COLLEGE of AMERICAN PATHOLOGISTS

CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia

Sarah Cannon Research Institute

PHC Webinar Series

Haydar Frangoul, MD, MS

October 19, 2021

Webinar Host

- This series is sponsored by the Personalized Healthcare Committee (PHC)
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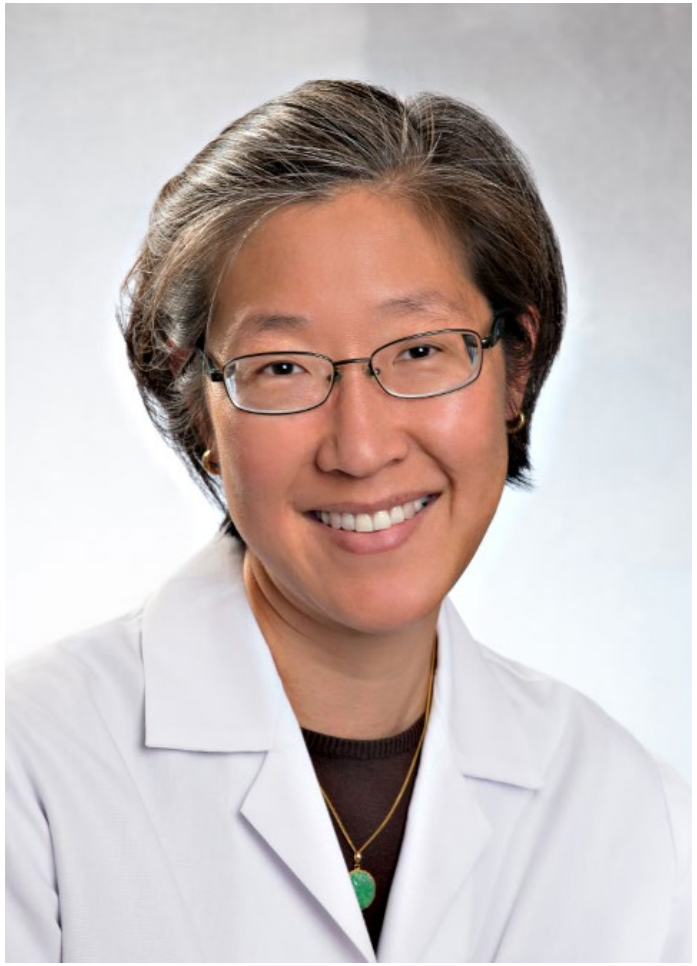

Housekeeping

- This presentation will be recorded. The recording and PDF will go out to all registrants in one week
- All lines are muted during the presentation
- Please send in your questions as you think of them via the “Question Box” in your control panel

Haydar Frangoul, MD, MS

- Director of the Pediatric Stem Cell Transplant program at Tristar Centennial Children's Hospital and the Sarah Cannon Research Institute in Nashville Tennessee.
- Completed his MD degree at the American University of Beirut followed by Pediatric residency at Duke University. He then went on to complete a fellowship in Pediatric Hematology/Oncology and Stem Cell Transplant at the University of Washington and the Fred Hutchinson Cancer Center.
- Leadership positions in the Children Oncology group, and Pediatric Blood and Marrow Transplant Consortium.
- One of the leading investigators in a clinical trial using CRISPR-Cas9 gene editing for patients with sickle cell disease and transfusion dependent thalassemia.

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Conflict of Interest

- **Vertex Pharmaceutical Steering committee membership**

Sickle Cell Disease (SCD)

- Inherited disorder of hemoglobin affecting 1 in 400 AA newborns in the US
- 270,000 infants born worldwide
- Results from a point mutation in codon 6 of the β-globin chain that results in an amino acid substitution.
- SCD leads to chronic hemolysis and a vasculopathy that involves virtually every organ.
- Chronic, debilitating condition, leading to high rates of disability and unemployment.

Hassell KL.. *Am J Prev Med. 2010*

Several genotypes may give rise to severe SCD

Patients with severe SCD experience frequent VOCs

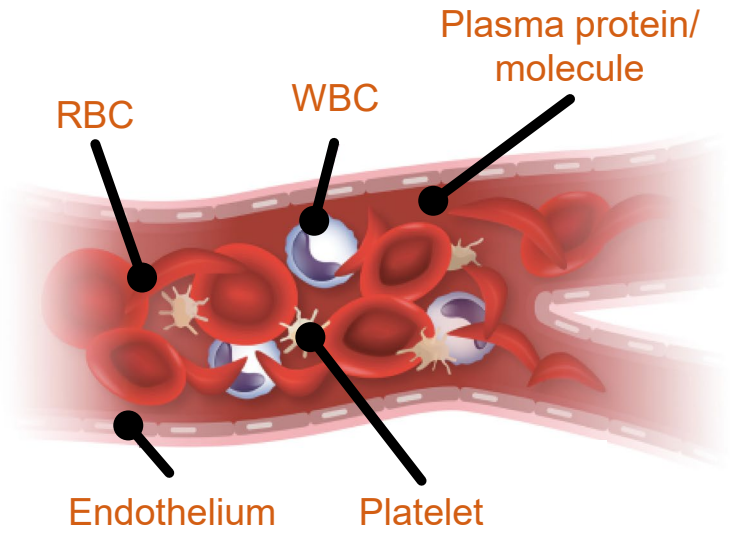
- VOCs are severe pain events caused by blockages of blood vessels, initiated by the sickled RBCs resulting from HbS polymerization

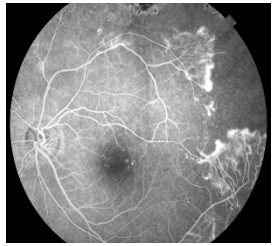
Multiple genotypes can lead to the presence of HbS and frequent VOCs, including:

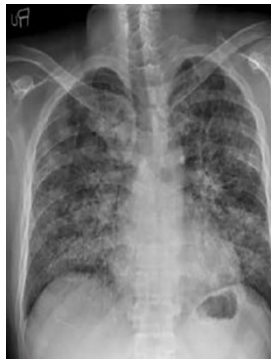
- Two copies of Sickle Hemoglobin Variant (HbSS)
- One sickle hemoglobin variant and one beta-0* (HbS / β^0) or non-beta-0 variant (HbS / β^+)
- One sickle hemoglobin variant and one other hemoglobin variant (HbSC or $HbSD^{Punjab}$, $HbSO^{Arab}$)

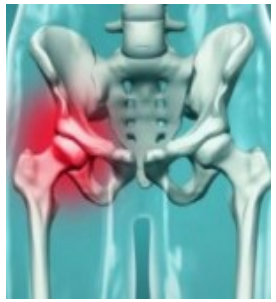
1. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010; 2. Cappellini MD, et al. *Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT)*. 3rd ed. Thalassaemia International Federation; 2014.

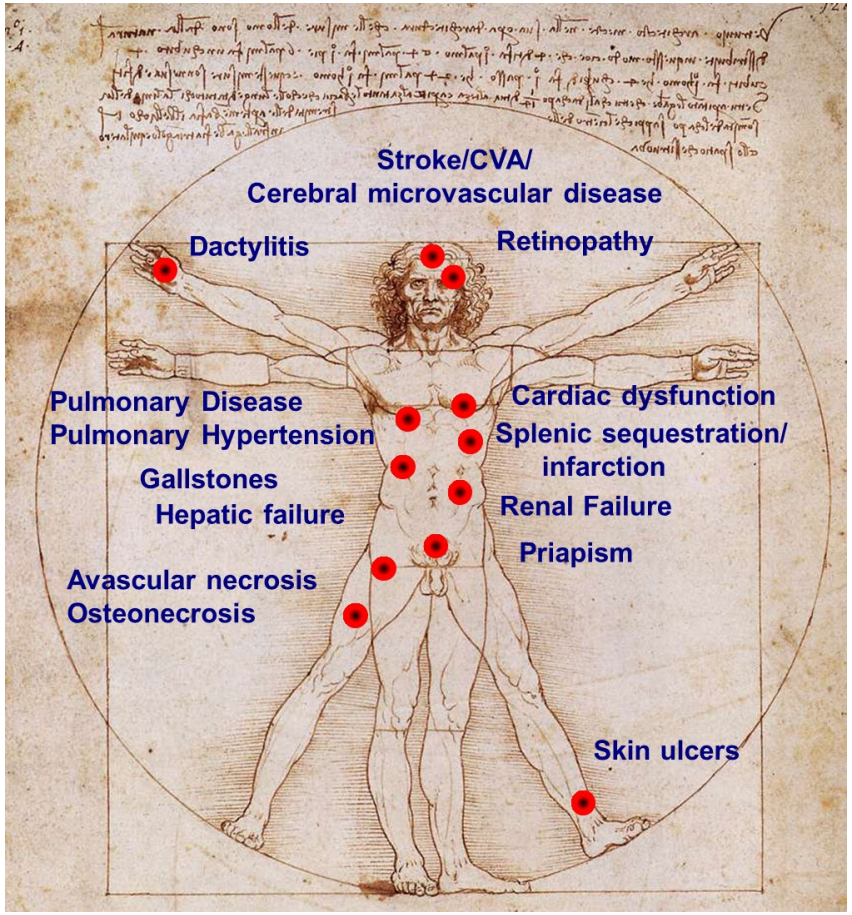
Sickle cell disease complex vascular pathophysiology

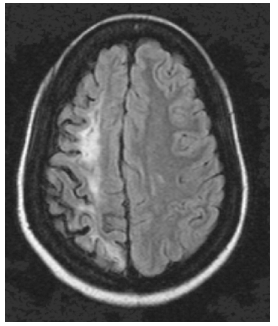


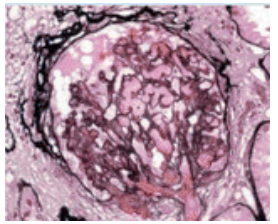


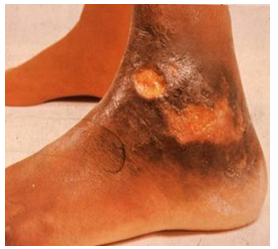






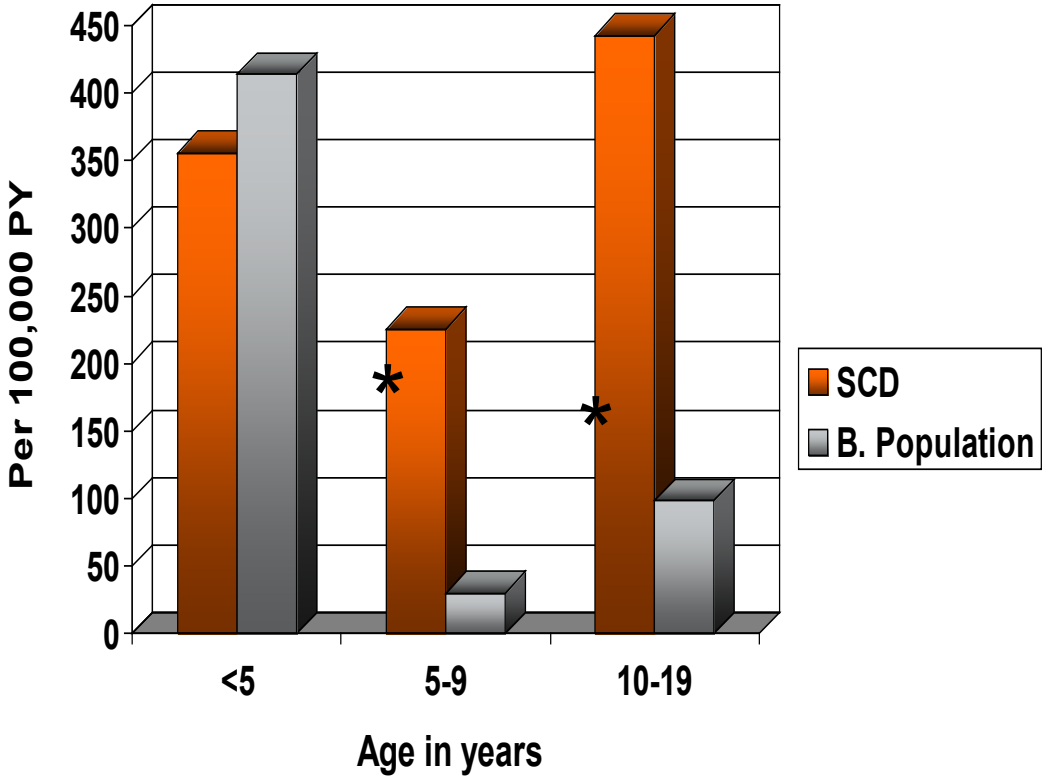






Sickle Cell Disease Mortality in Children State of Tennessee

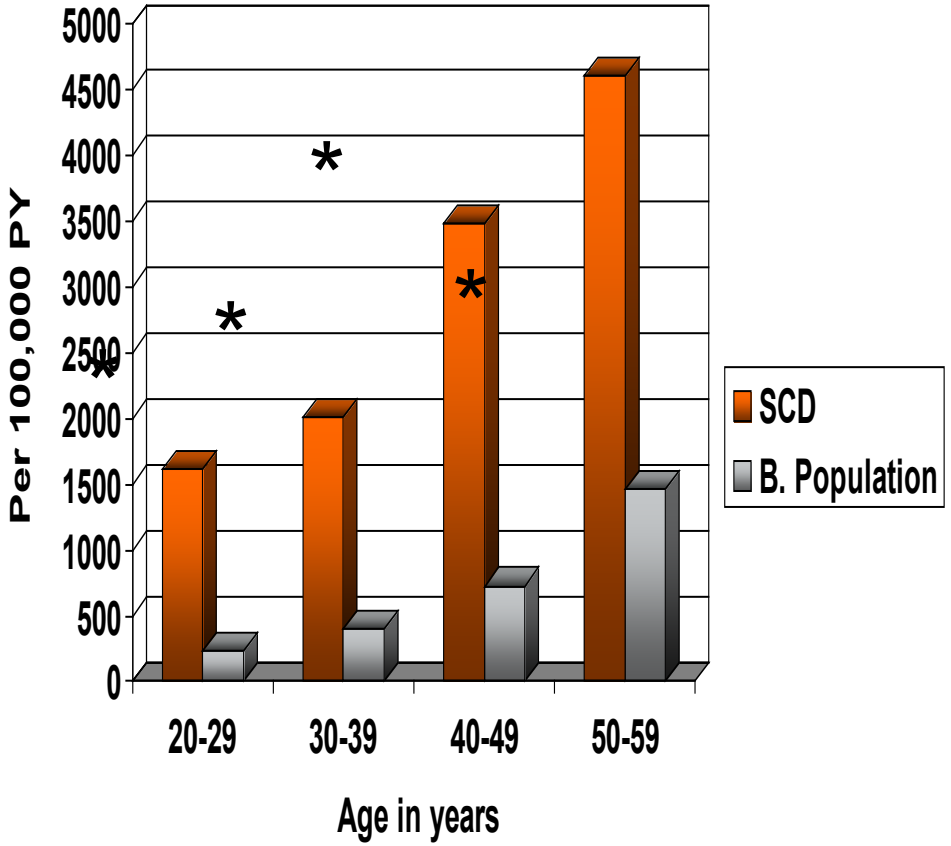
- Patients <5 years did not have increased mortality
- Patients 5-9 had a 7.7 fold increased risk of death (p<0.001)
- Patients 10-19 had a 4.5 fold increased risk of death (p<0.001)



Shankar *et al Am. J. Hem 2005*

Sickle Cell Disease Mortality in Children State of Tennessee

- Overall mortality in adults was 3-6 times higher than the control population for all adult age groups.

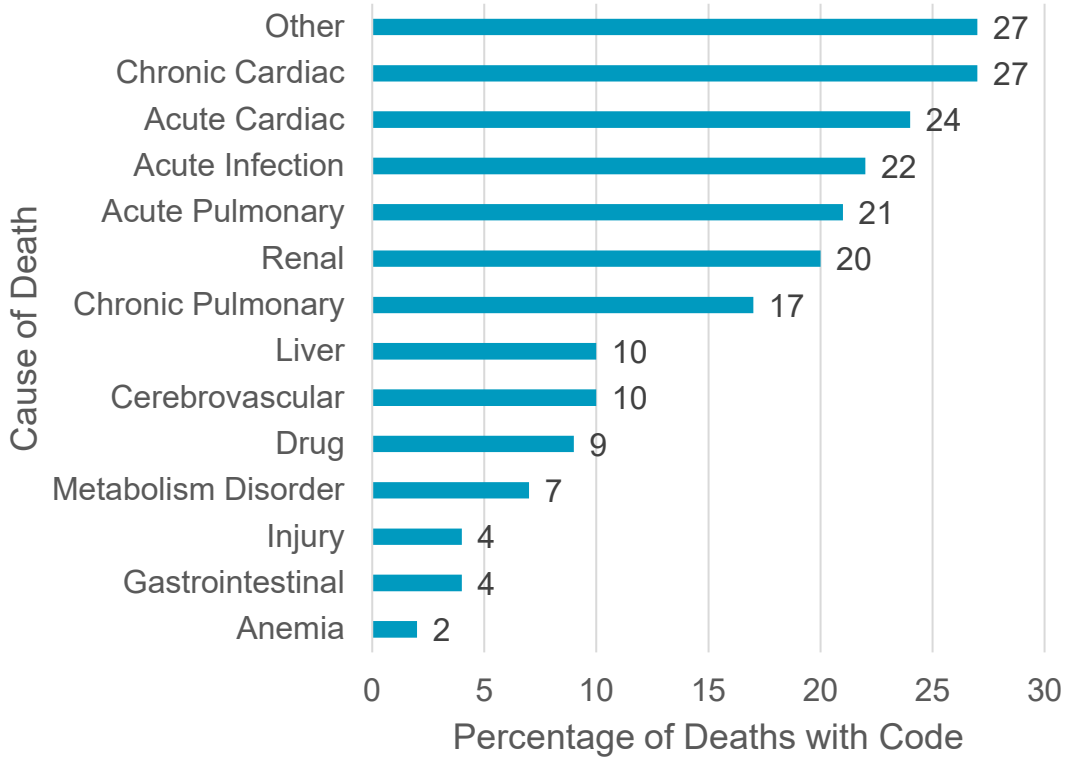


Shankar *et al Am. J. Hem 2005*

SCD Morbidity and Mortality

- **In the US the cost of caring for patients with SCD exceeds 1 billion dollars annually.**

- **In a study of adults from 2003-2016 the median survival was 48 years.**



Years 2015-2017, all ages

Payne AB, et al. *Ann Emerg Med*. 2020;.
Debaun et al. *Blood 2019*

Sickle Cell Disease Therapy

- Supportive care
- Penicillin prophylaxis
- Pneumococcal vaccination
- Transfusion therapy
- Hydroxyurea, ↑ HbF, Glutamic acid, Crizanlizumab, and Voxelotor
- *Allogeneic Stem Cell transplant is the only curative therapy*
  - *Only ~10% of the patients have HLA identical donor*

Transfusion Dependent β-Thalassemia

- 1.5% of the world population, and around 40,000 affected infants are born each year, with half of them classified as transfusion-dependent.
- β-Thalassemia is caused by mutations resulting in a single nucleotide substitution, small deletions or insertions within the β-globin gene or in rare cases, gross deletions.
- More than 350 β-thalassemia mutations have been described
  - β^{+} denoting mild mutations that cause a relative reduction of β-globin chain synthesis
  - β^{0} referring to severe mutations that can lead to a complete absence of β-globin chain product

Taher AT. *NEJM. 2021*

Several genotypes may give rise to severe TDT

Patients with TDT require RBC transfusion every 2-5 weeks

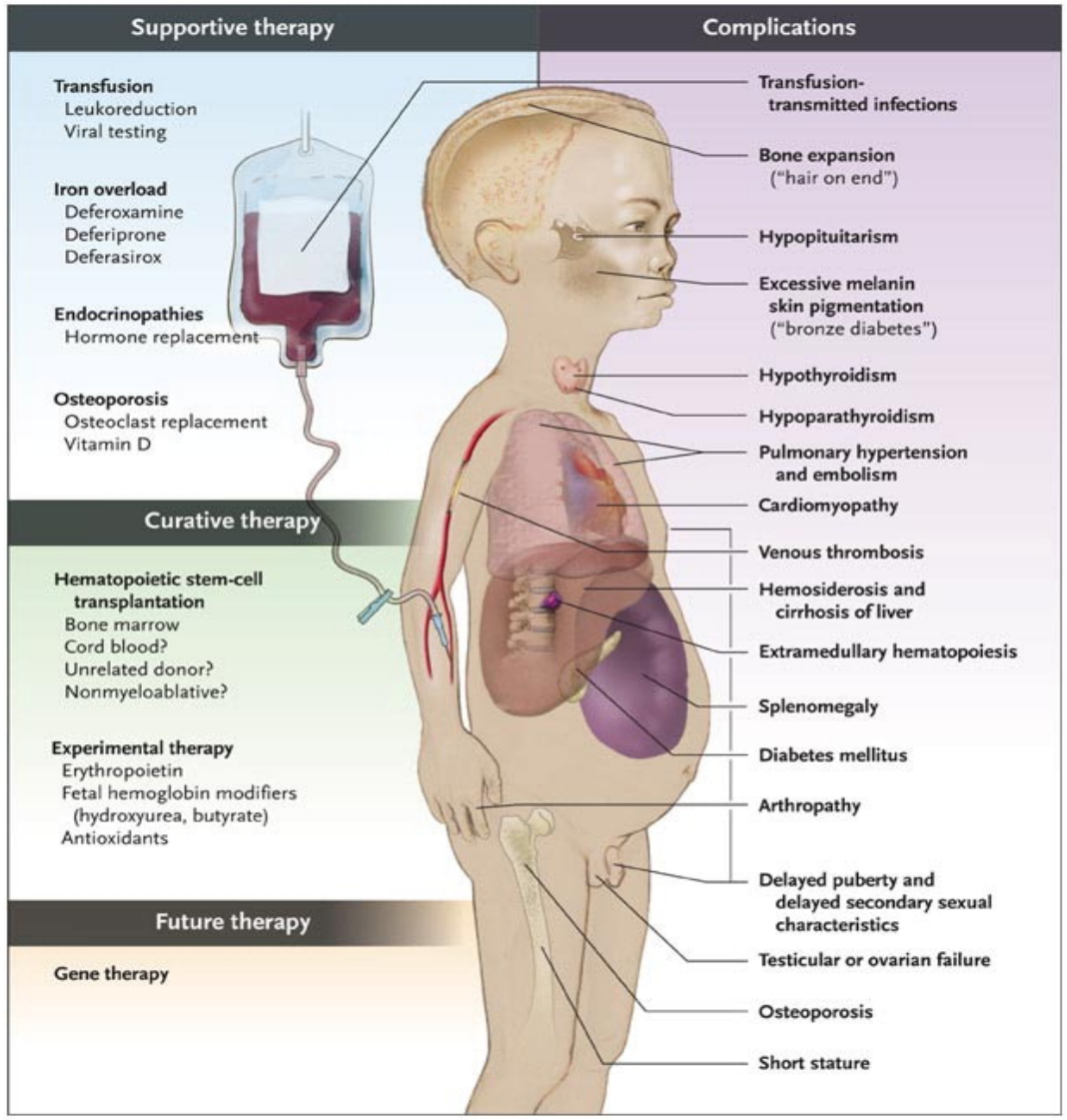
- Lifelong frequent transfusion is required due to the lack of functional hemoglobin

Multiple genotypes can result in little to no functional beta-globin and lead to TDT, including:

- Two copies of beta-0 variant (β^0 / β^0)
- One beta-0 and one non-beta-0 variant (such as β^0 / β^+ or β^0 / HbE)

1. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010; 2. Cappellini MD, et al. *Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT)*. 3rd ed. Thalassaemia International Federation; 2014.

Clinical Manifestations Of β-thalassemia



Galanello R, et al. *Orphanet J Rare Dis.* 2010;5:11.

Iron Overload

- Liver, heart, endocrine organs

Thrombosis (especially if splenectomized)

Bone and Joint Manifestations

- Osteoporosis/Fractures
- Arthropathy

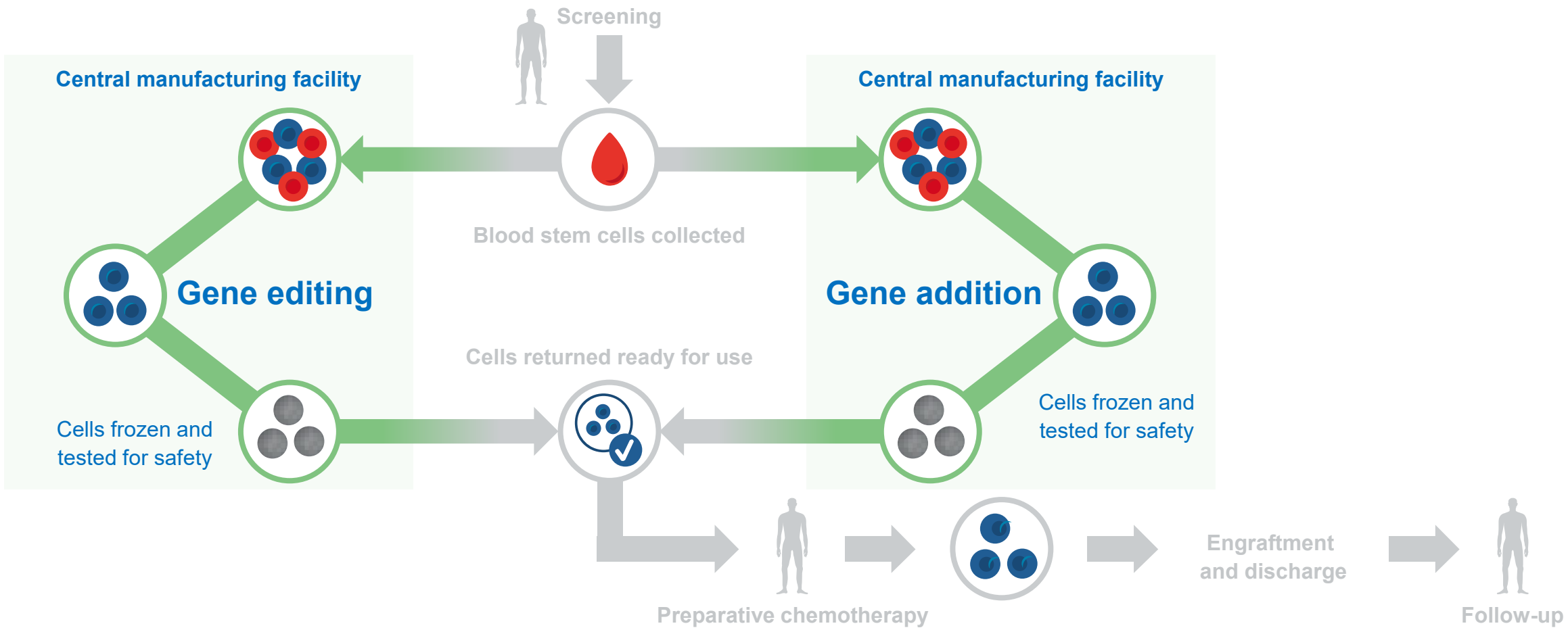
Cardiopulmonary (anemia, pulmonary hypertension)

Transfusion Dependent β-Thalassemia Therapy

- Red blood transfusions with extended antigen typing to minimize the risk of alloimmunization
- Monitoring iron overload using liver and cardiac MRI
- Iron Chelation therapy
- Luspatercept (recently approved in the US and Europe) it blocks SMAD2/3 signaling, and enhance erythroid maturation
- Allogeneic bone marrow transplant from HLA identical sibling

Taher AT. *NEJM. 2021*

Gene therapy and gene-editing process

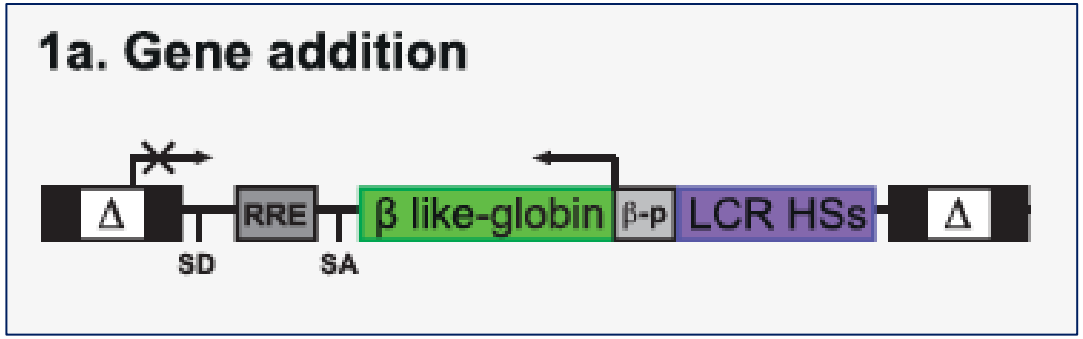


Gene Addition Approach

Gene Therapy for Beta Thalassemia

- Used a self-inactivating Lentiviral vector. It encodes a mutated adult β-globin ($\beta^{A(T87Q)}$).

- Largest experience is using leniviral vector encoding a modified β-globin gene βT87Q-globin including an anti-sickling mutation.



Cavazzana-Cavo M et al. *Nature 2010*

Gene Addition Approaches to treating Hemoglobinopathies

- In 2012 a report of an 18-year-old with β^{E}/β^{0} who received an ex vivo transduced bulk BM CD34 cells with 0.6 vector copy per cell
  - Discontinue transfusions 1 year post transplant
  - At last, follow up patient hemoglobin ranged from 9-10 g/dL with 36% being β^{T87Q}

- In 2017 a report of a 13-year-old with β^{s}/β^{s} who received an ex vivo transduced bulk BM CD34 cells.
  - At 15 months patient hemoglobin was 11.8g/dL with 50% being β^{T87Q}

Cavazzana-Calvo *Nature 2010*
Ribeil JA *NEJM 2017*

Gene Addition Approaches to treating Hemoglobinopathies

Initial Challenges:

- **Low vector copy**
  - Improved manufacturing to increase vector copy number
- **Using bone marrow as cell source for patients with sickle cell disease**
  - GCSF contraindicated
  - Use single agent plerixafor was well tolerated and resulted in adequate CD34 collection

HGB-206 Group C: Patient Characteristics for ITT Population

N=43 Patients who Started Cell Collection

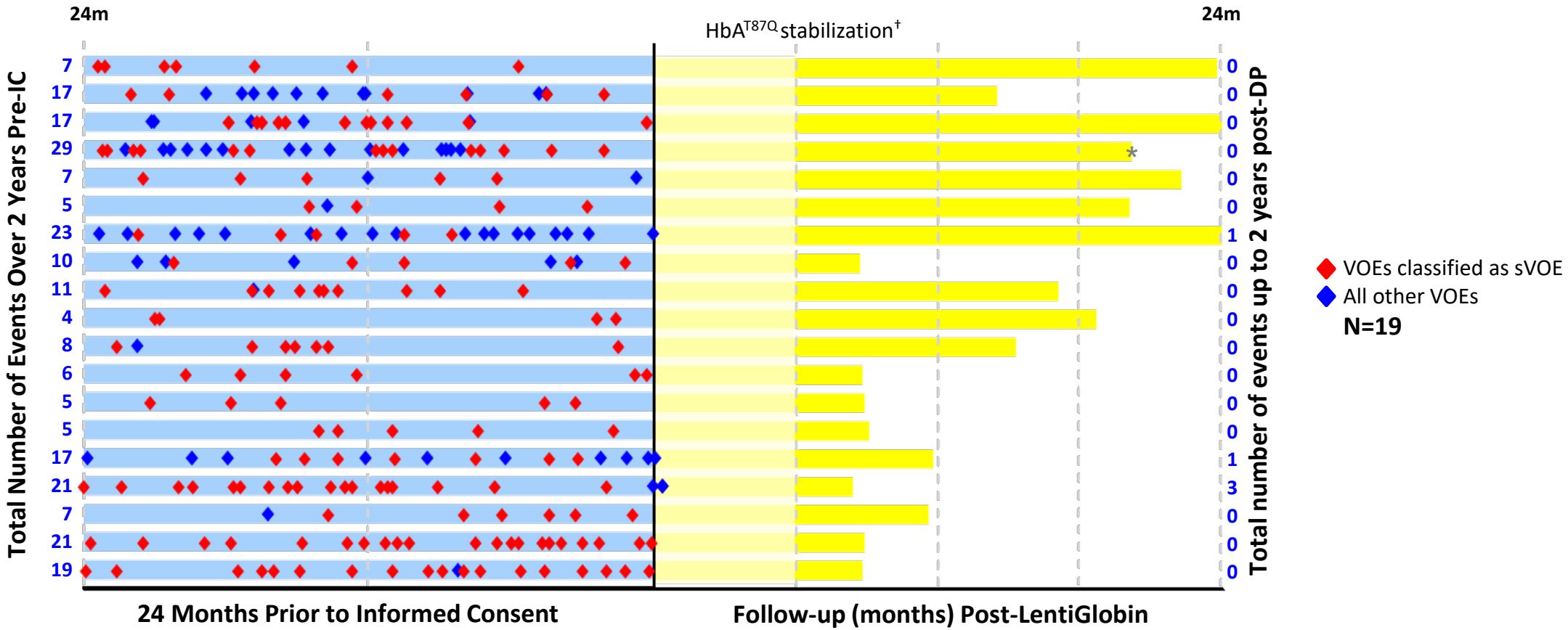
Parameter	N=43	
Age at consent, years, median (min–max)	**24** (12–38)	
Age category 18–50 years, n 12– < 18 years, n	 **34** **9**	
Gender, n	**18F 25M**	
Genotype, n	**40 β^S/β^S 2 β^S/β^0 1 β^S/β^+**	
SCD History	**All patients**	**Patients with ≥4 sVOE at baseline**
sVOEs*, n Annualized no. of events, median (min–max)	**39** **3.5** (0.5–16.0)	**36** **3.5** (2.0–16.0)
ACS, n Annualized no. of events, median (min–max)	**10** **0.5** (0.5-1)	**9** **0.5** (0.5-1)
Priapism, n	**2**	**2**
VOEs*, n Annualized no. of events, median (min–max)	**39** **4** (2.0–34.5)	**36** **4.3** (2.0-34.5)
Any history of stroke, n	**6**	**0**

HGB-206 Group C: Treatment and Drug Product Characteristics

N=32 Infused Patients

Parameter	N=32 Median (min–max)
Treatment characteristics	
No. of mobilization cycles	**2** (1–4)
CD34+ cells collected per mobilization cycle, x10^6 cells/kg	**10.4** (3.9–55.4)
Estimated average busulfan AUC, min*µmol[†]	**4843.0** (1445*–7322)
Neutrophil engraftment, ANC ≥ 500 /µl x 3 days, days	**19.5** (12–35)
Platelet engraftment, platelets > 50k /µl x 3 days, days[‡]	**30** (18–136)
Duration of hospitalization[§], days	**35** (26–65)
Drug product characteristics	
Vector copy number (average/patient), copies/diploid genome	**3.8** (2.3–5.7)
CD34+ cells transduced (average/patient), %	**80.2** (63–93)
CD34+ cell dose, x10^6 cells/kg	**6.8** (3.0–24.0)

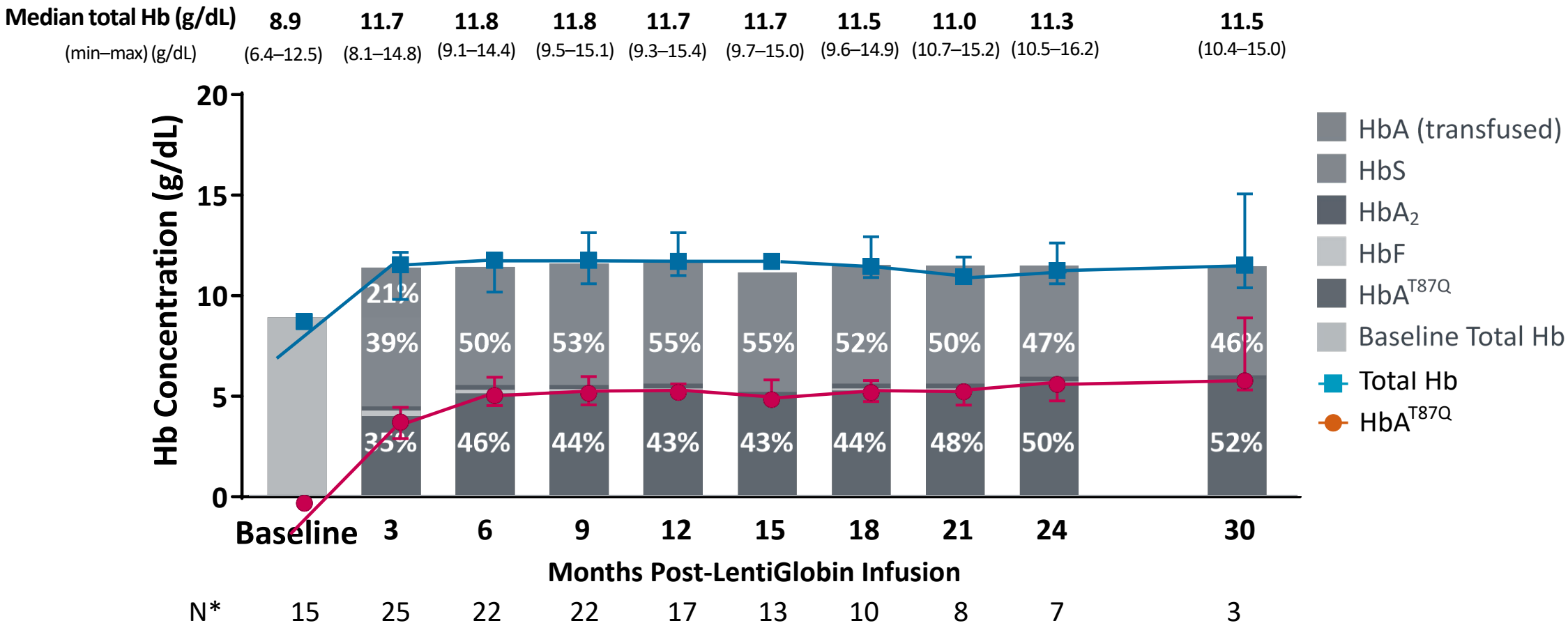
HGB-206 Group C: Complete Resolution of VOEs ≥6 Months Post-LentiGlobin Treatment



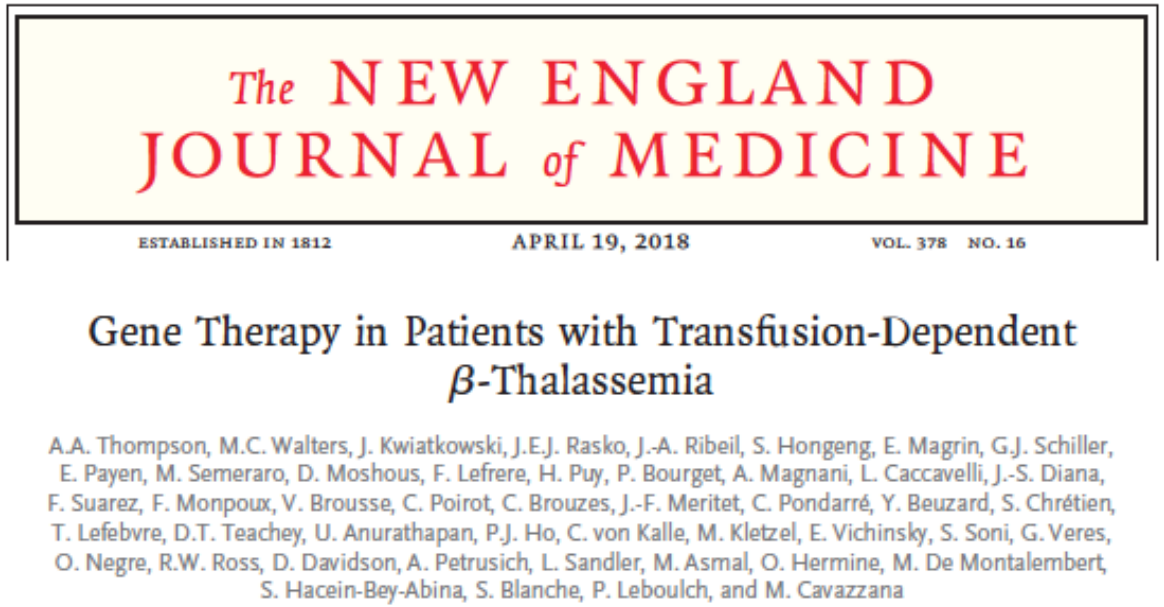
Median (min–max) annualized VOE rate	5 (2.0–14.5)	0 (0–4.3)

- No VOEs occurred after stabilization of HbA^{T87Q} expression† (last VOE at Day 22 post-LentiGlobin infusion)

HGB-206 Group C: Median HbA^{T87Q} ≥ 40% at ≥ 6 Months Post-LentiGlobin Treatment



- 22 patient ages 12-35 with TDT and a median follow up of 26 months
- 12/13 patients with non-β^0/ β^0 are transfusion independent at last follow up
- 3/9 patients with β^0/ β^0 or IVS1-110 mutation were transfusion independent


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 19, 2018 VOL. 378 NO. 16

Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia

A.A. Thompson, M.C. Walters, J. Kwiatkowski, J.E.J. Rasko, J.-A. Ribeil, S. Hongeng, E. Magrin, G.J. Schiller, E. Payen, M. Semeraro, D. Moshous, F. Lefrere, H. Puy, P. Bourget, A. Magnani, L. Caccavelli, J.-S. Diana, F. Suarez, F. Monpoux, V. Brousse, C. Poirot, C. Brouzes, J.-F. Meritet, C. Pondarré, Y. Beuzard, S. Chrétien, T. Lefebvre, D.T. Teachey, U. Anurathapan, P.J. Ho, C. von Kalle, M. Kletzel, E. Vichinsky, S. Soni, G. Veres, O. Negre, R.W. Ross, D. Davidson, A. Petrusich, L. Sandler, M. Asmal, O. Hermine, M. De Montalembert, S. Hacein-Bey-Abina, S. Blanche, P. Leboulch, and M. Cavazzana

Gene addition therapy approaches to treatment of hemoglobinopathies

Limitations:

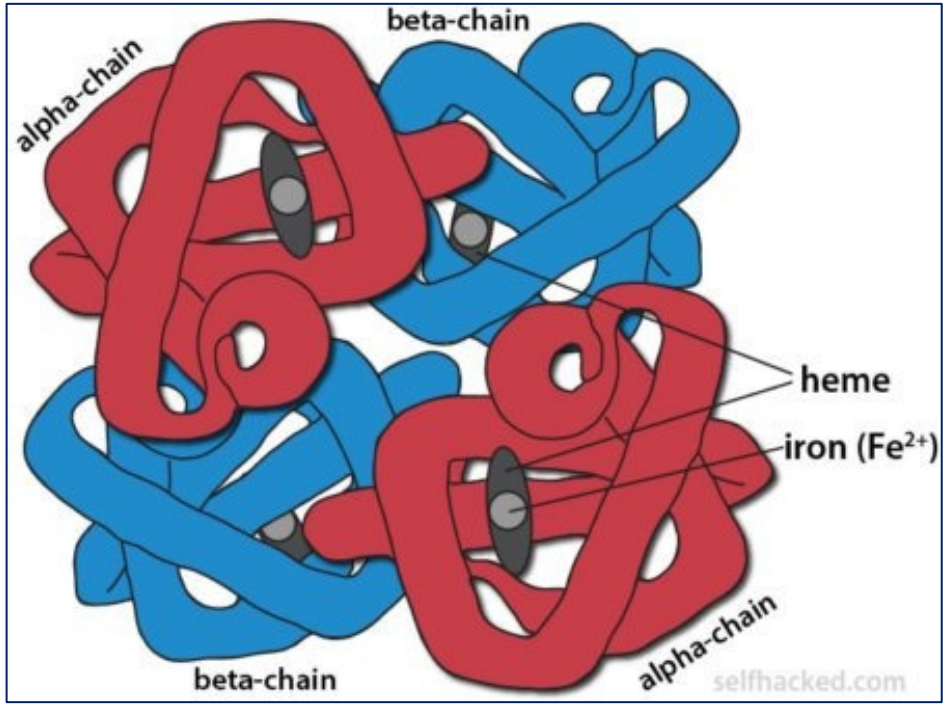
- Random insertion site
- Recent report of MDS and AML in patients with sickle cell disease receiving LentiGlobin gene therapy for sickle cell disease (ClinicalTrials.gov: NCT02140554 and NCT04293185)[1]
  - One patient developed MDS that evolved to AML 3 years post treatment
  - One patient developed AML 5.5 years post therapy
  - One patient with Trisomy 8, 6 months post therapy with no dysplasia or increased blasts
- Absence of data in patients with SCD and CNS disease

https://www.businesswire.com/news/home/20210216005442/en/

Gene Editing Approach to Increase Fetal Hemoglobin production

Hemoglobin

- Hemoglobin (Hb), the protein that carries oxygen from the lungs to the tissues, is a tetramer composed of 2 α-like globin chains and 2 β-like globin chains.

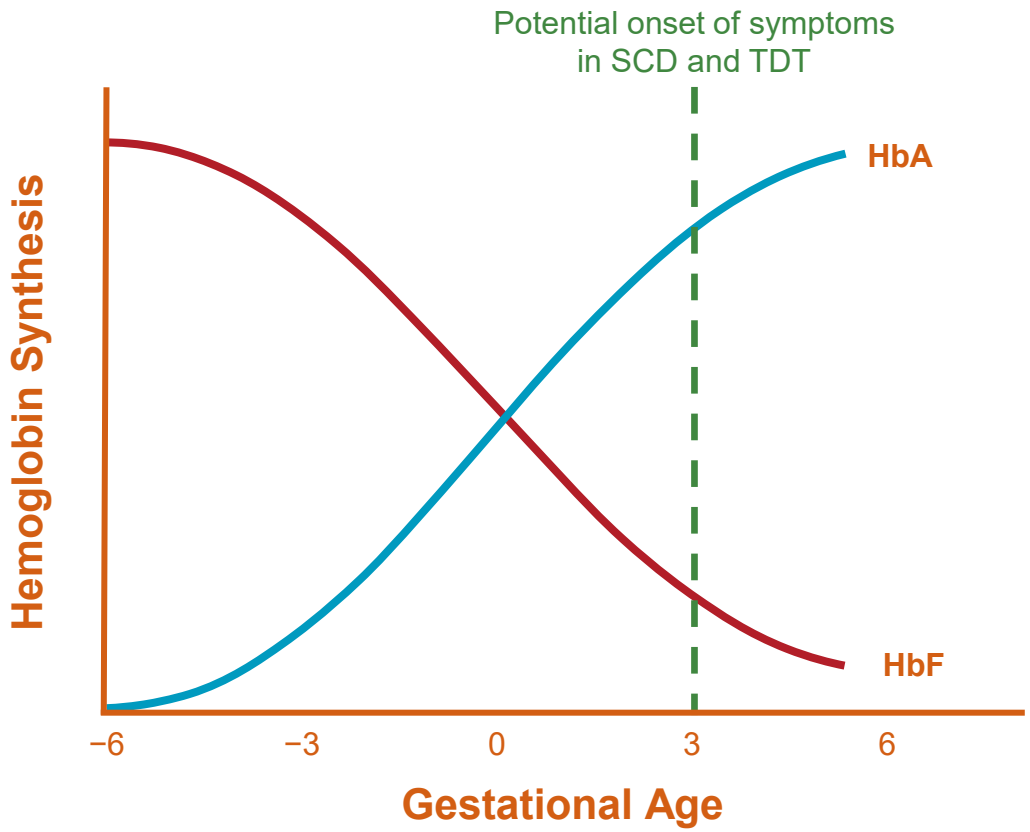


Sankaran VG et al. *Cold Spr Presp 2013*

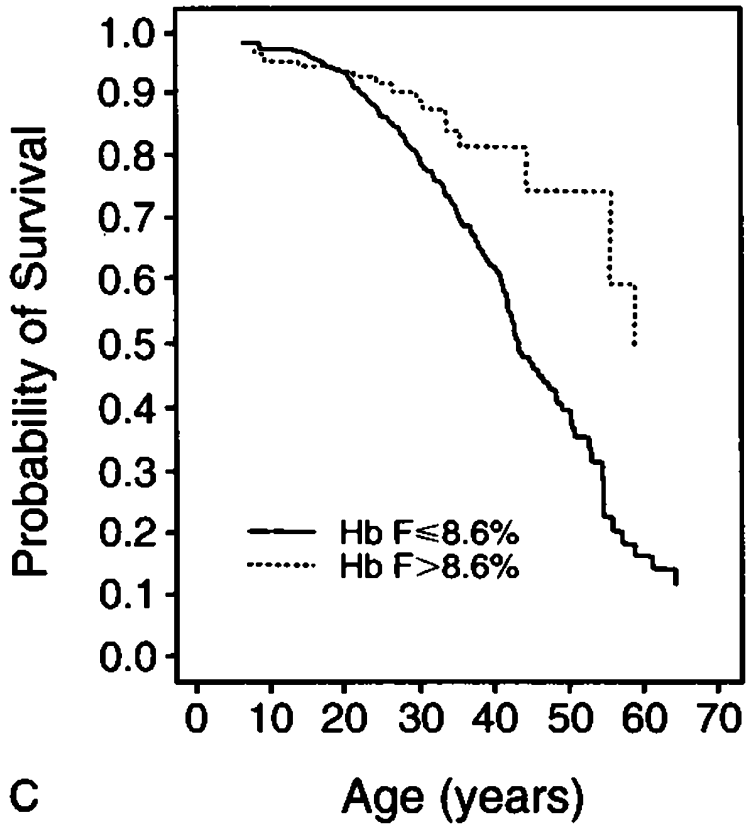
Symptoms arise as hemoglobin switches from fetal to adult[1,2]

- The main type of hemoglobin in early life is HbF
- A few months after birth, HbF is replaced with HbA
- In patients with SCD / TDT, the onset of symptoms occurs as HbF switches to HbA, which is affected by disease-causing mutations

- Hemoglobin switching timeline



Protective Effect of Fetal Hemoglobin



ORIGINAL ARTICLE

Mortality In Sickle Cell Disease -- Life Expectancy and Risk Factors for Early Death

Orah S. Platt, Donald J. Brambilla, Wendell F. Rosse, Paul F. Milner, Oswaldo Castro, Martin H. Steinberg, and Panpit P. Klug*et al.

June 9, 1994

- **In 3764 patients in the pre-hydroxyurea era, HbF > 8.6% was associated with improved survival**

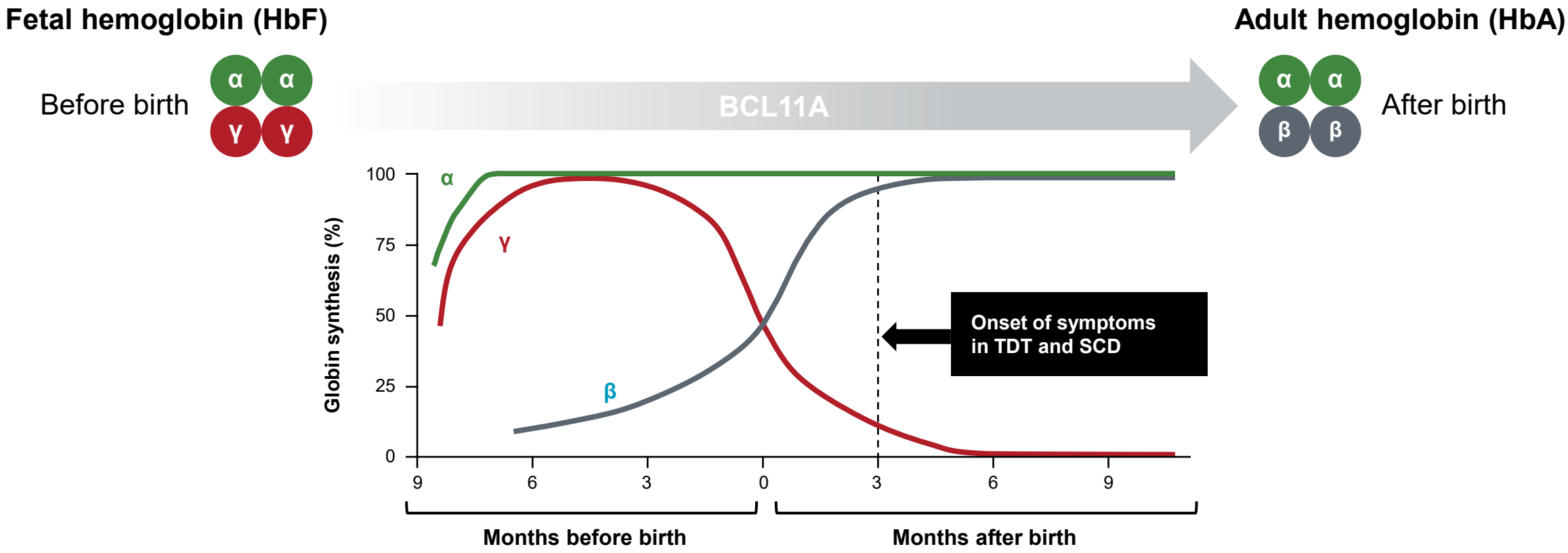
Protective Effect of Fetal Hemoglobin

- Janet Watson in 1948 observed that the blood of young children with SCD showed less sickling and attributed this to the residual HbF that exists in early life.
- Adults affected by SCD express unusually high levels of HbF and that these individuals present with a much milder course of SCD
- The phenomenon was named hereditary persistence of fetal hemoglobin (HPFH)
- In 2007, a series of genome-wide association studies (GWAS) identified BCL11A gene as a modulator of HbF levels

Watson J, *Am J of Med 1948*
Jacob GF *et al. Br J of Hem 1958*
Menzel Set al. *Nat Gen 2007*

Symptoms arise as hemoglobin switches from fetal to adult

- **BCL11A is a transcription factor responsible for the repression of fetal hemoglobin expression[1]**

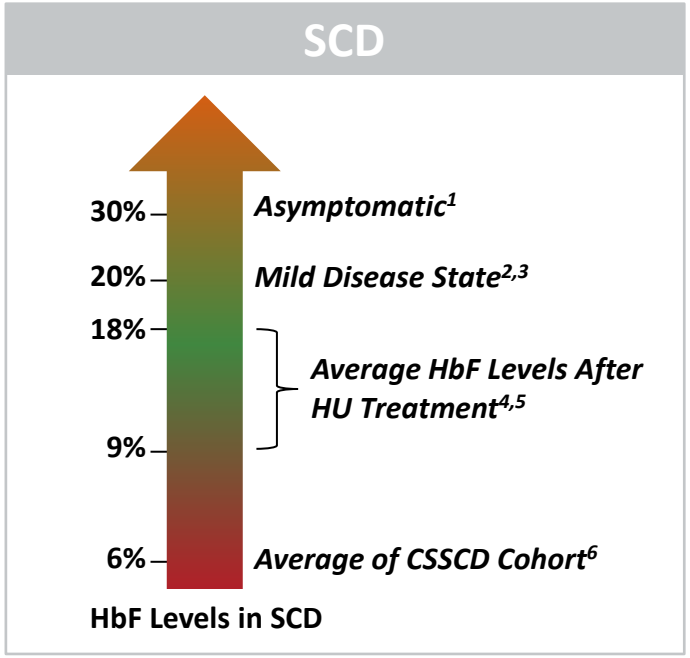


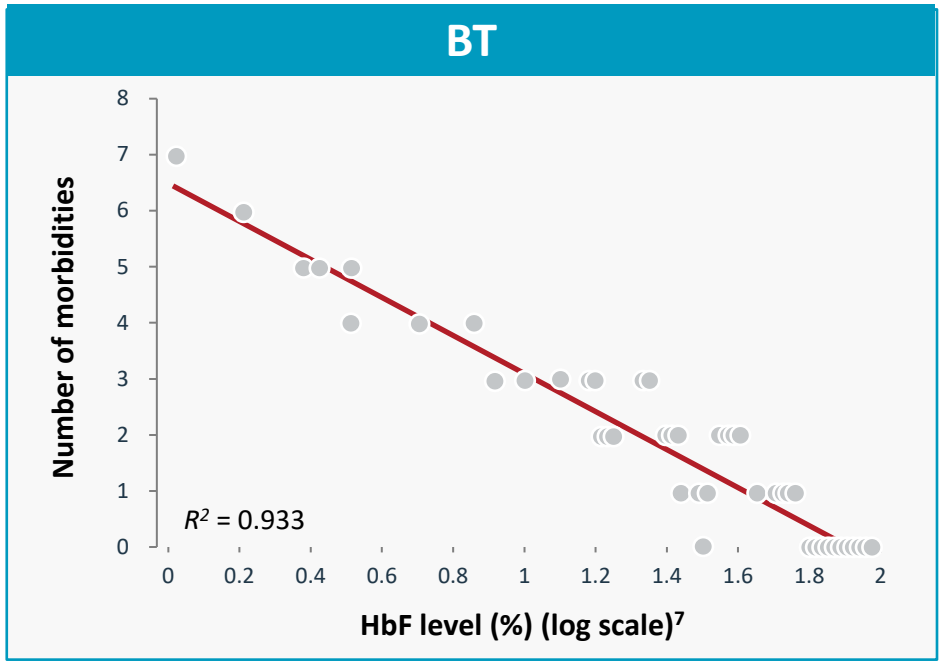
SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

1. Frangoul H, et al. *N Engl J Med*. 2021;384:252-260.

Persistence of HbF can Alleviates Symptoms in Patients with SCD and β Thalassemia

A subset of patients with β-T or SCD continue to express HbF into adulthood, a condition known as hereditary persistence of HbF, and these patients experience reduced or no symptoms with no detrimental effects[8-10]





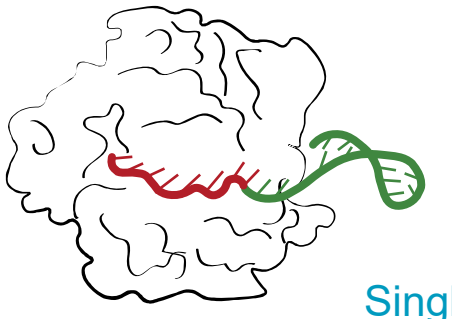
BT, beta-thalassemia; CSSCD, Cooperative Study of Sickle Cell Disease; HbF, fetal hemoglobin; HU, hydroxyurea; SCD, sickle cell disease.

1. Ngo DA, et al. *Br J Haematol*. 2012;156:259-264. 2. Akinsheye I, et al. *Blood*. 2011;118:19-27. 3. Alsultan A, et al. *Am J Hematol*. 2012;87:824-826. 4. Nevitt, SJ et al. *Cochrane Database Syst Rev*. 2017;4:CD002202. 5. Fitzhugh CD, et al. *PLoS One*. 2015;10:e0141706. 6. Platt OS, et al. *N Engl J Med*. 1991;325:11-16. 7. Musallam K, et al. *Blood*. 2012;119:364-367. 8. Murray N, et al. *Br J Haematol*. 1988;69:89-92. 9. Conley CL, et al. *Blood*. 1963;21:261-281. 10. Bank A. *Blood*. 2006;107:435-443.

CRISPR-Cas9 as a gene-editing tool[1,2]

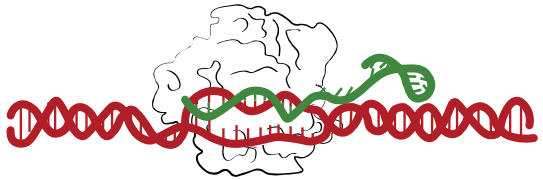
CRISPR-Cas9 consists of the Cas9 enzyme and the single-guide RNA

Cas9 endonuclease



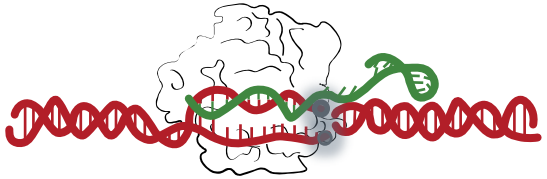
Single-guide RNA

Cas9 and the single-guide RNA form a complex and function as a unit to edit the target DNA only at precise locations



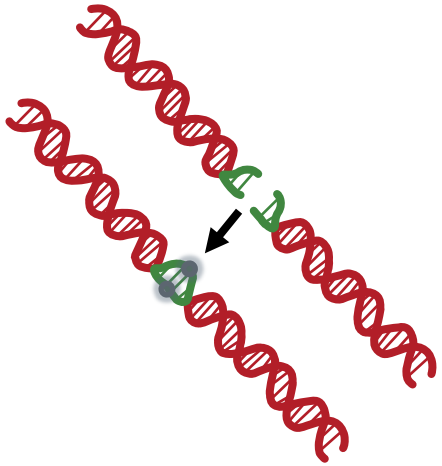
Single-guide RNA binds both the target DNA and the Cas9 endonuclease

During repair of the edited DNA, a change in the target DNA sequence is introduced



Cas9 endonuclease editing DNA, double-strand edit

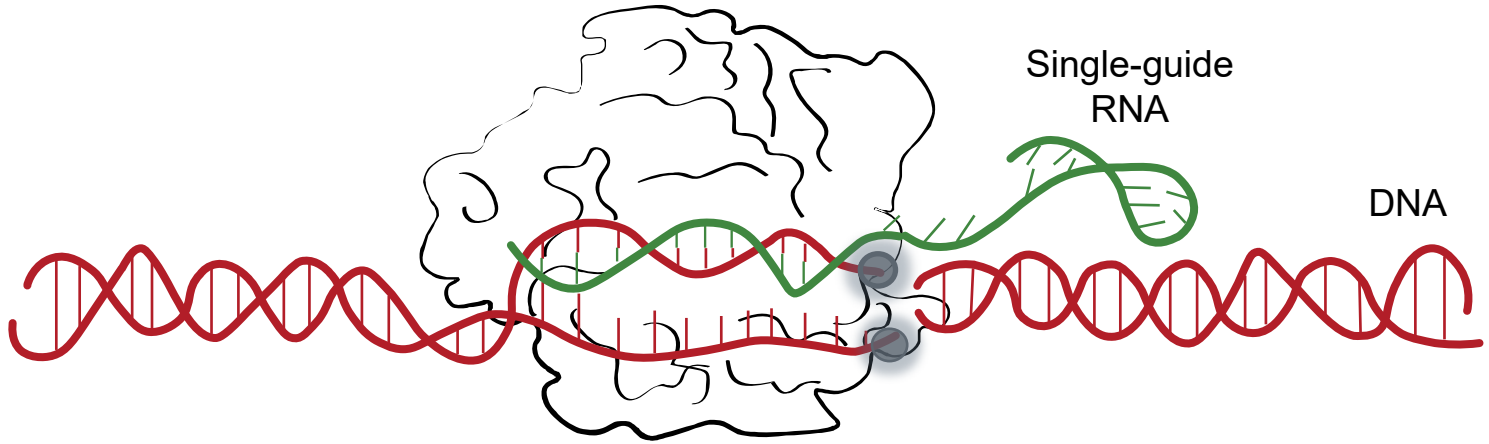
The change to the target DNA sequence inactivates the gene or alters the function of the DNA



Using CRISPR-Cas9-based gene editing to target *BCL11A*

- Our goal is to edit the specific region of the *BCL11A* gene to **decrease the expression of the BCL11A protein** and increase the expression of HbF[1]

Cas9 endonuclease



Nobel Prize in Chemistry Awarded to 2 Scientists for Work on Genome Editing

Emmanuelle Charpentier and Jennifer A. Doudna developed the Crispr tool, which can change the DNA of animals, plants and microorganisms with high precision.

"One of gene technology's sharpest tools: the CRISPR-Cas9 genetic scissors"[2]

CRISPR: clustered regularly interspaced short palindromic repeats; HbF: fetal hemoglobin; RNA: ribonucleic acid.

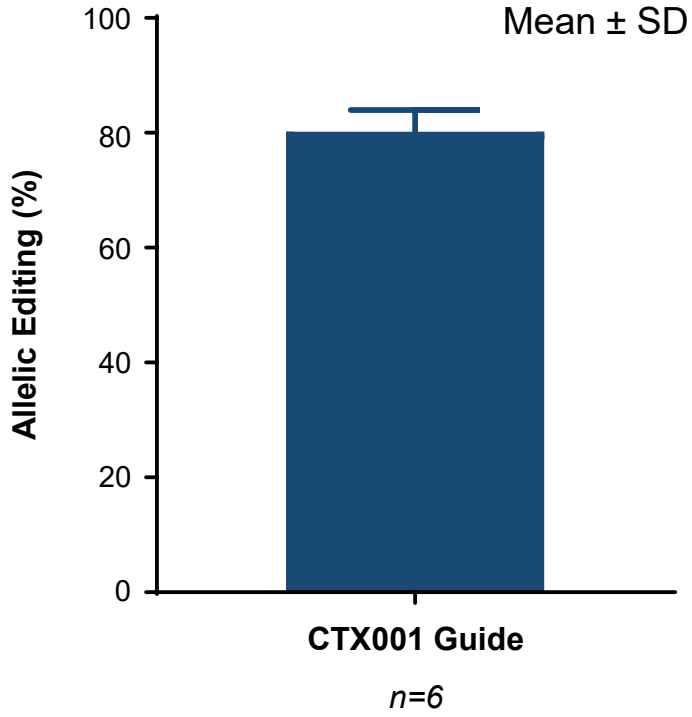
1. Frangoul H, et al. *N Engl J Med*. 2021;384:252-260; 2. The Royal Swedish Academy of Sciences. The Nobel Prize in Chemistry 2020, 2020. https://www.nobelprize.org/uploads/2020/10/popular-chemistryprize2020.pdf.

Manufacturing process optimized to achieve high editing rates[1]

Multiple CRISPR-Cas9 parameters optimized:

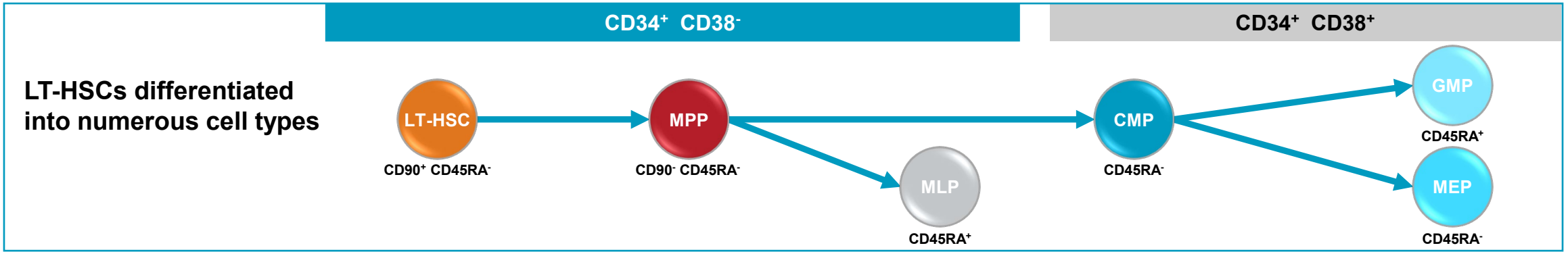
- Cas9 + gRNA ribonucleoprotein (RNP) vs. mRNA
- gRNA sequences and chemical modifications
- Nuclear localization sequences
- Synthesis and purification methods
- Manufacturing

Editing efficiency at clinical scale in human CD34⁺ cells in vitro

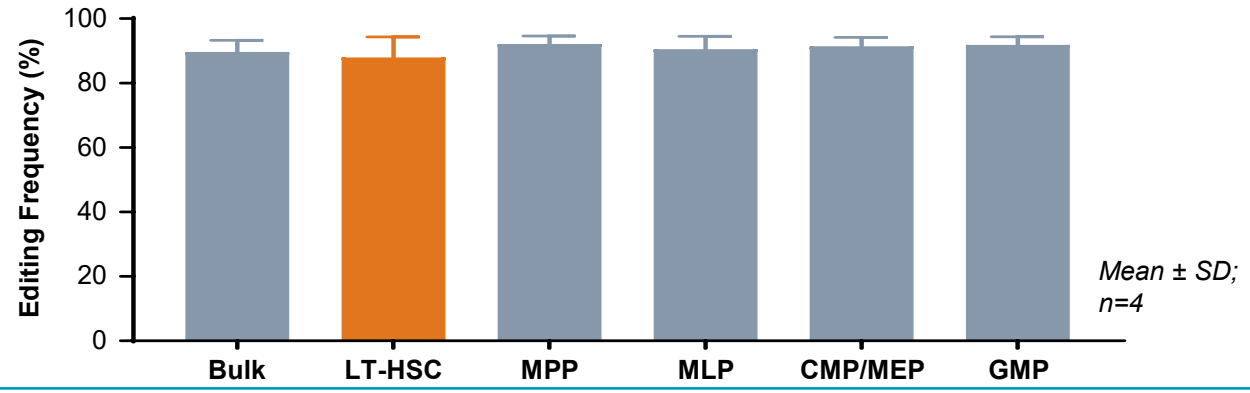


Efficient editing in long-term hematopoietic stem cells

Similar data observed in process development and process-qualified samples from four healthy donors



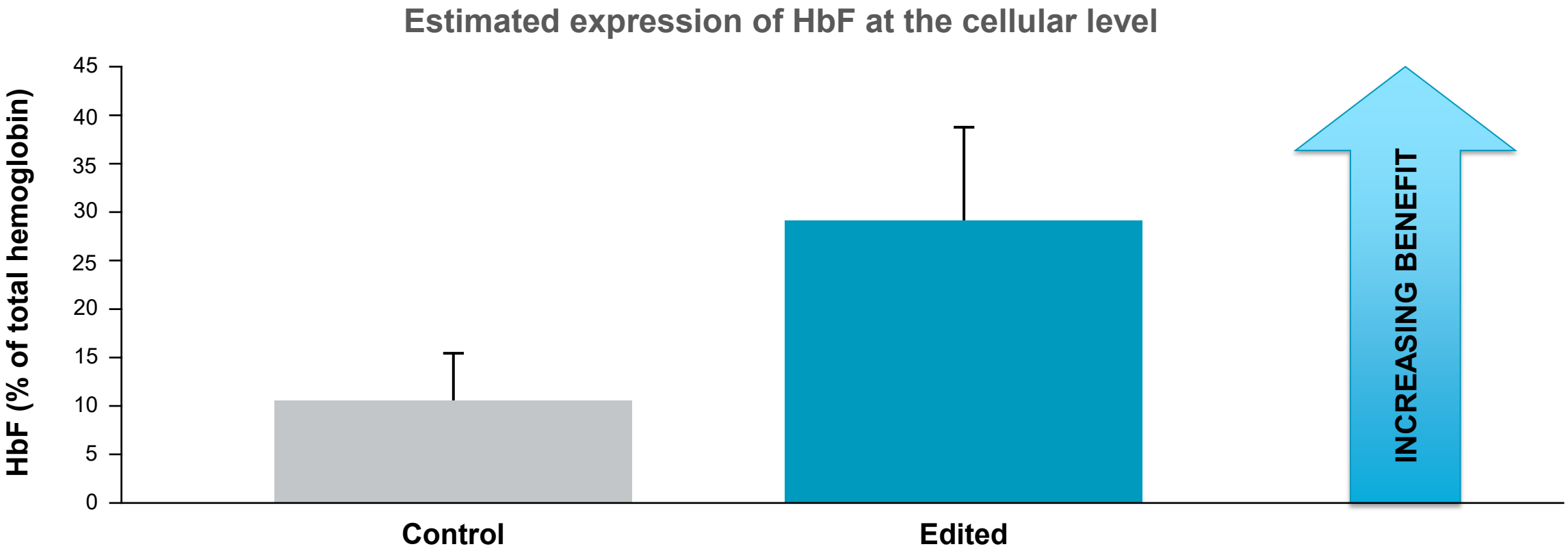
HIGH RATES OF EDITING ACHIEVED IN ALL CELL TYPES, INCLUDING LT-HSCs



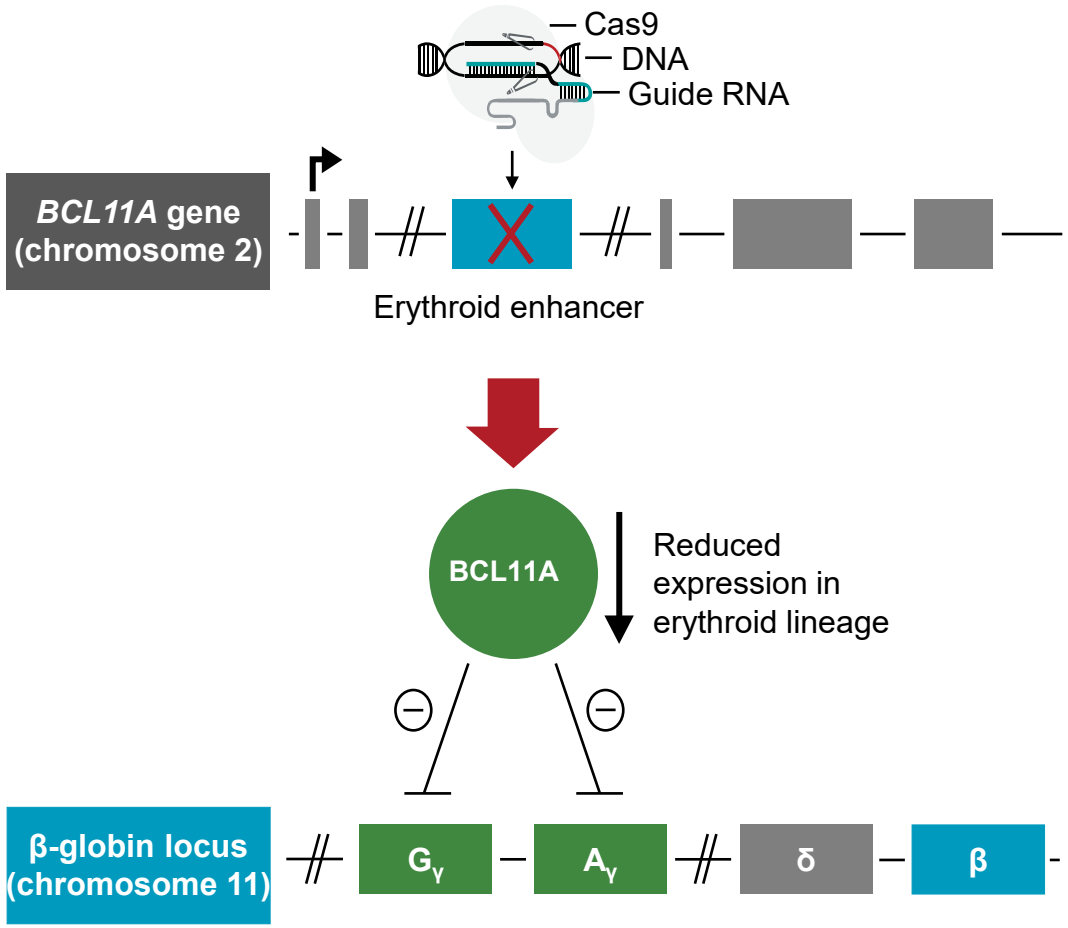
EDITING DOES NOT AFFECT PREVALENCE OF LT-HSCs

POPULATION	PERCENTAGE OF CELLS	
	Mock	*Edited*
Bulk CD34+	95	94
LT-HSC	7.8	8.0
MPP	19	16
MLP	13	8.5
CMP/MEP	11	11
GMP	8.4	13

Meaningful increases in HbF were achieved in human stem cells edited with CRISPR-Cas9 in preclinical studies[1]



CRISPR-Cas9-Mediated Editing of *BCL11A* Increases HbF Levels[1]



- Naturally occurring genetic polymorphisms in *BCL11A* are associated with elevated HbF and decreased severity of TDT and SCD[2-4]
- BCL11A suppresses expression of HbF
- Editing of *BCL11A* results in reactivation of γ-globin expression and formation of HbF ($\alpha 2\gamma 2$) in mouse models
- CTX001 is produced using ex vivo editing of the erythroid enhancer region of *BCL11A* in $CD34^+$ HSPCs and reduces erythroid-specific expression of BCL11A
- Infusion of CTX001 leads to an increase in HbF levels in erythroid cells in vivo

HbF: fetal hemoglobin; HSPCs: hematopoietic stem progenitor cells; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

1. Figure modified from Canver MC, Orkin SH. *Blood*. 2016;127:2536-2545; 2. Murray N, et al. *Br J Haematol*. 1988;69:89-92; 3. Conley CL, et al. *Blood*. 1963;21:261-281; 4. Bank A. *Blood*. 2006;107:435-443.

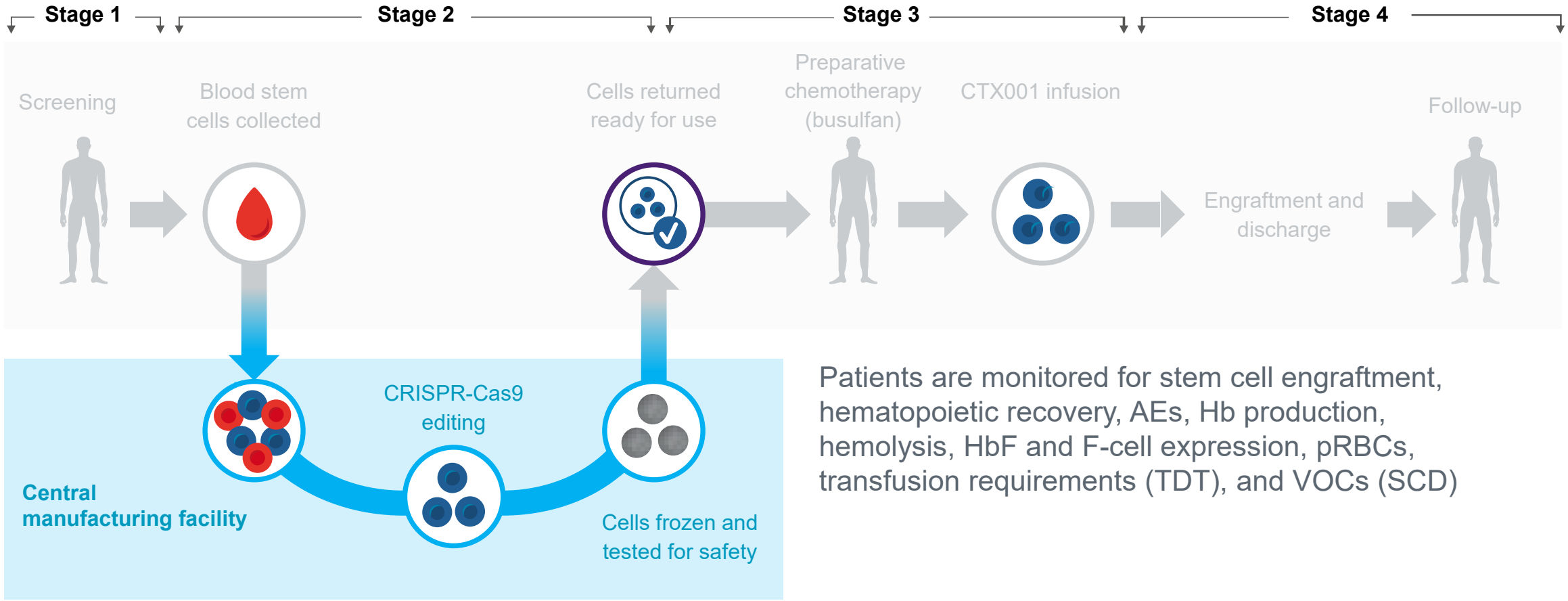
Studies in Patients With Transfusion-dependent β-Thalassemia (TDT) and Sickle Cell Disease (SCD) Are Ongoing

	CLIMB THAL-111	CLIMB SCD-121
Design	Phase 1 / 2, international, multicenter, open-label, single-arm study (NCT03655678)	Phase 1 / 2, international, multicenter, open-label, single-arm study (NCT03745287)
Target enrollment	45 patients aged 12 to 35 years with TDT, including β^0 / β^0 genotypes, defined as a history of at least 100 mL/kg/year or 10 units/year of pRBC transfusions in the previous 2 years	45 patients aged 12 to 35 years with severe SCD and a history of ≥2 vaso-occlusive crises per year over the previous 2 years
Primary endpoints	Proportion of patients achieving sustained transfusion reduction of 50% for at least 6 months starting 3 months after CTX001 infusion	Proportion of patients with HbF ≥20% sustained for at least 3 months starting 6 months after CTX001 infusion

Here, we present safety and efficacy results from the first 10 patients infused with CTX001

HbF: fetal hemoglobin; pRBC: packed red blood cell; SCD: sickle cell disease; TDT: transfusion-dependent β-thalassemia.

In the clinic: CTX001 – an autologous ex vivo CRISPR-Cas9 gene-edited therapy[1]



Patients are monitored for stem cell engraftment, hematopoietic recovery, AEs, Hb production, hemolysis, HbF and F-cell expression, pRBCs, transfusion requirements (TDT), and VOCs (SCD)

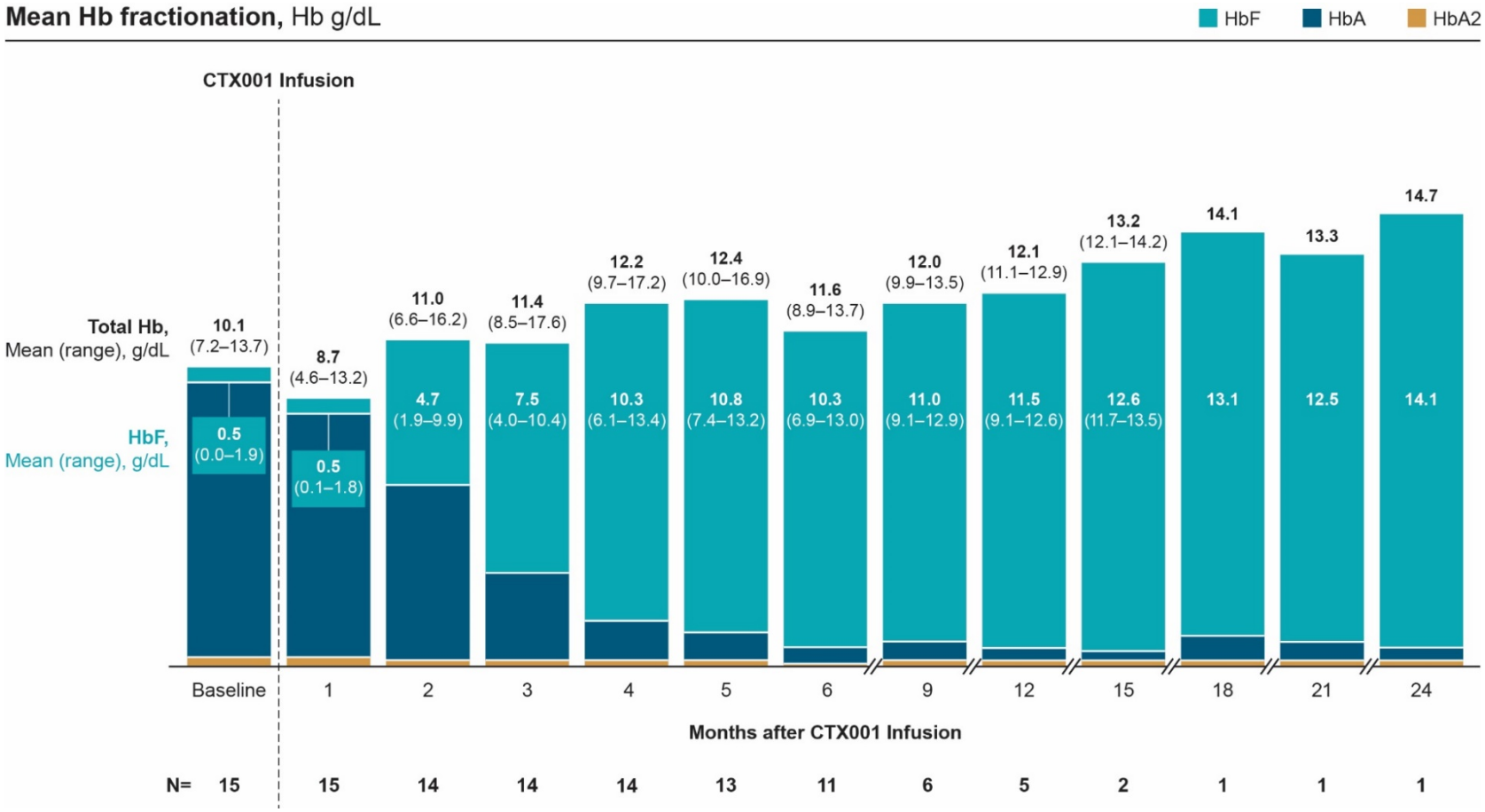
TDT: Patient Baseline and Treatment Characteristics

Patients with *≥3-month follow-up (n=15)*

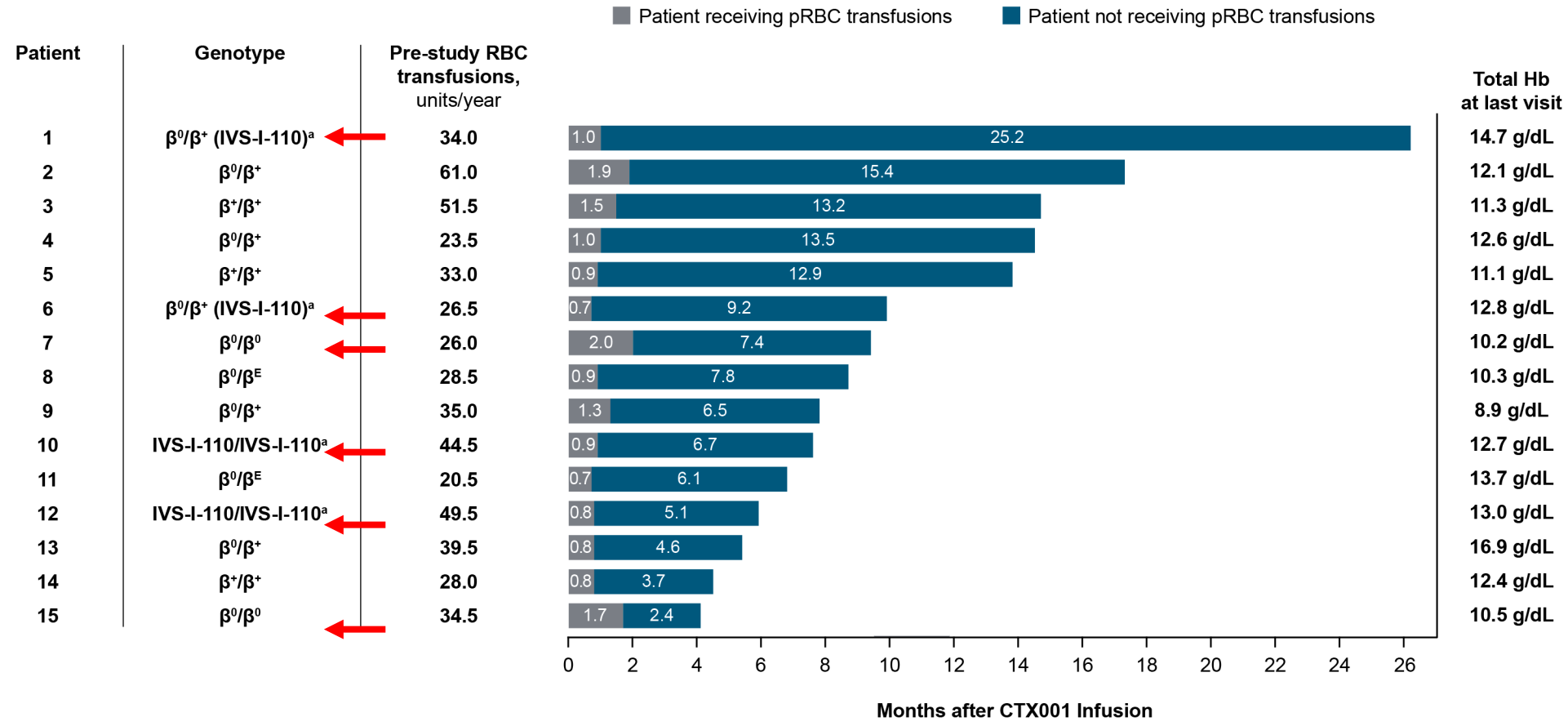
Patient characteristics		
Genotype, n	β^+ / β^+	**2**
	β^0 / β^+ **or** β^0 / β^E	**3/2**
	β^0 / β^+ (IVS-I-110)[a]	**4**
	β^0 / β^0	**4**
Gender, Female/Male, n		**9/6**
Age at consent, years Median (range)		**23** (18 – 32)
Pre-study pRBC transfusions[b] Units/year, median (range)		**34.0** (20.5–61.0)

Treatment characteristics	Median (range)
Drug product cell dose, $CD34^+$ cells × 10^6/kg	**11.6** (3.5 – 16.6)
Neutrophil engraftment,[c] Study Day[d]	**29** (19 – 39)
Platelet engraftment,[e] Study Day[d]	**40** (29 – 56)
Duration of follow-up, Months	**8.7** (4.0 – 26.6)

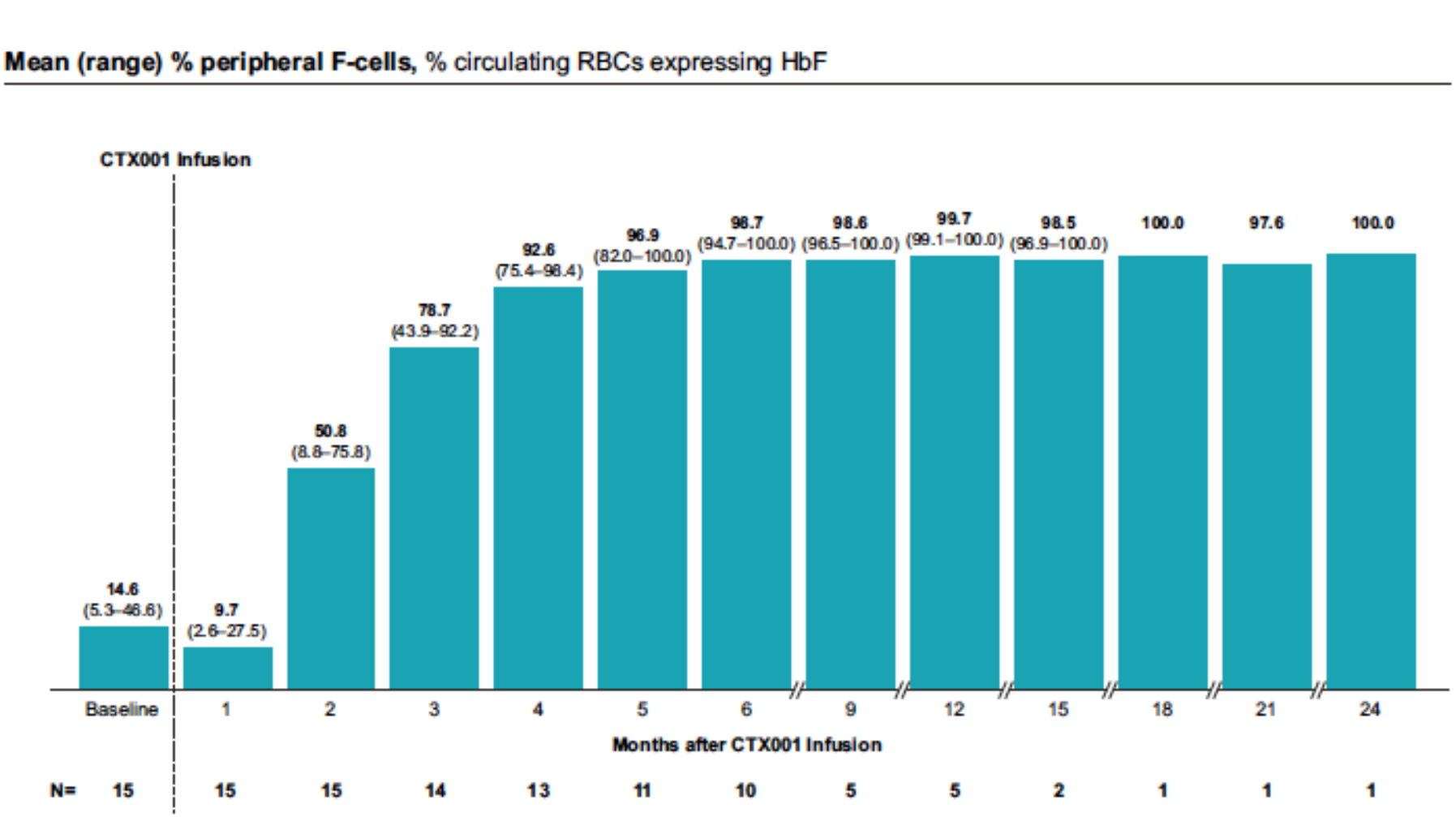
TDT: All patients demonstrated increased total Hb and HbF[1]



TDT: Patients have stopped receiving transfusions within 2 months of CTX001 infusion[1]



TDT: Pancellular Expression of HbF Is Maintained



Durable BCL11A Editing Observed in CD34+ Bone Marrow Cells

	Proportion of edited alleles in CD34+ bone marrow cells[a], %		
	6-month visit	12-month visit	24-month visit
Patient 1	78.1	76.1	80.9
Patient 2	41.8	53.3	
Patient 3	72.6	69.5	
Patient 4	76.6	81.0	
Patient 5	88.1	88.2	

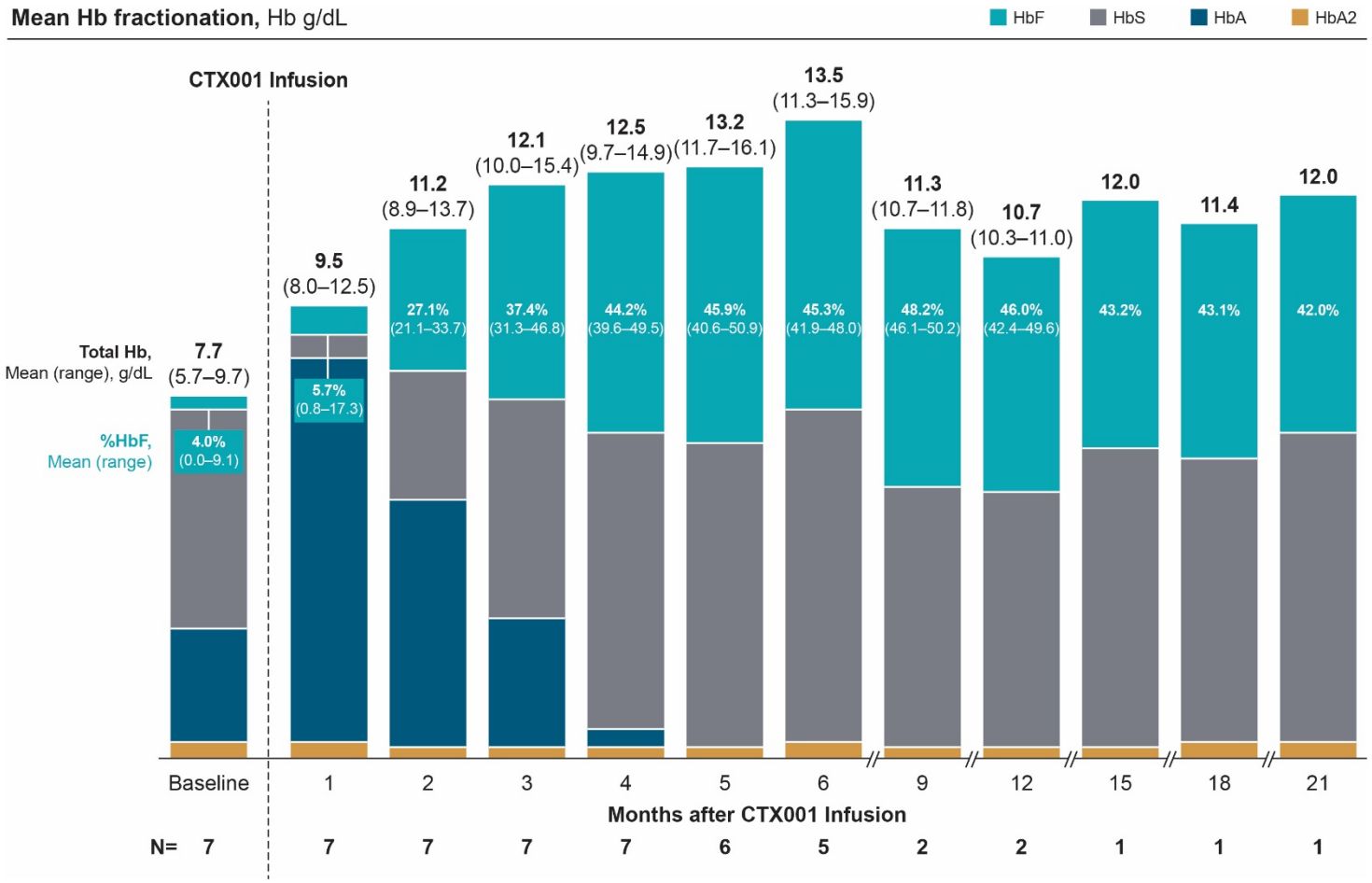
SCD: Patient Baseline and Treatment Characteristics

Patients with *≥3-month follow-up (n=7)*

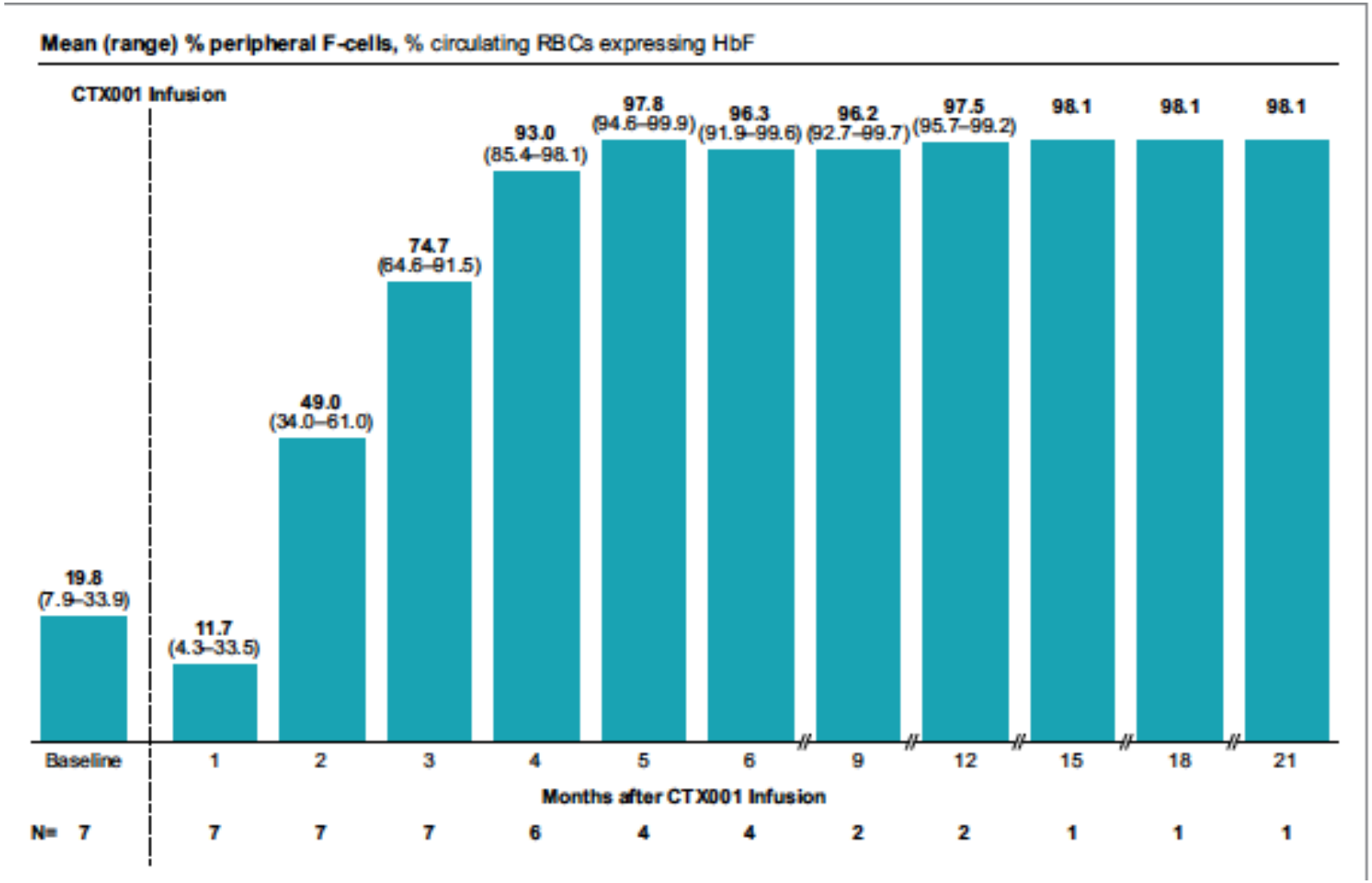
Patient characteristics		
Genotypes, n	β^S / β^S	**7**
Gender, Female/Male, n		**3/4**
Age at consent, years Median (range)		**22** (19 – 34)
Pre-study VOCs VOCs/year[a], Median (range)		**5.5** (2.5 – 9.5)

Treatment characteristics	Median (range)
Drug product cell dose,[b] $CD34^+$ cells × 10^6/kg	**3.3** (3.1 – 3.9)
Neutrophil engraftment,[c] Study Day[d]	**25** (17 – 33)
Platelet engraftment,[e] Study Day[d]	**33** (30 – 53)
Duration of follow-up, Months	**7.6** (4.9 – 22.4)

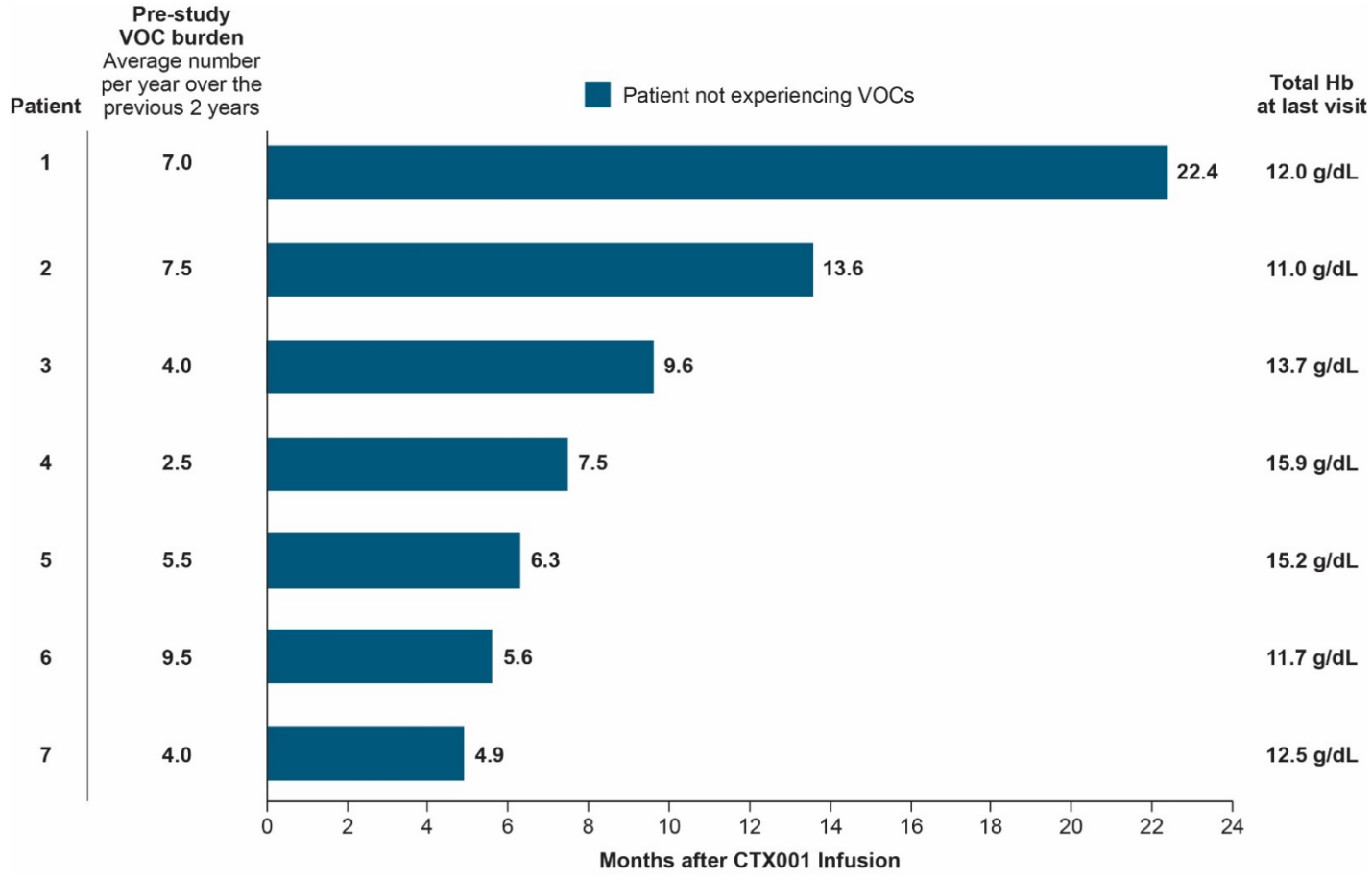
SCD: All patients demonstrated increased total Hb and HbF[1]



SCD: Pancellular Expression of HbF Is Maintained



SCD: All patients infused with CTX001 remain VOC-free[1]



Durable BCL11A Editing Observed in CD34+ Bone Marrow Cells

- Bone marrow editing assessments were performed at 6 months and 12 months of F/U
- The mean proportion of edited alleles in CD34+ bone marrow cells was 85.5% (range: 80.4% to 93.1%) in the 4 patients with data available at 6 months post CTX001 infusion
- In the 2 patients with at least 12 months of follow-up post CTX001 infusion, the proportion of edited alleles was maintained in bone marrow cells over the duration of follow-up (in the first patient, 81.4% and 80.4% at Months 6 and 12, respectively [22.4 months of total follow-up]; and in the second patient, 87.3% and 87.1% at Months 6 and 12, respectively [13.6 months of total follow-up])

Gene editing approaches to treatment of hemoglobinopathies

Limitations:

- Short follow up
- Need for high dose chemotherapy
- Absence of data in patients with SCD and CNS disease

Conclusions

- Gene therapy approaches can offer an alternative to allogeneic stem cell transplant especially for patients who lack an HLA identical donor
- The data for gene addition approaches using a Leniviral vector is encouraging, additional studies are required to determine the risk of secondary malignancy in patients with sickle cell disease
- The preliminary data with CRISPR-Cas9 gene editing of BCL11A is encouraging, in both SCD and TDT patients.
- Additional follow is required to determine the long-term safety and persistence of the gene modified cells in the marrow

Gene-editing treatment shows promise for sickle cell disease

By MARION RENAULT December 5, 2020

AP

1st Patients To Get CRISPR Gene-Editing Treatment Continue To Thrive

December 15, 2020 · 5:02 AM ET

Heard on Morning Edition

ROB STEIN

4-Minute Listen + PLAYLIST

npr

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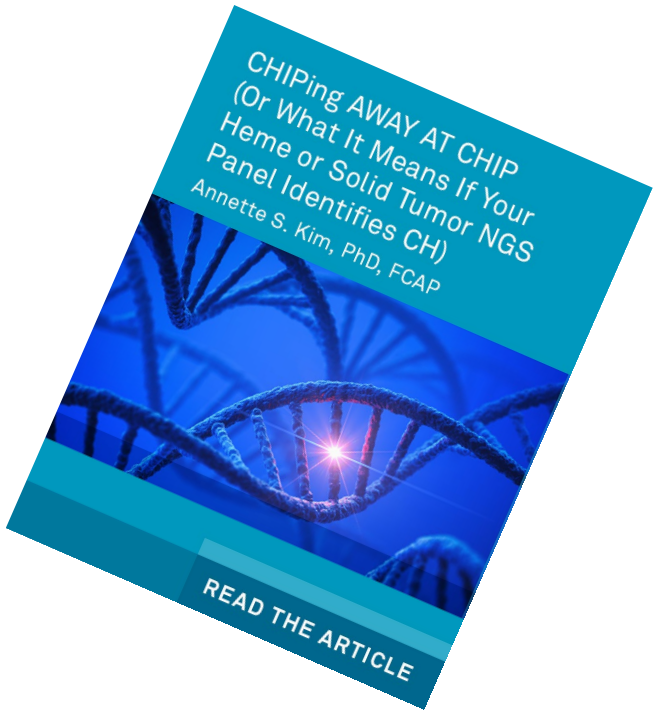
    Member Resources > Precision Medicine



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THANK YOU!

Thank you for attending our webinar,

"CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia"

by Haydar Frangoul, MD, MS

For comments about this webinar or suggestions for upcoming webinars, please contact phcwebinars@cap.org.

NOTE: There is no CME/CE credit available for today's free webinar. The PDF of the presentation will be sent out in a week.

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