspnea (1 patient); muscle spasms, facial swelling (1 patient); and dizziness (1 patient); all day 1 events, excluding muscle spasms and facial swelling. †All related TEAEs were Grade ≤2 except 1 nonserious Grade 3 allergic facial swelling 11 weeks post-infusion that resolved the same day and was assessed as possibly related to risto-cel by investigator. ‡One patient died 4 months post-risto-cel infusion likely related to idiopathic pneumonia syndrome secondary to busulfan conditioning and unrelated to risto-cel as previously reported.

HSCT, hematopoietic stem cell transplantation; SCD, sickle cell disease; TEAE, treatment-emergent adverse event

Conclusions

- Patients required **low number of stem cell collection cycles** and achieved **rapid engraftment**, potentially leading to enhanced safety of the risto-cel treatment regimen and reduction in treatment burden
- The safety profile **consistent** with busulfan conditioning, autologous HSCT, and underlying SCD
- **No severe VOCs** were reported by investigators post-engraftment to date
- Treatment with risto-cel resulted in **substantial reduction in HbS <40%** through **rapid and robust pancellular production of anti-sickling HbF >60%**
- Improvement or resolution of anemia, hemolysis, erythropoietin, and sickling in patients suggests recovery of **normal RBC health and function**
- Novel base editing with risto-cel offers a **one-time potentially transformative therapy** as an option for patients with SCD that may **decrease treatment burden** for patients, families, and healthcare facilities