Enhanced CD34+ cell mobilizations, collections, and comparable safety profile with fixed-dose versus weight-based plerixafor dosing in patients with sickle cell disease receiving autologous CD34+ base-edited hematopoietic stem cells (ristoglogene autogetemcel; BEAM-101) in the ongoing BEACON study

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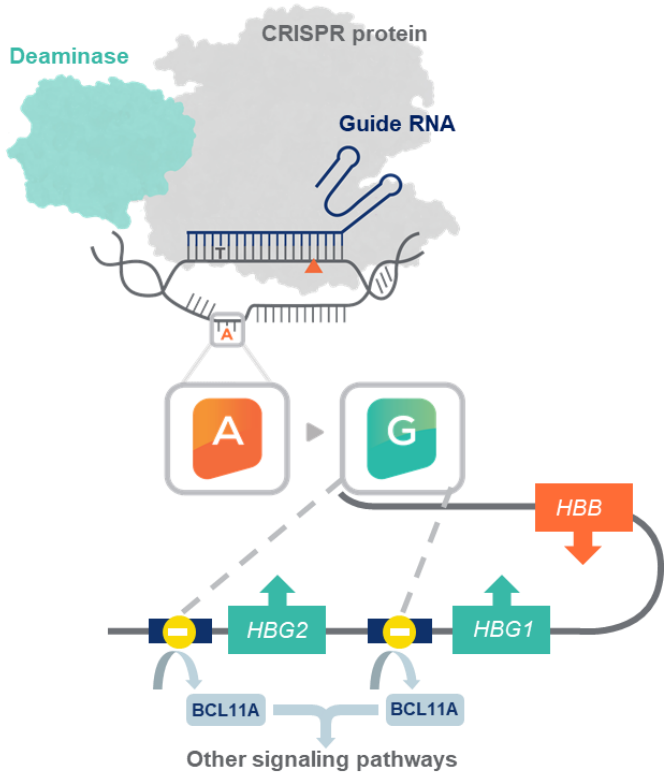
67th ASH 2025

Disclosures

BEACON is a Phase 1/2 clinical study evaluating the safety and efficacy of risto-cel (BEAM-101) in patients with SCD and sVOCs

Base editing with risto-cel[1,2]



BEACON treatment process[1]

1. Screening and eligibility
   - Age from ≥12 years to ≤35 years
   - SCD with β^S/β^S, β^S/β^0, or β^S/β^+ genotypes
   - ≥4 sVOCs in 24 months before screening
2. HSPC collection and risto-cel manufacturing
   - Mobilization cycle: ≤4 collection days
     - Manufacturing process: median of 3 collection days
     - Back-up/rescue cells: 1 collection day
   - Additional mobilization cycles performed as needed
3. Myeloablative conditioning with PK-adjusted busulfan, followed by risto-cel administration
4. Follow-up for 24 months after, followed by enrollment into a 13-year long-term follow-up study

Select endpoints
- Time to engraftment
- Proportion of patients sVOC-free for 12 consecutive months*
- Total Hb, HbF, HbS levels

BEACON study: NCT05456880

*From 60 days after last RBC transfusion

A, adenine; BCL11A, B-cell lymphoma/leukemia 11A; CRISPR, clustered regularly interspaced short palindromic repeats; G, guanine; Hb, hemoglobin; *HBB*, hemoglobin subunit beta; HbF, fetal hemoglobin; *HBG*, hemoglobin subunit gamma; HbS, sickle hemoglobin; HSPC, hematopoietic stem and progenitor cell; PK, pharmacokinetic; RBC, red blood cell; SCD, sickle cell disease; sVOC, severe vaso-occlusive crisis

1. Beam Therapeutics Inc. Protocol BTX-AUT-001; 2. Beam Therapeutics Inc. Investigator's brochure BEAM-101. 2022

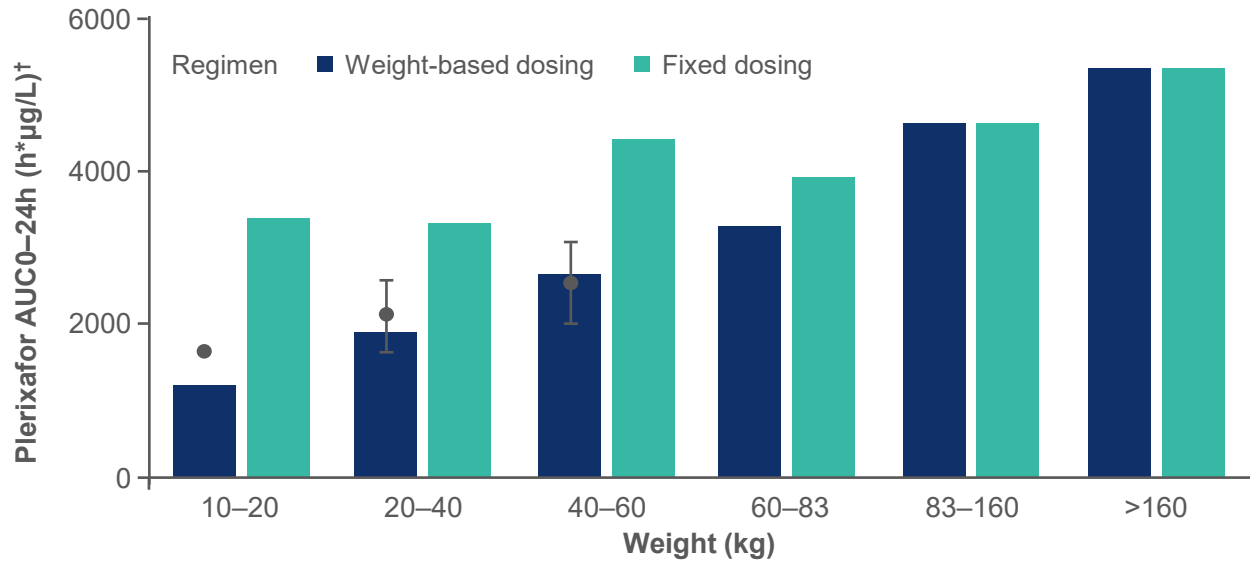
Fixed-dose plerixafor regimen has been previously shown to enhance HSPC mobilization into peripheral blood

- Dose optimization can **improve mobilization** and **lower the number of collection cycles**, which can **decrease patient burden and hospital resource utilization**[1,2]
- Detailed PKPD modeling (weight-based and fixed dosing) based on data from literature was conducted to characterize robustly the exposure and mobilization profiles of plerixafor in pediatric and adult patients with SCD in different weight categories

Weight category, kg*	Weight-based dosing, mg/kg	Fixed dosing, mg
>83	0.24	-
60–83	0.24	20
40–60	0.24	20

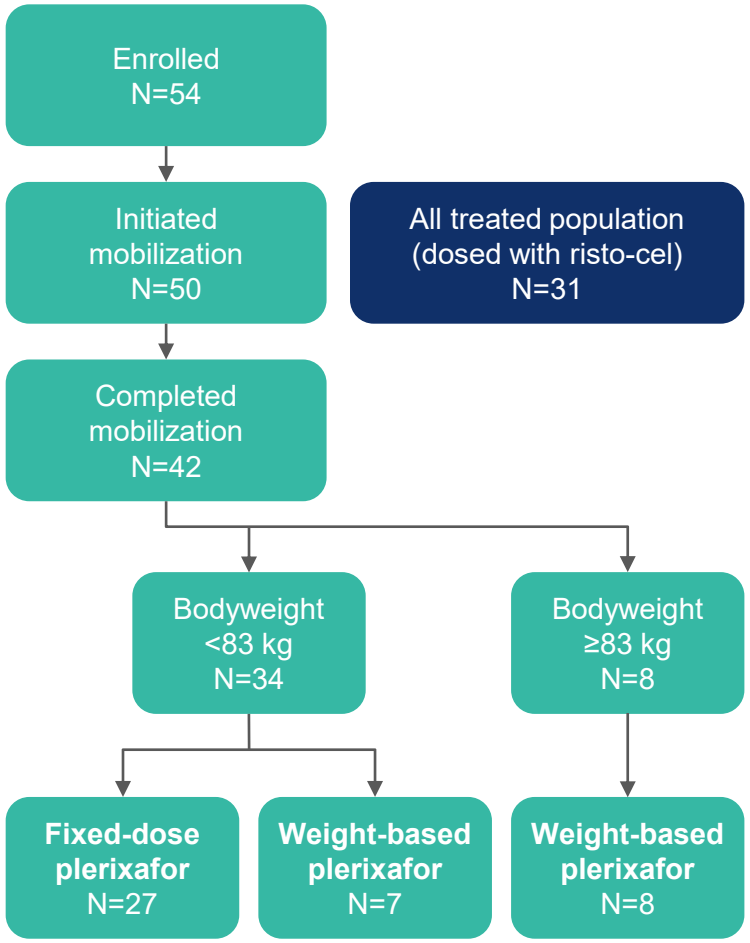
In this presentation, we report comparisons of HSPC mobilization and collection efficacy, and evaluate the safety profile of weight-based versus fixed-dose plerixafor in the BEACON clinical study

PKPD model: a modified tiered dosing regimen was developed to match plerixafor exposures in lower-weight patients with those observed in a standard 83-kg patient[3]



*Weight category modeling was also carried out for 20–40 kg (12.5-mg dose) and 10–20 kg (10-mg dose); table includes only the weight categories included in the BEACON clinical study; †grey bars indicate observed data
AUC0–24h, area under the concentration-time curve from time zero to 24 hours; HSPC, hematopoietic stem and progenitor cell; PKPD, pharmacokinetic and pharmacodynamic; SCD, sickle cell disease
1. Esrick E, et al. Blood Adv 2018;2:2505–2512; 2. MOZOBIL: package insert. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022311s018lbl.pdf (Accessed November 12, 2025);
3 Beam Therapeutics Inc. Protocol BTX-AUT-001

Baseline demographics and characteristics of patients enrolled in the BEACON clinical study, by plerixafor dosing group



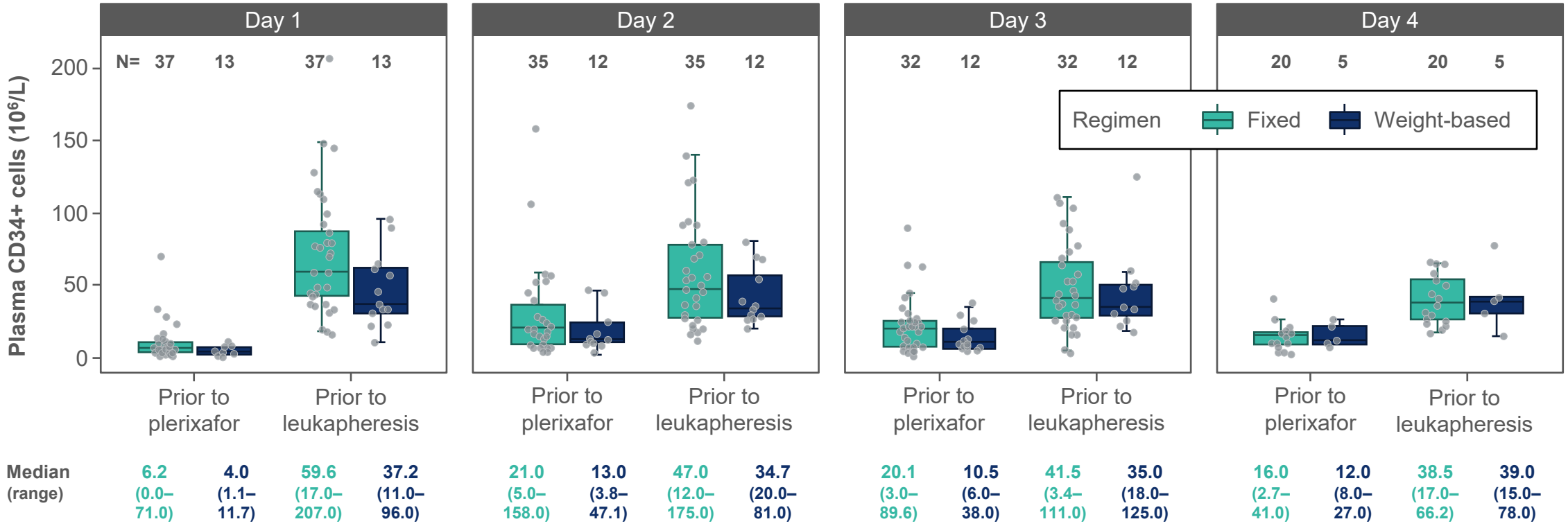
Baseline characteristics	All treated population N=31	Fixed-dose plerixafor (<83 kg) N=27	Weight-based plerixafor (<83 kg) N=7	Weight-based plerixafor (≥83 kg) N=8
Mean (range) age, years	22.8 (16–34)	20.6 (12–30)	22.0 (19–27)	25.8 (19–34)
Age <18 years, n (%)	1 (3.2)	5 (18.5)	0	0
Sex, n (%)				
Male	16 (51.6)	13 (48.1)	3 (42.9)	6 (75.0)
Female	15 (48.4)	14 (51.9)	4 (57.1)	2 (25.0)
Mean (range) weight, kg	66.8 (46–134)	57.3 (42–76)	61.1 (52–74)	97.6 (79–134)
Genotype, n (%)				
β^S/β^S	28 (90.3)	25 (92.6)	6 (85.7)	7 (87.5)
β^S/β^+	2 (6.5)	1 (3.7)	0	1 (12.5)
Median (range) investigator-reported sVOCs* in 2 years prior to study start	7 (4–60)	6 (3–60)	10 (7–13)	6.5 (4–41)
Mean (SD) total plerixafor dose, mg	115.3 (80.5)	92.6 (45.5)	89.4 (32.6)	186.5 (114.1)
Mean (SD) plerixafor dose per apheresis day, mg	20.1 (3.9)	20 (0)	14.8 (2.1)	24.4 (4.1)

Data cutoff August 6, 2025. *To qualify as an 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 intravenous or intramuscular 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

ACS, acute chest syndrome; Hb, hemoglobin; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; sVOC, severe vaso-occlusive crisis; VOC, vaso-occlusive crisis

More CD34+ cells were mobilized with fixed-dose plerixafor than weight-based dosing

CD34+ plasma profile in patients with bodyweight ≤83 kg



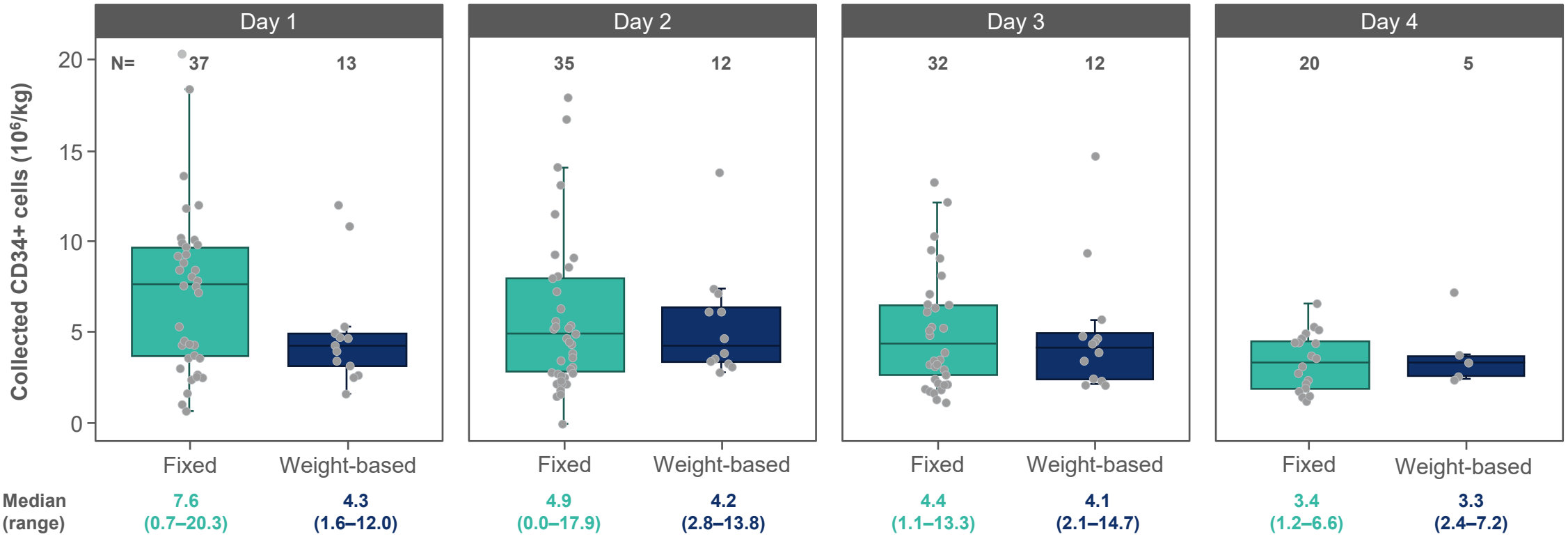
	Day 1				Day 2				Day 3				Day 4			
	Prior to plerixafor		Prior to leukapheresis		Prior to plerixafor		Prior to leukapheresis		Prior to plerixafor		Prior to leukapheresis		Prior to plerixafor		Prior to leukapheresis	
	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based	Fixed	Weight-based
Median (range)	6.2 (0.0–71.0)	4.0 (1.1–11.7)	59.6 (17.0–207.0)	37.2 (11.0–96.0)	21.0 (5.0–158.0)	13.0 (3.8–47.1)	47.0 (12.0–175.0)	34.7 (20.0–81.0)	20.1 (3.0–89.6)	10.5 (6.0–38.0)	41.5 (3.4–111.0)	35.0 (18.0–125.0)	16.0 (2.7–41.0)	12.0 (8.0–27.0)	38.5 (17.0–66.2)	39.0 (15.0–78.0)

A higher number of CD34+ cells were mobilized each day with fixed-dose plerixafor than weight-based dosing; Day 2 pre-dose CD34+ levels were higher in patients receiving fixed-dose plerixafor

Data cutoff August 6, 2025
Day 1 includes multiple entries per patient. Intrapatient variability in collection yield was low. Similar trends were observed when patients were counted once only

More CD34+ cells were collected with fixed-dose plerixafor than weight-based dosing

CD34+ cells collected by apheresis in patients with bodyweight ≤83 kg



A higher number of CD34+ cells were collected with fixed-dose than with weight-based dose regimen at each timepoint, with the highest number of cells being collected on Day 1

Data cutoff August 6, 2025

Patients receiving a fixed-dose regimen required fewer mobilization days and collection cycles to achieve dose

	Fixed-dose plerixafor (<83 kg) N=27	Weight-based plerixafor (<83 kg) N=7	Weight-based plerixafor (≥83 kg) N=8
Mobilization/apheresis days			
Median (range)	4.0 (2.0–12.0)	6.0 (4.0–11.0)	6.5 (3.0–16.0)
Mean (SD)	4.6 (2.3)	6.1 (2.5)	7.6 (4.7)
Stem cell collection cycles			
Median (range)	1 (1–3)	2 (1–3)	2 (1–5)
Risto-cel dose infused, $\times 10^6$ viable CD34+ cells/kg	N=18	N=6	N=7
Median (range)	5.9 (3.3–17.2)	5.7 (3.2–20.0)	8.4 (5.2–23.4)

- 70% of patients with bodyweight <83 kg who received fixed-dose plerixafor completed stem cell collection (including back-up collection) after a single cycle, compared with 38% of those receiving weight-based dosing
- For the 31 patients dosed:
  - Median (range) time from start of mobilization to drug product release was 2.9 (2.2–7.8) months
  - Median (range) time from start of mobilization to dosing was 4.5 (3.1–10.5) months

Fixed-dose plerixafor resulted in higher mobilization and collection of CD34+ cells, resulting in fewer stem cell collection cycles needed

Data cutoff August 6, 2025. Data are observational and not randomized or controlled
SD, standard deviation

The safety profile was comparable between fixed-dose plerixafor and weight-based dosing

Patients with, n (%)	Fixed-dose plerixafor (<83 kg) N=27	Weight-based plerixafor (<83 kg) N=7	Weight-based plerixafor (≥83 kg) N=8
AEs during mobilization period			
AEs 7 days from the start of plerixafor in each cycle	15 (55.6)	6 (85.7)	5 (62.5)
Grade ≥3 AEs	4 (14.8)	3 (42.9)	1 (12.5)
Related to plerixafor	1 (3.7)	1 (14.3)	0
Serious AEs	2 (7.4)	2 (28.6)	0
Related to plerixafor	1 (3.7)*	1 (14.3)†	0
Most common AEs related to plerixafor			
Acute kidney injury	1 (3.7)	0	0
Back pain	0	1 (14.3)	0
Bone pain	0	1 (14.3)	0
Diarrhea	0	1 (14.3)	0
Gingival pain	0	1 (14.3)	0
Headache	0	0	1 (12.5)
Nausea	3 (11.1)	1 (14.3)	2 (25.0)
Pain	0	1 (14.3)	0
Sickle cell anemia with crisis	0	1 (14.3)	0

- AEs observed during the mobilization period were consistent with plerixafor/leukapheresis
- Safety profile was comparable between fixed-dose and weight-based dose groups
- Plerixafor dosing over 4 days was well tolerated

Data cutoff August 6, 2025
*Acute kidney injury; †sickle cell anemia with crisis
AE, adverse event

Patients achieved rapid neutrophil and platelet engraftment following treatment with risto-cel (N=31)

Treatment characteristics	All treated population N=31*
Median (range) risto-cel dose infused, ×10^6 viable CD34+ cells/kg	6.2 (3.2–23.4)
Neutrophil engraftment	**N=28†**
Median (range) time to neutrophil engraftment, days	17.5 (12–30)
Median (range) duration of severe neutropenia (ANC <500 cells/μL), days	7 (1–17)
Platelet engraftment	**N=27‡**
Median (range) time to platelet engraftment, days	19 (11–53)

Data cutoff August 6, 2025
*Patients achieved neutrophil and platelet engraftment beyond the data cut; †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; HbF, fetal hemoglobin

The safety profile of the risto-cel 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)

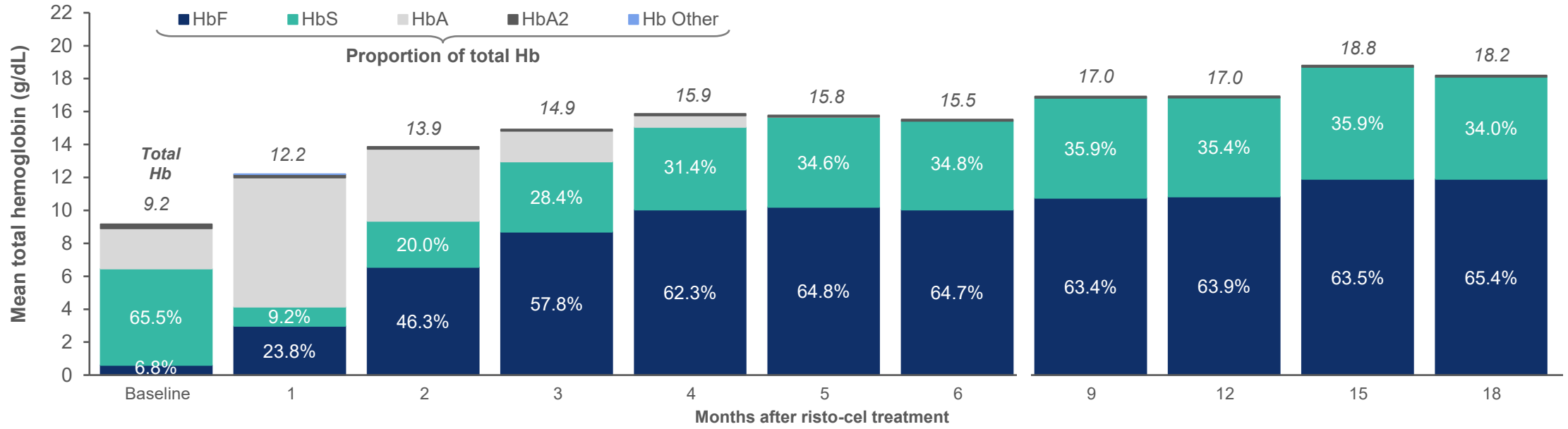
Data cutoff August 6, 2025

*Included cough, vomiting, dyspnea (one patient); muscle spasms, facial swelling (one patient); and dizziness (one patient); all Day 1 events, excluding muscle spasms and facial swelling; †all related TEAEs were Grade ≤2 except one non-serious 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 after 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

Patients achieved rapid and robust HbF induction with corresponding HbS reduction following risto-cel infusion (N=31)

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



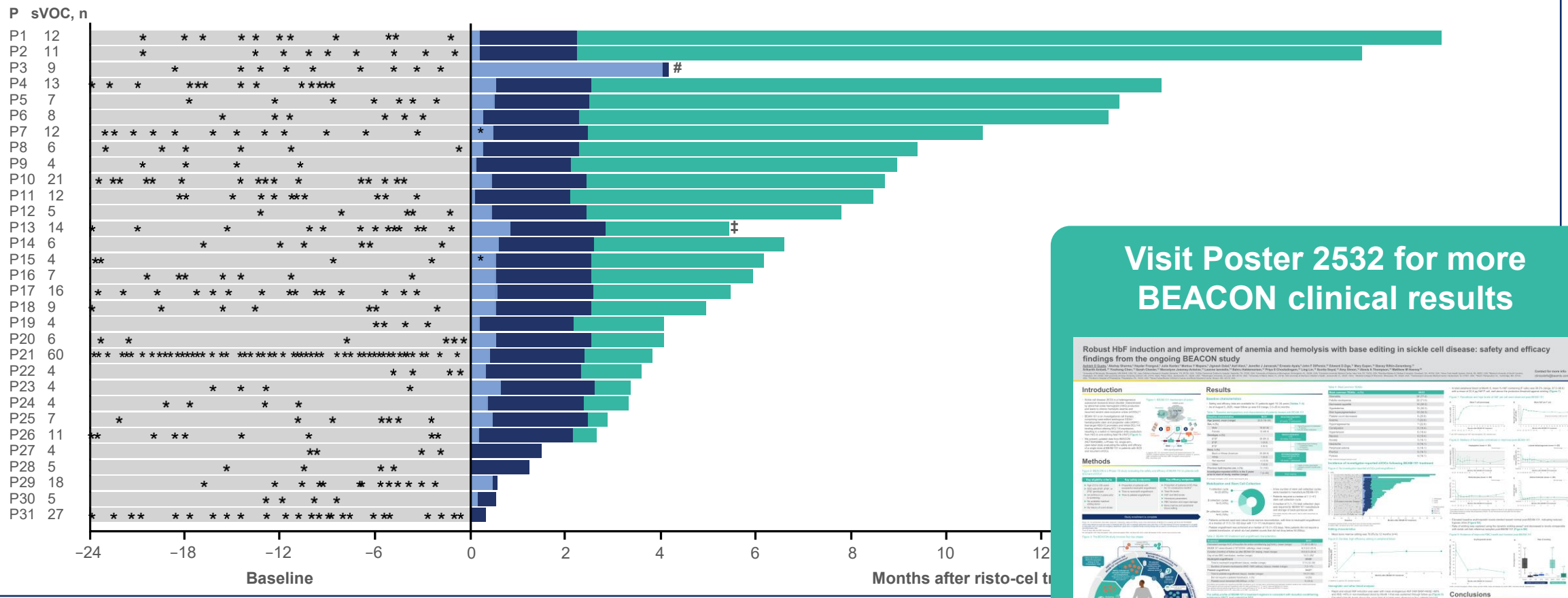
N=	31	27	26	22	17	17	13	6	5	2	1
HbF / (F+S)*	9%	69%	70%	67%	66%	65%	65%	64%	64%	64%	66%

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

Data cutoff August 6, 2025
*HbF % is calculated as a proportion (%) of untransfused blood (HbF/HbF+HbS)
Hb, hemoglobin; HbA, adult hemoglobin; HbF, fetal hemoglobin; HbS, sickle hemoglobin

No patients (N=31) experienced any investigator-reported sVOCs after engraftment

Investigator-reported sVOCs following treatment with risto-cel



Data cutoff August 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

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Conclusions

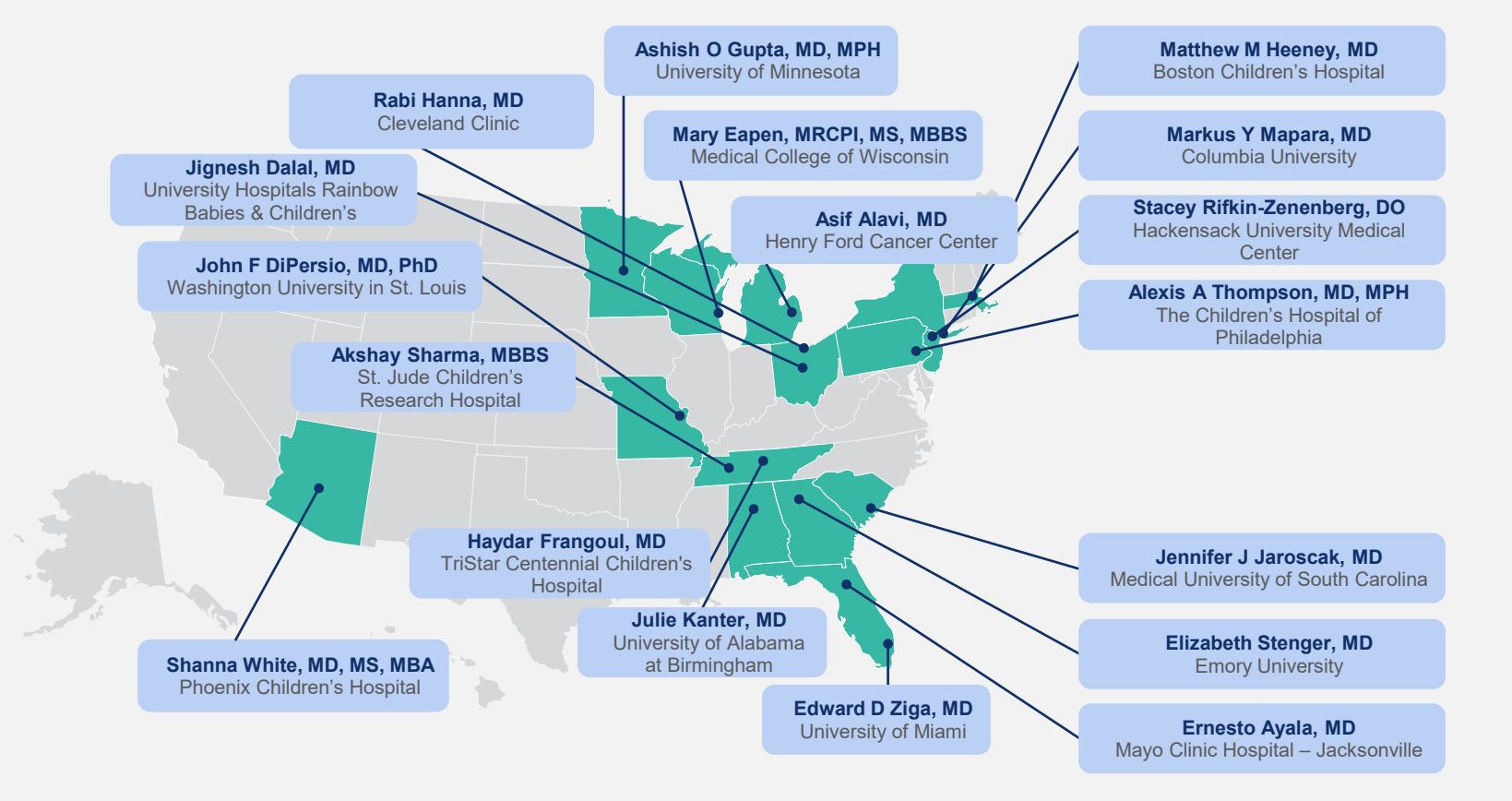
- Risto-cel's automated, closed, and wholly owned manufacturing process ensured **robust CD34+ cell yield** and **high editing efficiency** with **no manufacturing failures**
  - Median time from **start of first mobilization to drug product release was 2.9 (range 2.2–7.8) months**
- Efficacy and safety results from the ongoing BEACON clinical study show that risto-cel treatment demonstrated **rapid neutrophil and platelet engraftment** and **high editing efficiency**, resulting in **robust HbF production (>60%), decreased HbS (<40%)**, and improvement or resolution of anemia, sickling, and hemolysis
- **No investigator-reported sVOCs have occurred** after engraftment in any patients treated with risto-cel
- **More CD34+ cells were mobilized and collected** in patients receiving fixed-dose plerixafor compared with traditional weight-based dosing, resulting in **fewer stem cell collection cycles needed** to make risto-cel
  - This was particularly notable on Day 1, despite similar pre-dose CD34+ levels
- **Total administered dose of plerixafor was comparable between** fixed and weight-based dosing regimens
- **Four days of collection were well-tolerated** and the **safety profile was generally comparable** between fixed-dose and weight-based regimens; adverse events during the collection period were consistent with plerixafor/leukapheresis

Novel fixed-dose plerixafor utilized in the BEACON clinical study for stem cell collection resulted in shorter exposure duration and robust mobilization and cell collection, leading to fewer mobilization cycles, and may decrease the treatment burden for patients and healthcare facilities, compared with weight-based dosing

HbF, fetal hemoglobin; HbS, sickle hemoglobin; sVOC, severe vaso-occlusive crisis

Acknowledgments

Thank you to the study participants, their families, and their caregivers for their participation, and the study investigators for their contributions



This clinical study is sponsored by Beam Therapeutics

Medical editorial support was funded by Beam Therapeutics and provided by:
Kate Rees, PhD (Helios Medical Communications, part of Helios Global Group) and
Audrey W Hou, PharmD (Beam Therapeutics) under the guidance of the authors and in accordance with Good Publication Practice