

Terapia genica nelle emoglobinopatie: quali prospettive per il paziente pediatrico

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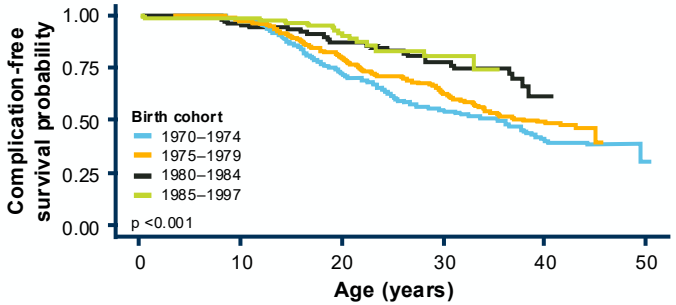
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LECCE, 12-14 ottobre 2026
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Disclosures of Franco Locatelli

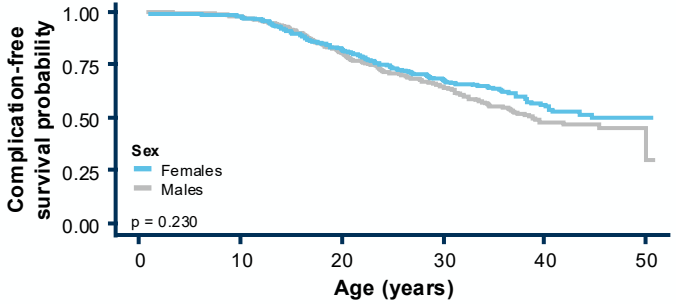
Name of Company	Research Support	Employee	Consultant	Stockholder	Speaker's Bureau	Advisory Board	Other
Miltenyi					X		
Amgen					X	X	
Novartis					X	X	
BMS					X		
GILEAD					X		
MEDAC					X	X	
Sanofi						X	
SOBI					X		
Vertex					X	X	

In Italy, the majority of complications of TDT appear in the second and third decades of life

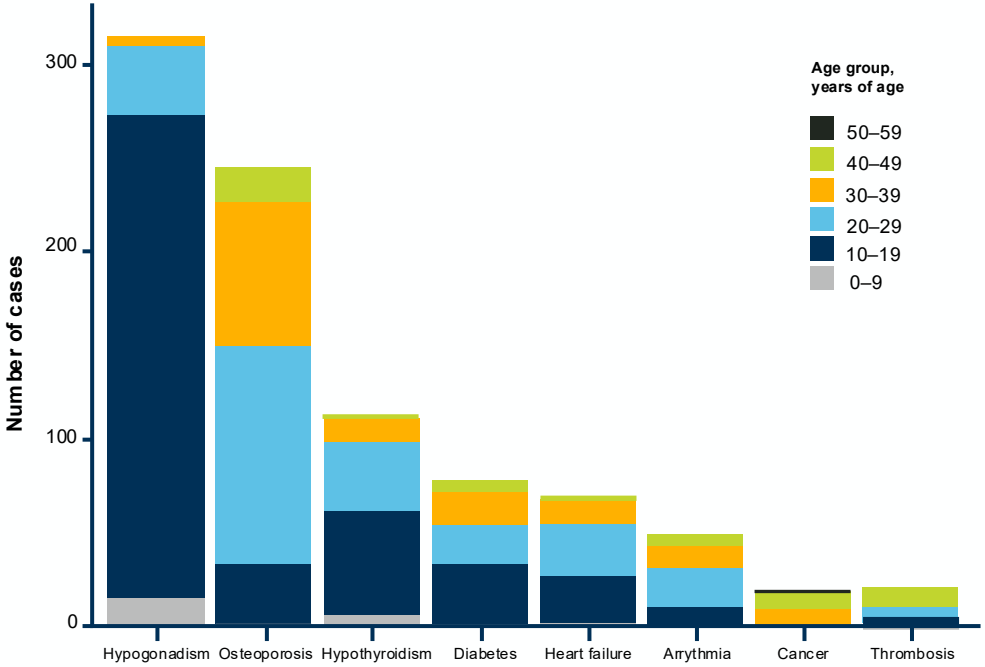
Complication-free survival[a] from birth, by birth cohort



Complication-free survival[a] from birth, by sex



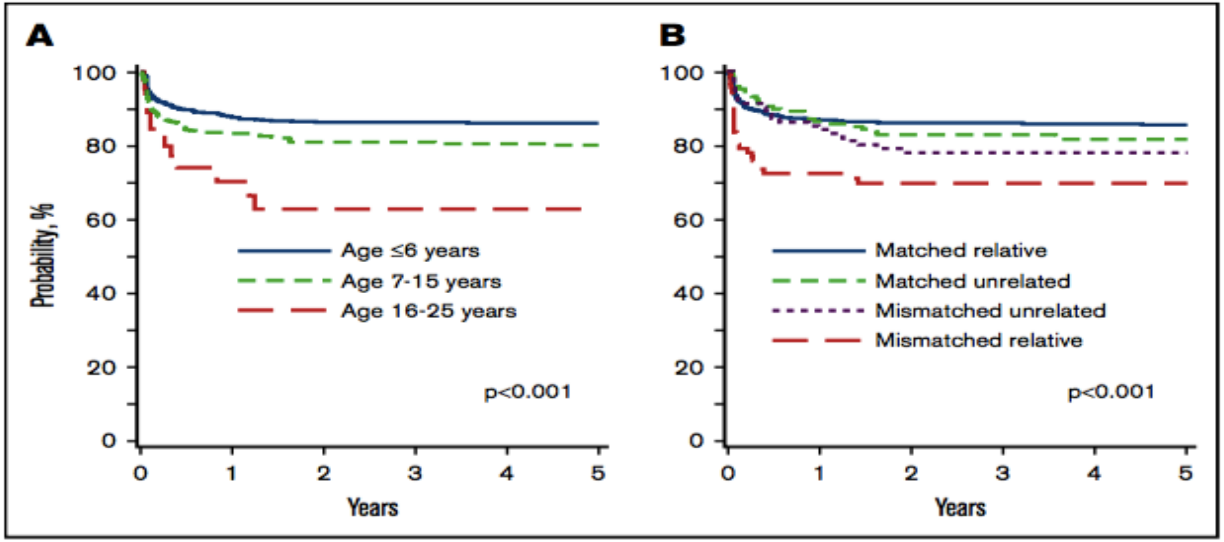
Distribution of age at presentation for different complications[b]



[a]Osteoporosis and hypogonadism excluded; [b]Human immunodeficiency virus excluded.
TDT, transfusion-dependent β-thalassaemia.
Forni GL, et al. Am J Hematol. 2023;98:381–87.

3

Related and unrelated donor transplantation for B-thalassemia major: results of an international survey



EFS by Age and Donor

Li C. et al. Blood Advances 2019; 3: 2562-2570

The paradigmatic model of gene therapy for haemoglobinopathies

More than one option

Gene therapy

Genome editing

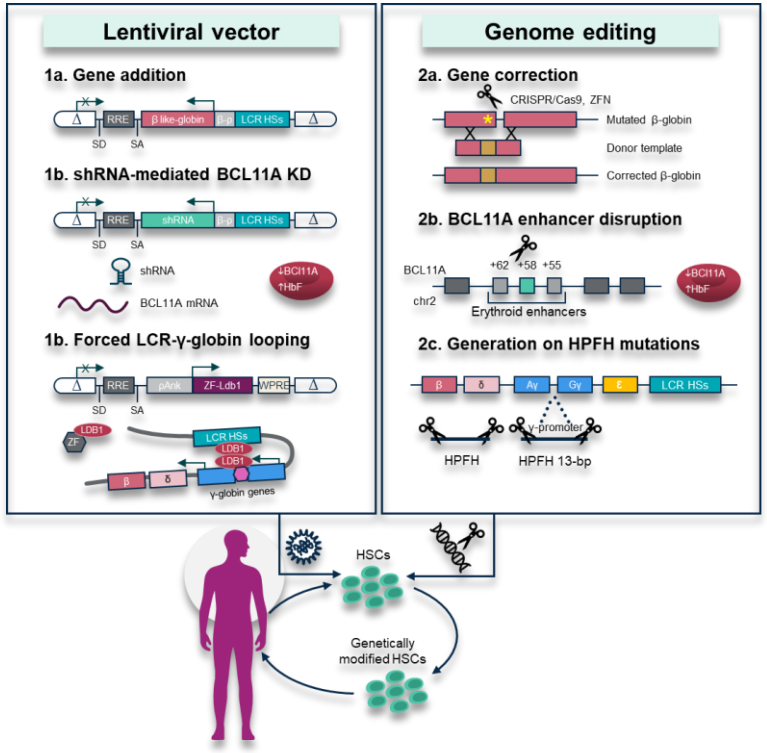
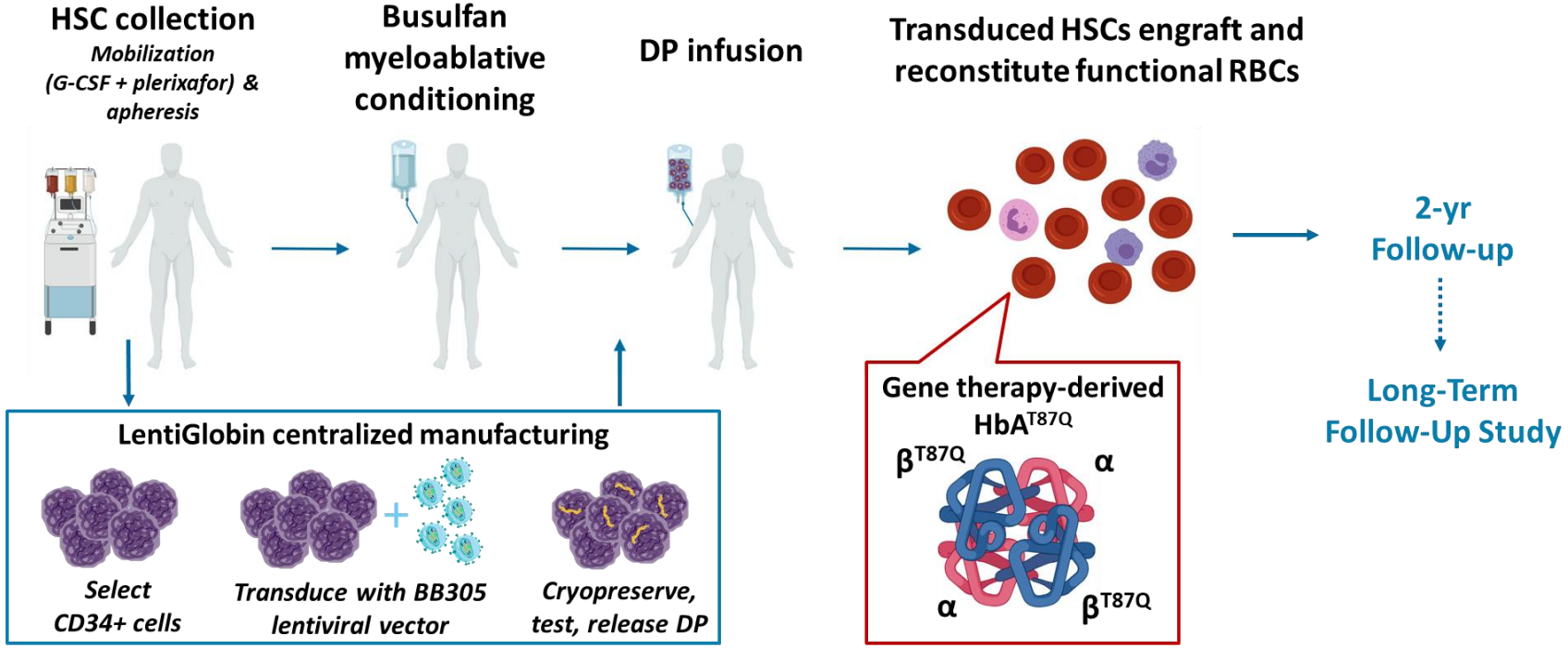


Figure adapted from Cavazzana M et al. Mol Therapy. 2017.

BCL11A, B-cell lymphoma/leukaemia 11A; CRISPR, clustered regularly interspaced short palindromic repeats; HbF, foetal haemoglobin; HPFH, hereditary persistence of foetal haemoglobin; HSC, haematopoietic stem cell; KD, knockdown; LCR, locus control region; mRNA, messenger ribonucleic acid; RRE, rev-responsive element; SA, splicing acceptor; SD, splicing donor; shRNA, short hairpin ribonucleic acid; ZFN, zinc-finger nucleases.

1. Cavazzana M, et al. *Mol Therapy*. 2017;25(5):1142–1154.

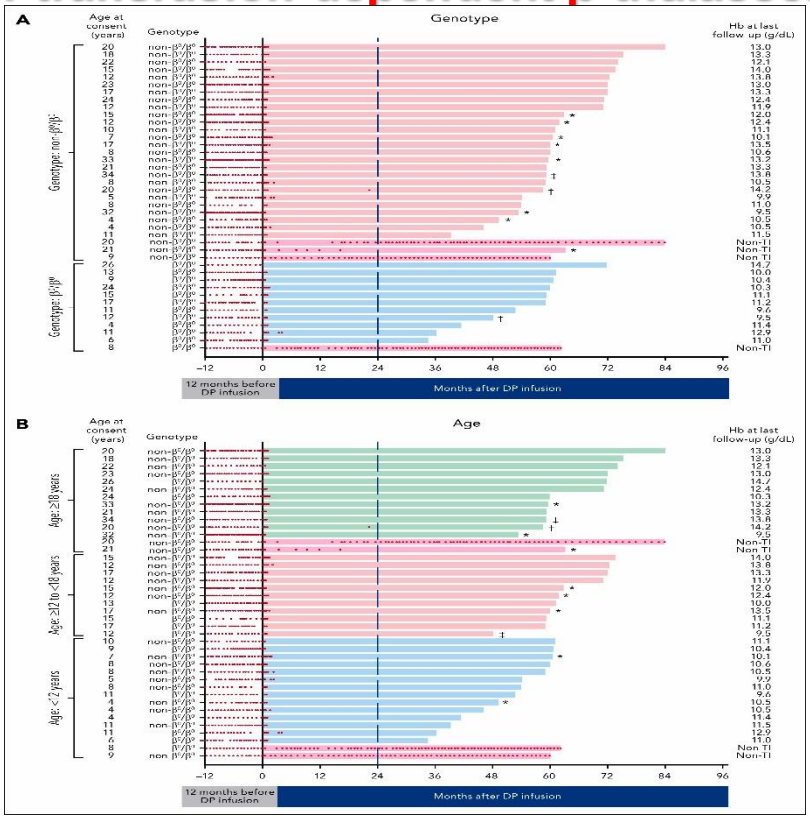
HGB-205, -204, -207, -212 studies of beti-cel gene therapy in TDT



DP, drug product; G-CSF, granulocyte-colony stimulating factor; HSC, hematopoietic stem cell; RBC, red blood cell.

1. Locatelli F et al. Blood. 2018;132:1025.

Long-term efficacy and safety results of betibeglogene autotemcel gene therapy for transfusion-dependent β-thalassemia



Janet L. Kwiatkowski,Alexis A. Thompson,Jennifer Schneiderman,Isabelle Thuret,Andreas E. Kulozik,Evangelia Yannaki,Marina Cavazzana,Suradej Hongeng,Timothy S. Olson,Martin G. Sauer,Adrian J. Thrasher,Ashutosh Lal,John E. J. Rasko,Joachim B. Kunz,Melissa A. Kinney,Anjulika Chawla,Shamshad Ali,Ge Tao,Himal L. Thakar,Clark Paramore,Niki Witthuhn,Mark C. Walters, Franco Locatelli, Long-term efficacy and safety results of betibeglogene autotemcel gene therapy for transfusion-dependent β-thalassemia, Blood, 2026,

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Helping hematologists conquer blood diseases worldwide

EU CT 2025-522160-32-00

A single arm, open label, multicenter, single-dose, phase 2b clinical study evaluating efficacy and safety of gene therapy using autologous CD34+ hematopoietic stem cells transduced with the GLOBE lentiviral vector using an improved transduction protocol in subjects with transfusion-dependent beta-thalassemia

9 TDT patients aged 3-35 years old

- At least 2 subjects will be children with an age comprised between 3 and 12 and at least 2 will be adolescent (13-17 years)
- At least 2 out of 9 subjects must have B0/B0 or B0/B0-like genotype

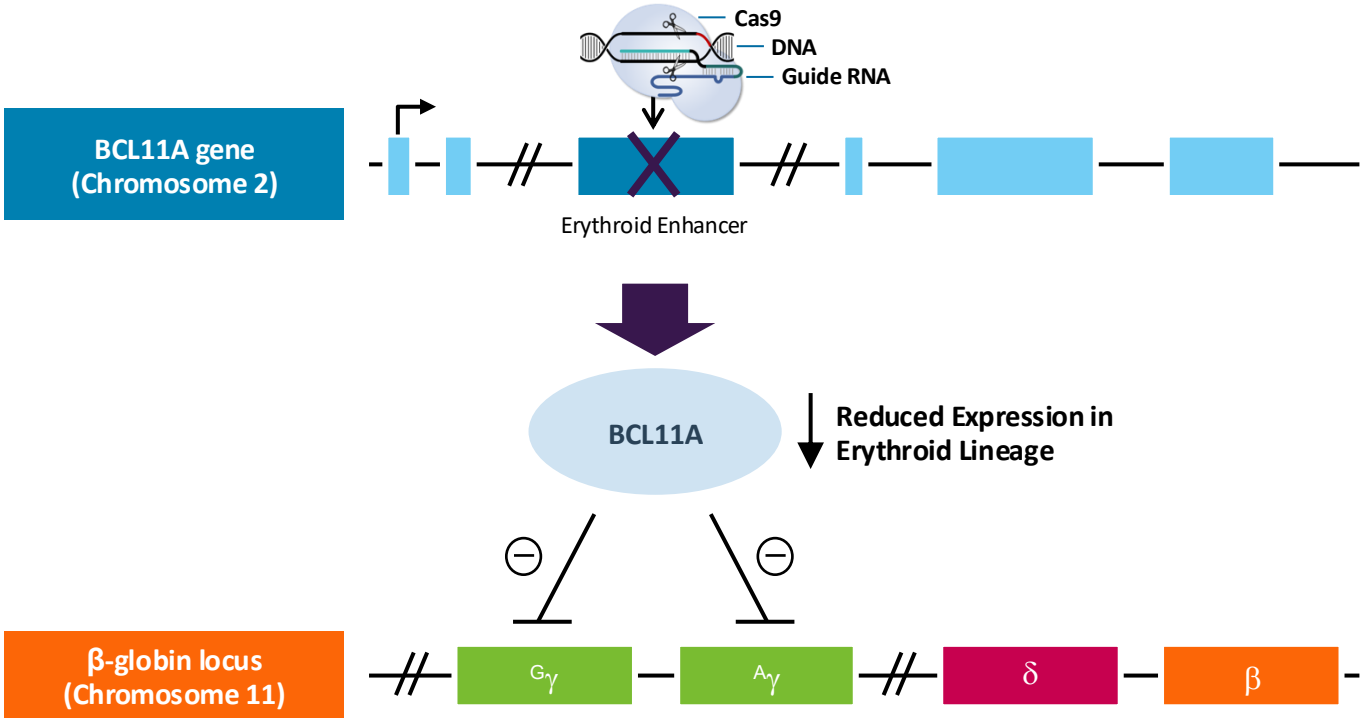
2 Clinical Sites involved

IRCCS Ospedale San Raffaele, Milan
PI: Prof. Alessandro Aiuti

IRCCS Ospedale Pediatrico Bambino Gesù, Rome
PI: Prof. Franco Locatelli



This approach disrupts the BCL11A erythroid enhancer, which plays a major role in the silencing of γ-globin expression



Disruption of the erythroid enhancer region of BCL11A leads to re-expression of γ-globin (HbF)

1. CRISPR Therapeutics, 2018; 2. NCT03655678, available at https://clinicaltrials.gov/ct2/show/NCT03655678 (accessed February 2020).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia

F. Locatelli, P. Lang, D. Wall, R. Meisel, S. Corbacioglu, A.M. Li, J. de la Fuente, A.J. Shah, B. Carpenter, J.L. Kwiatkowski, M. Mapara, R.I. Liem, M.D. Cappellini, M. Algeri, A. Kattamis, S. Sheth, S. Grupp, R. Handgretinger, P. Kohli, D. Shi, L. Ross, Y. Bobruff, C. Simard, L. Zhang, P.K. Morrow, W.E. Hobbs, and H. Frangoul, for the CLIMB THAL-111 Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Exagamglogene Autotemcel for Severe Sickle Cell Disease

H. Frangoul, F. Locatelli, A. Sharma, M. Bhatia, M. Mapara, L. Molinari, D. Wall, R.I. Liem, P. Telfer, A.J. Shah, M. Cavazzana, S. Corbacioglu, D. Rondelli, R. Meisel, L. Dedeken, S. Lobitz, M. de Montalembert, M.H. Steinberg, M.C. Walters, M.J. Eckrich, S. Imren, L. Bower, C. Simard, W. Zhou, F. Xuan, P.K. Morrow, W.E. Hobbs, and S.A. Grupp, for the CLIMB SCD-121 Study Group*

Gene editing approaches: approval by regulatory agencies

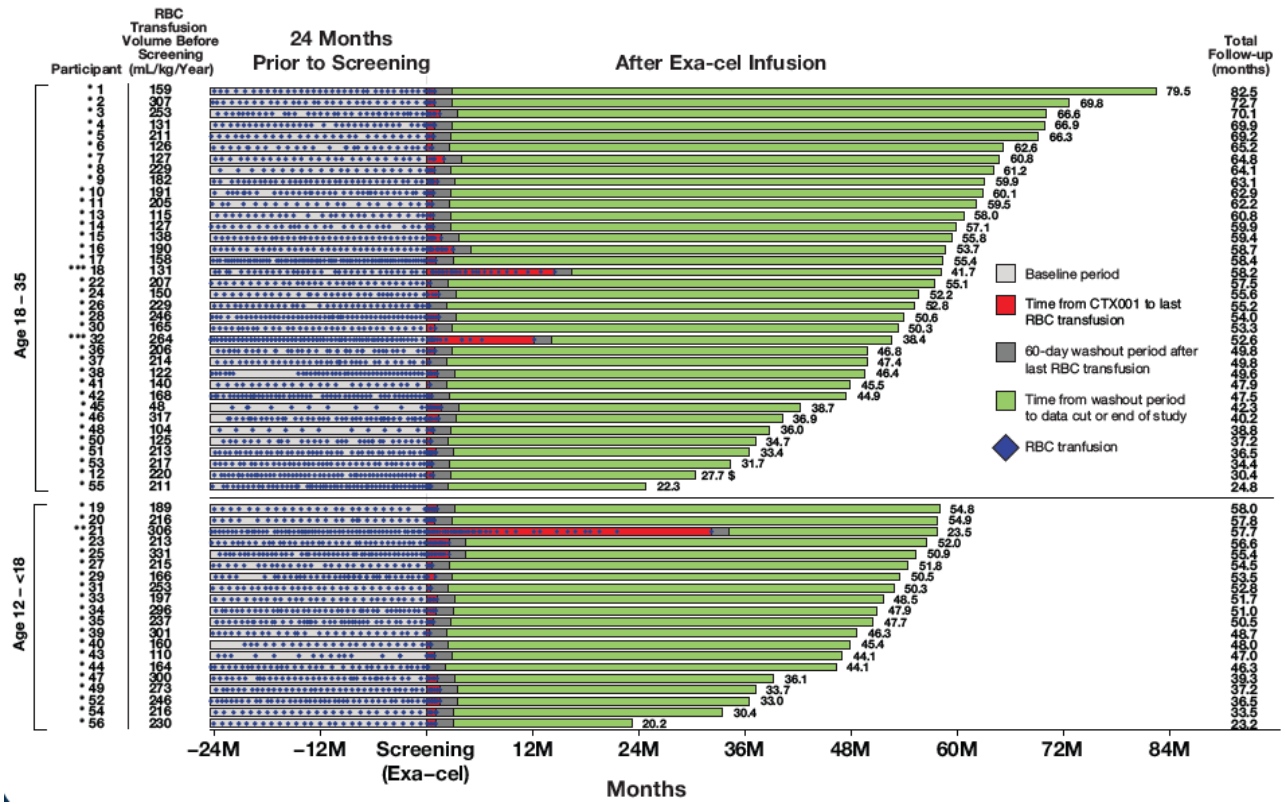
Both FDA, at the end of 2023, and EMA, at the beginning of 2024, have approved the gene editing appoach aimed at re-activating the synthesis of HbF in patients above the age of 12 years. In particular:

- **Exacel is indicated for the treatment of transfusion-dependent β-thalassemia (TDT), including β^0/β^0 genotypes, defined as a history of ≥100 mL/kg/year or ≥10 units/year of packed RBC transfusions in the previous 2 years, in patients 12 years of age and older for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-matched related HSC donor is not available.**

- **Exacel is indicated for the treatment of severe sickle cell disease (SCD) in patients 12 years of age and older with recurrent vaso-occlusive crises (VOCs, namely a history of ≥2 severe VOCs per year in the previous 2 years) for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-matched related HSC donor is not available**

Durable Transfusion Independence Achieved After Exa-cel (CLIMB THAL-111 and 131)

Transfusion independence achieved in 98% and maintained for up to 6.6 Years



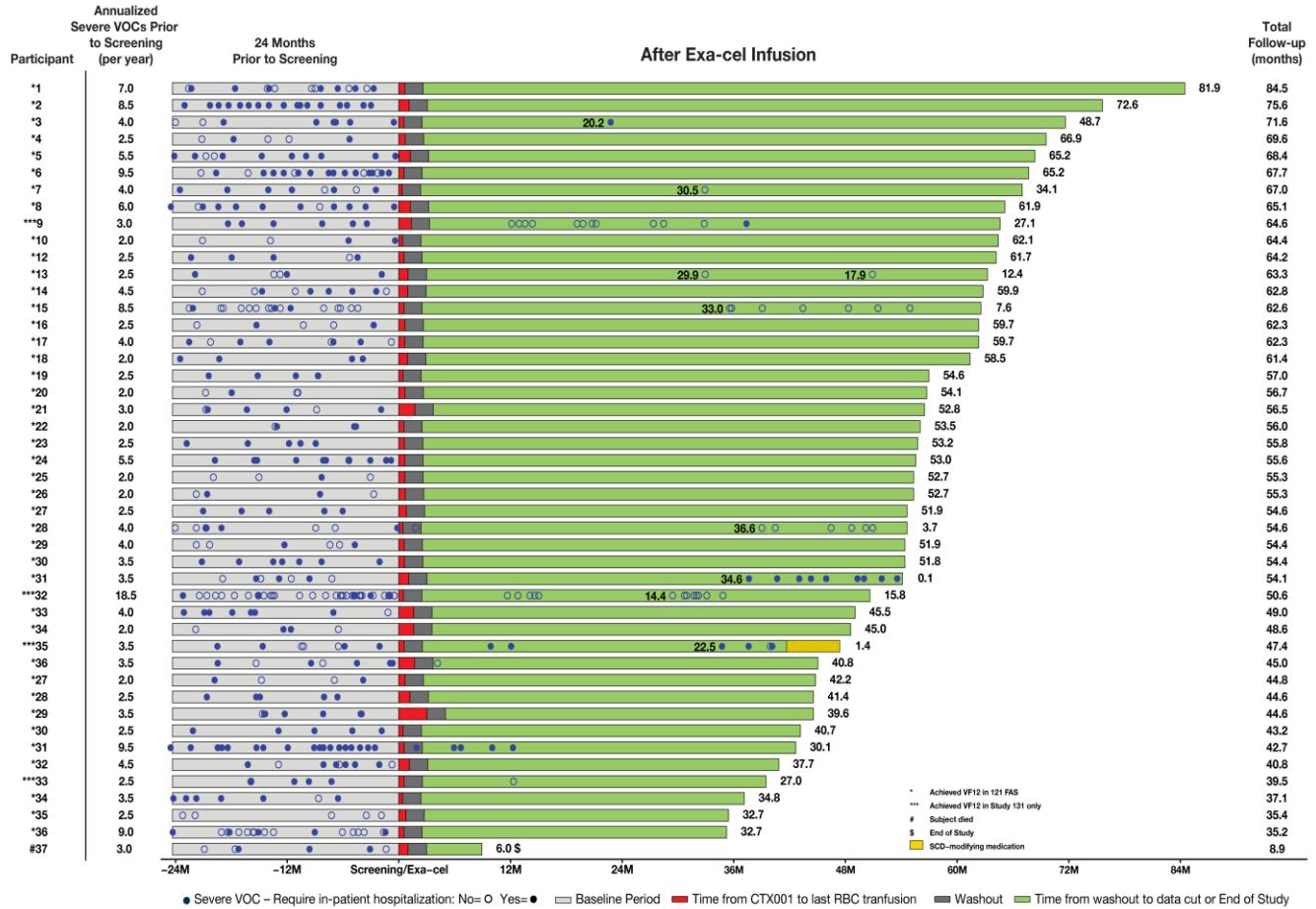
- 98% (55/56) of participants achieved TI12 in CLIMB THAL-111 and CLIMB-131 combined
  - Similar efficacy response observed in adults aged ≥18 years and adolescents aged ≥12 to <18 years
- Mean duration of transfusion independence is 4.0 years (range: 1.7 to 6.6)
- 1 participant who has not yet achieved TI12 (weighted average Hb has not reached 9 g/dL for 12 months) has been transfusion-free for 2 years

Data shown are as of Nov 2025

* Achieved TI12 in CLIMB-111; **Did not achieve TI12 (due to not having weighted average Hb ≥9 g/dL); ***Achieved TI12 in CLIMB-131 only

EOS: end of study**; exa-cel:** exagamglogene autotemcel; **Hb:** hemoglobin; **RBC:** red blood cell; **TI12:** transfusion independent for ≥12 consecutive months while maintaining a weighted average Hb ≥9 g/dL.

Duration of Freedom from Severe Vaso-occlusive Crises and Inpatient Hospitalizations for Severe Vaso-occlusive Crises After Exa-cel Infusion



Locatelli F et al. EBMT 2026 Annual Meeing, Presidential Symposium

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

CRISPR-Cas12a Gene Editing of *HBG1* and *HBG2* Promoters to Treat β-Thalassemia

Haydar Frangoul, M.D.,[1,2] Rabi Hanna, M.D.,[3] Mark C. Walters, M.D.,[4,5] Roy L. Kao, M.D.,[6] Clinton Carroll, M.D., M.S.C.I.,[1] Meghann McManus, D.O., M.P.H.,[1] Kai-Hsin Chang, Ph.D.,[7] Michael C. Jaskolka, Ph.D.,[7] Keunpyo Kim, Ph.D.,[7] Qifeng Yu, Ph.D.,[7] Nnenna Badamosi, M.D., M.P.H.,[7] Baisong Mei, M.D., Ph.D.,[7] Olubunmi Afonja, M.D.,[7] and Alexis Thompson, M.D., M.P.H.,[8] for the EdiThal Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

CRISPR-Cas12a Gene Editing of *HBG1* and *HBG2* Promoters to Treat Sickle Cell Disease

Rabi Hanna, M.D.,[1] Haydar Frangoul, M.D.,[2,3] Luis Pineiro, M.D.,[4] Christopher McKinney, M.D.,[5] Markus Mapara, M.D., Ph.D.,[6] Jignesh Dalal, M.D.,[7] Hemalatha G. Rangarajan, M.D.,[8] Harold Atkins, M.D.,[9] Akshay Sharma, M.B., B.S.,[10] Kai-Hsin Chang, Ph.D.,[11] Michael C. Jaskolka, Ph.D.,[11] Keunpyo Kim, Ph.D.,[11] Qifeng Yu, Ph.D.,[11] Baisong Mei, M.D., Ph.D.,[11] Olubunmi Afonja, M.D.,[11] and Mark C. Walters, M.D.,[12,13] for the RUBY Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Base Editing of *HBG1* and *HBG2* Promoters for Sickle Cell Disease

A.O. Gupta,[1] A. Sharma,[2] H. Frangoul,[3,4] J. Kanter,[5] M.Y. Mapara,[6] J. Dalal,[7] A. Alavi,[8] J.J. Jaroscak,[9] E. Ayala,[10] J.F. DiPersio,[11] E.D. Ziga,[12] M. Eapen,[13] S. Rifkin-Zenenberg,[14] A.C. Minella,[15] Y. Chen,[15] S. Chesler,[15] S. Ambati,[15] T.S. Bowman,[15] B. Habtemariam,[15] M. Joseney-Antoine,[15] P.S. Chockalingam,[15] L. Lin,[15] S. Goyal,[15] A. Simon,[15] A.A. Thompson,[16] and M.M. Heeney,[17] for the BEACON Investigators*

More Options for Gene Editing in Hemoglobinopathies

Franco Locatelli, M.D., Ph.D.[1,2]

Table 1. Trials of Gene-Editing Therapies in Sickle Cell Disease and β-Thalassemia.*

Variable	Exa-cel	Reni-cel	Risto-cel
Manufacturer	Vertex Pharmaceuticals	Editas Medicine	Beam Therapeutics
Mechanism of action	Disruption of the erythroid-specific enhancer of *BCL11A* by CRISPR-Cas9	Disruption of *HBG1* and *HBG2* promoters by CRISPR-Cas12a	Base editing of *HBG1* and *HBG2* promoters
Age range — yr	12–35	12–50 for SCD; 18–35 for TDT	12–35
No. of patients with SCD treated	44 (32 adults and 12 adolescents)	28 adults	31 (30 adults and 1 adolescent)
No. of patients with TDT treated	52 (34 adults and 18 adolescents)	9 adults	Not treated
Median duration of follow-up (range) — mo	19.3 (0.8–48.1) for SCD; 20.4 (2.1–48.1) for TDT	9.5 (0.7–25.2) for SCD; 17.5 (3.8–23.4) for TDT	6.6 (0.3–20.4)
Current status of development	Approved by most regulatory agencies	Discontinuation of product development	Clinical trial active, not recruiting
Trials involving children	Ongoing	NA	NA

* Exagamglogene autotemcel (exa-cel) was assessed in patients with transfusion-dependent β-thalassemia (TDT)[8] and in those with sickle cell disease (SCD).[9] Studies involving children with SCD or TDT are ongoing.[13] Renizgamglogene autogedtemcel (reni-cel) was evaluated in patients with SCD[10] and in those with TDT.[11] Ristoglogene autogetemcel (risto-cel) was assessed in patients with SCD.[12] *HBG1* and *HBG2* encode the γ-chains that are part of the fetal hemoglobin tetramere. CRISPR denotes clustered regularly interspaced short palindromic repeats, and NA not available.

Original Article

Exa-cel in Children with Transfusion-Dependent β-Thalassemia or Sickle Cell Disease

Haydar Frangoul, M.D., Josu de la Fuente, M.D., Ph.D., Yogi Chopra, M.D., Roland Meisel, M.D., Persis J. Amrolia, M.D., Ph.D., Mattia Algeri, M.D., Akshay Sharma, M.B., B.S., Maria Domenica Cappellini, M.D., Selim Corbacioglu, M.D., Antonis Kattamis, M.D., Stephan Lobitz, M.D., Mariane de Montalembert, M.D., Ph.D., Damiano Rondelli, M.D., Sujit Sheth, M.D., Martin H. Steinberg, M.D., Mark C. Walters, M.D., Kevin Boerner, M.D., Tina Liu, Ph.D., Sakellarios Zairis, M.D., Ph.D., William Hobbs, M.D., Ph.D., Stephan A. Grupp, M.D., Ph.D., Franco Locatelli, M.D., Ph.D.

N Engl J Med
Volume 395(10):947-958
September 10, 2026



The NEW ENGLAND JOURNAL of MEDICINE

Phase 3 CLIMB THAL-141 and CLIMB SCD-151 Studies

	CLIMB THAL-141 (NCT05356195)	CLIMB SCD-151 (NCT05329649)
Study Design	Global, multicenter, open-label, single-arm, 2-year Phase 3 trials of a single infusion of exa-cel	
Participants	2 to 11 years of age[a] with TDT defined as a history of ≥100 mL/kg/year in the previous 2 years or for participants initiating transfusion therapy <2 years before signing consent, RBC transfusions at least every 3-4 weeks for ≥6 months	2 to 11 years of age[a] with a history of ≥2 severe VOC events per year for the previous 2 years before enrollment and Hydroxyurea failure unless Hydroxyurea intolerant
Primary Efficacy Endpoint	Proportion of participants **transfusion independent for ≥12 consecutive months** while maintaining a weighted average hemoglobin ≥9 g/dL (**TI12**)	Proportion of participants who **do not have any severe VOCs for ≥12 consecutive months** (**VF12**)
Selected Secondary and Other Efficacy Endpoints	Duration of **transfusion independence for participants who achieved T112** • Total Hb and HbF levels, F-cell % over time • Allelic editing at the intended locus in bone marrow CD34⁺ HSCs and peripheral blood cells over time	• Proportion of participants **free from inpatient hospitalization for severe VOCs for ≥12 months** (**HF12**) • Duration of severe VOC free for participants who achieved VF12 and HF12

CLIMB 131 (NCT04208529)

Global, multicenter, open-label, rollover Phase 3 study to provide up to 15 years of long-term efficacy and safety follow-up

[a] Currently enrolled cohort includes participants aged 5-11 years; younger cohort aged 2-4 years to follow

exa-cel, exagamglogene autotemcel; **F-cells,** erythrocytes expressing HbF; **Hb**, hemoglobin; **HbF**, fetal hemoglobin; **HF12**, free from inpatient hospitalizations for severe VOCs for ≥12 months; **HSCs**, hematopoietic stem cells; **RBC**, red blood cell; **TDT,** transfusion-dependent β-thalassemia; **TI12**, maintained weighted average Hb ≥9 g/dL without RBC transfusions for at least 12 consecutive months any time after exa-cel infusion; **VF12**, free from severe VOCs for ≥12 consecutive months; **VOC**, vaso-occlusive crisis

TDT and SCD Participants Aged 5-11 Years: Key Treatment Characteristics

Characteristics	TDT N = 15[e]	SCD N = 11[e]
Duration (months) of follow-up after exa-cel, median (range)	16.0 (2.2, 32.1)	16.9 (7.6, 33.1)
Busulfan cAUC exposure[a], median (range), mg*h/L	79.4 (56.8, 94.6)	72.9 (52.7, 86.1)
Neutrophil Engraftment (days)[b]		
Time to neutrophil engraftment, median (range)	30 (19, 38)	28 (20, 37)
Duration of neutropenia (ANC <500 cells/µL), median (range)	22 (10, 31)	20 (11, 28)
Platelet Engraftment (days)[c]		
Time to platelet engraftment, median (range)	51 (22, 82)	47 (24, 78)
Time (days) to hospital discharge[d], median (range)	37 (23, 132)	34 (29, 45)
Participants who received G-CSF prior to neutrophil engraftment, n (%)	12 (80.0)	6 (54.5)

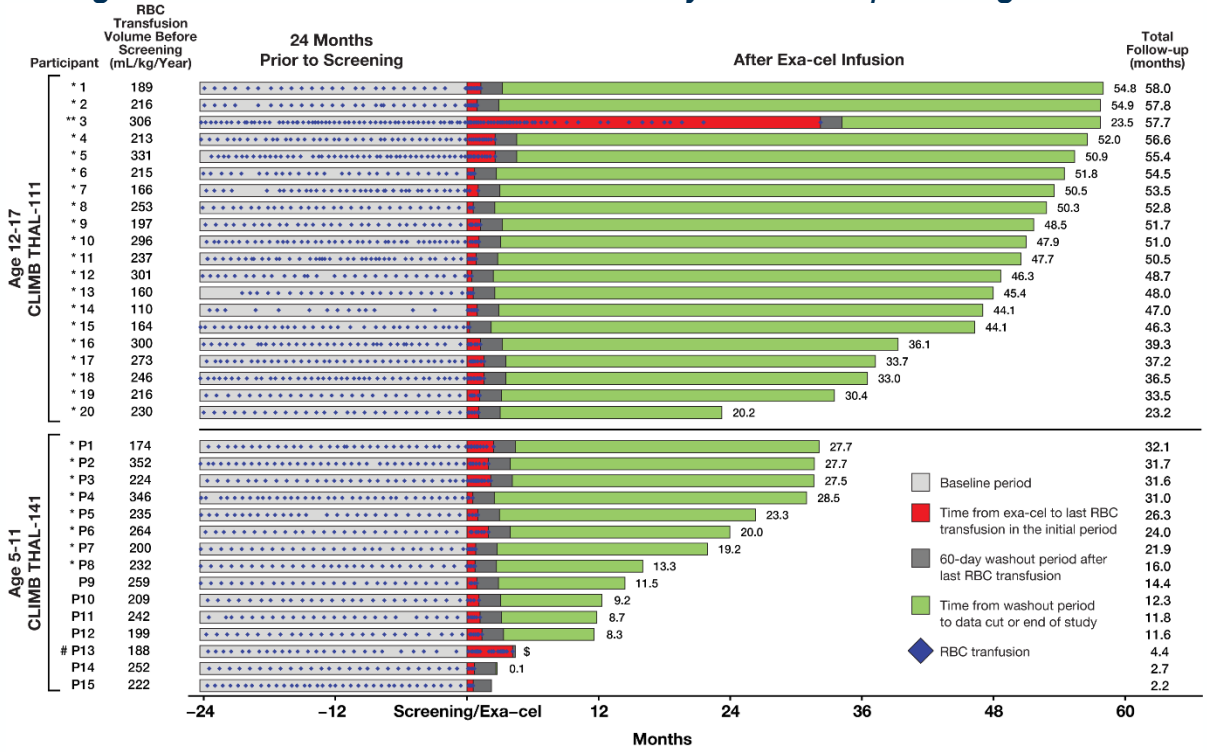
All participants engrafted neutrophils. In CLIMB-THAL-141, 12 out of 13 participants engrafted platelets. One participant was not evaluable for platelet engraftment due to confounding factors (severe VOD and platelet transfusions).
Data shown are as of January 2026 for CLIMB THAL-141 and CLIMB SCD-151

[a] Protocol-specified cAUC range was 82 mg*h/L (range: 74 – 90 mg*h/L) for q6h and qd dosing. Dosing was amended during the study to q6h dosing only.
[b] Defined as the first day of 3 consecutive measurement of absolute neutrophil count ≥500 cells/µL on 3 different days.
[c] Defined as the first day of 3 consecutive measurement of unsupported (no platelet transfusion in last 7 days) platelet count ≥20,000/µL (TDT) / ≥50,000/µL (SCD) on 3 different days.
[d] Defined as the number of days from exa-cel infusion to hospital discharge following neutrophil engraftment.
[e] FAS includes all participants who received exa-cel infusion

exa-cel, exagamglogene autotemcel; **cAUC**, cumulative area under the concentration versus time curve; **FAS**, Full Analysis Set; **N**, total sample size; **n**, size of subsample; **q6h**, every 6 hours; **qd**, once daily; **SCD**, sickle cell disease; **TDT**, transfusion-dependent β–thalassemia; VOD, venoocclusive disease

Children with TDT Achieved Transfusion Independence After Exa-cel Infusion

Participants Aged 5-11 Years Have Similar Efficacy As Participants Aged 12-17 Years



* Participants in the PES who achieved TI12 in parent study

** Participants in the PES who did not achieve TI12 in parent study. One participant has stopped RBC transfusions and has been transfusion free for 23.5 months. The participant has not yet achieved TI12 as weighted average of Hb has not reached 9 g/dL.

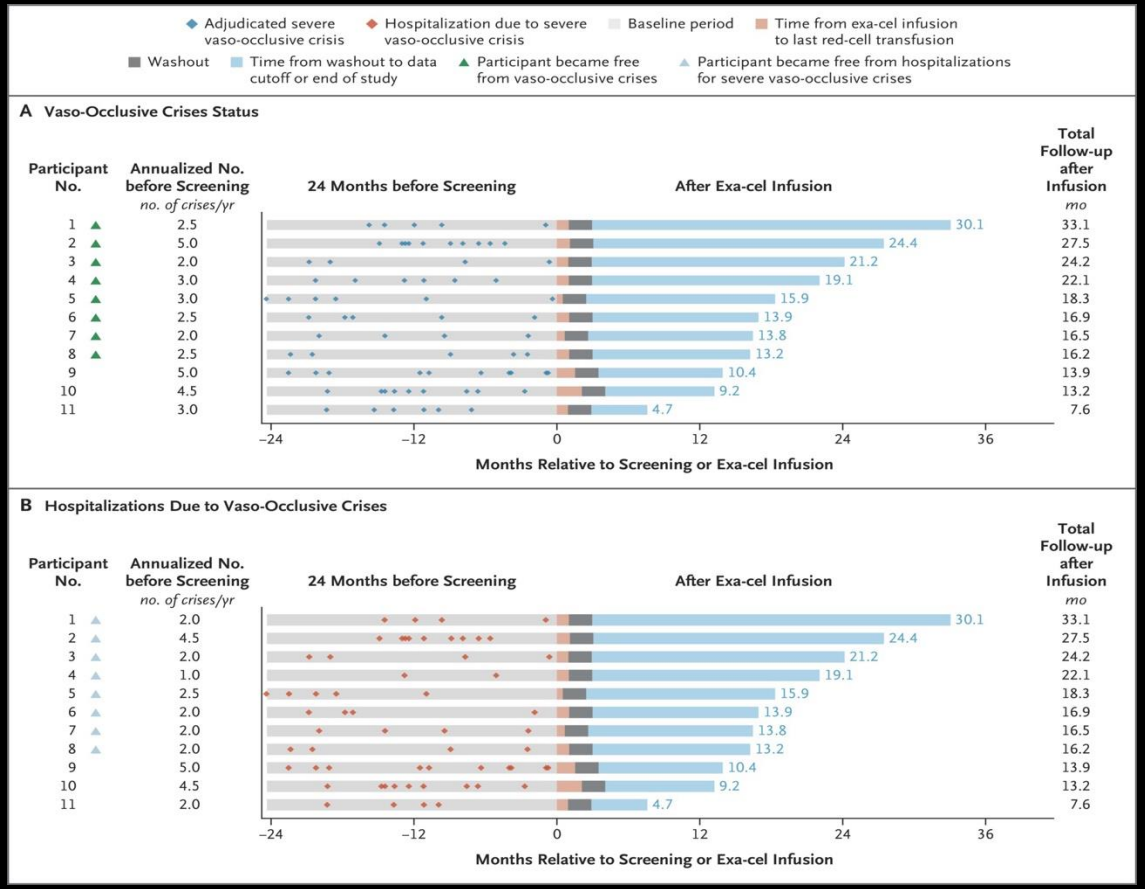
\# Participant experienced severe veno-occlusive disease related to busulfan, with multi-organ failure and subsequently died.

Based on data cut-off date of January 2026 for CLIMB THAL-111/CLIMB-131 and CLIMB THAL-141/CLIMB-131

exa-cel, exagamglogene autotemcel; **M**, month; **PES**, Primary Efficacy Set; **RBC**, red blood cell; **TDT**, transfusion-dependent β-thalassemia; **TI12**, maintained weighted average Hb ≥9 g/dL without RBC transfusions for at least 12 consecutive months any time after exa-cel infusion

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Vaso-occlusive Crises and Hospitalizations after Exa-cel Infusion in Children with Sickle Cell Disease (CLIMB SCD-151).

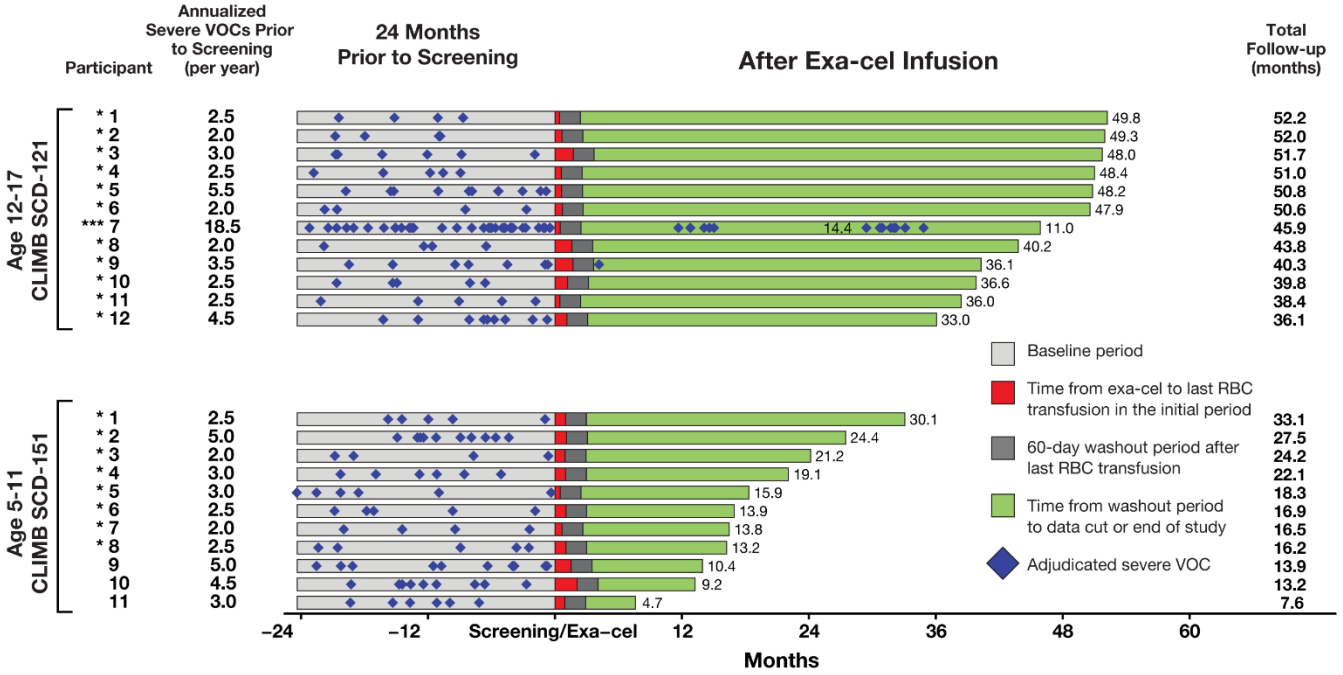


Frangoul H et al. N Engl J Med2026;395:947-958

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Children with SCD Were Free of VOCs After Exa-cel Infusion

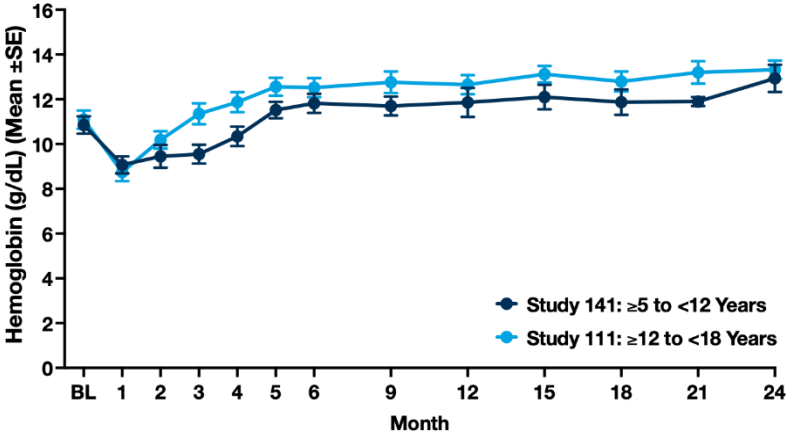
Participants Aged 5-11 Years Have Similar Efficacy As Participants Aged 12-17 Years



* Participants in the PES who achieved VF12 in parent study.
** Participants in the PES who did not achieve VF12 in parent study
*** Participants in the PES who achieved VF12 in Study 131 only
Based on data cut-off date of January 2026 for CLIMB SCD-121/CLIMB-131 and CLIMB SCD-151/CLIMB-131
RBC, red blood cell; **HSCT**, hematopoietic stem cell transplantation; **VF12**, free from severe VOC for ≥12 consecutive months; **VOC**, vaso-occlusive crisis

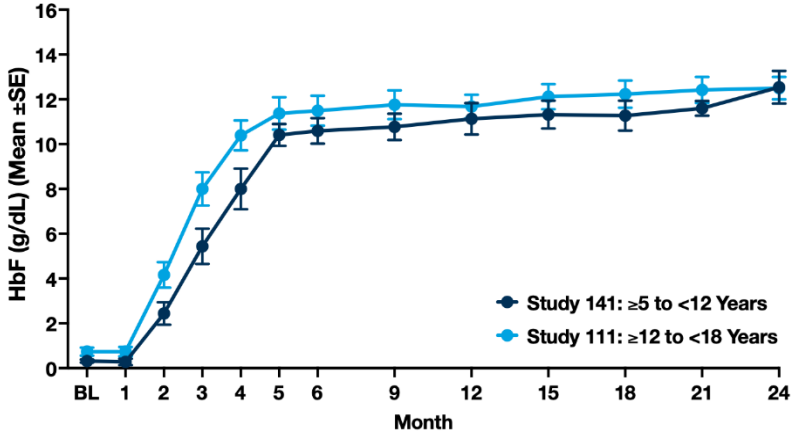
TDT: Durable Increases in Total Hb and HbF in Participants Aged 5-11 Years With Normalization of Total Hb Similar to Adolescents and Adult Participants

Total Hb



n for 141:	13	12	13	13	13	12	10	8	7	7	6	4	4
n for 111:	19	20	20	20	20	20	20	20	20	20	20	19	19

HbF



n for 141:	13	12	13	12	12	12	10	8	7	7	6	4	4
n for 111:	19	20	20	20	20	19	20	20	19	20	18	19	19

Data shown as of July 2025 for participants in CLIMB TDT-141 (5-11 years) compared with adolescent (≥12 to <18 years) participants in CLIMB THAL-111

- **Total Hb:** Mean Total Hb levels increased to normal age-adjusted ranges[a]
- **HbF:** Mean HbF levels increased in pediatric participants similarly as adolescent and adult participants[1]
  - Similar pancellular HbF distribution across age groups: mean proportion of F-cells >99% after Month 6

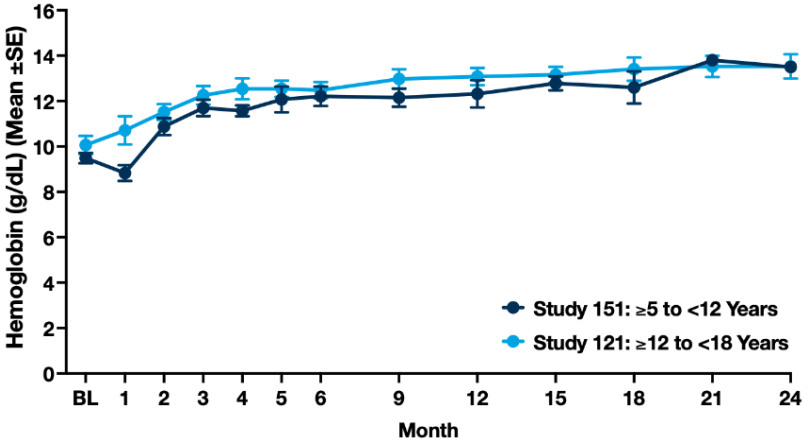
[a] 11.5 g/dL is LLN for Hb for participants aged 5-11 years

1. Refer to CLIMB THAL-111 ASH poster #6089

F-cells, erythrocytes expressing HbF; **Hb**, hemoglobin; **HbF**, fetal hemoglobin; **LLN**, lower limit of normal; **TDT**, transfusion-dependent β-thalassemia

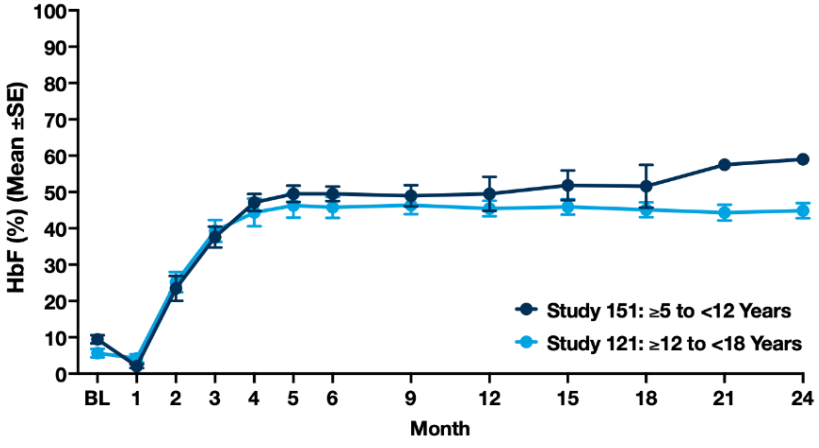
SCD: Durable Increases in Mean Total Hb and HbF in Participants Aged 5-11 Years With Increases in HbF% to ≥40% Similar to Adolescents and Adult Participants

Total Hb



n for 151:	11	11	10	10	10	10	10	8	5	4	3	1	1
n for 121:	12	11	12	12	12	12	12	12	12	12	12	12	12

HbF



n for 151:	11	10	10	9	10	9	10	7	5	4	3	1	1
n for 121:	12	11	12	12	12	12	12	12	12	12	12	12	12

Data shown as of July 2025 for participants in CLIMB SCD-151 (5-11 years) compared with adolescent (≥12 to <18 years) participants in CLIMB SCD-121

- **Total Hb**: Mean Total Hb levels increased to a normal age-adjusted range[a]
- **HbF**: Mean HbF% increased to ≥40% similarly as adolescent and adult participants[1]
  - Similar pancellular HbF distribution across age groups: mean proportion of F-cells >98% after Month 6

[a] 11.5 d/dL is LLN for Hb for participants aged 5-11 years

1. Refer to CLIMB SCD-121 ASH poster #2537

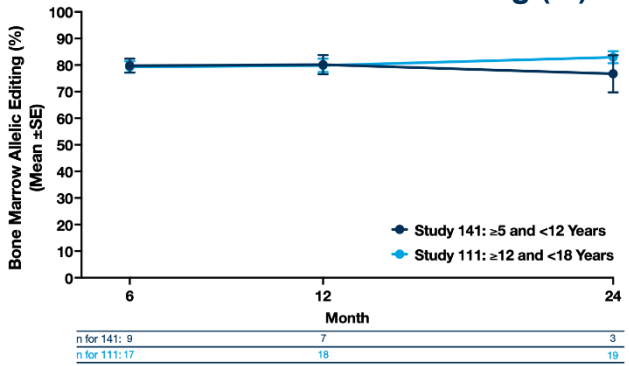
F-cells, erythrocytes expressing HbF; **Hb**, hemoglobin; **HbF**, fetal hemoglobin; **SCD**, sickle cell disease

TDT & SCD: Durable Bone Marrow & Peripheral Blood Allelic Editing in Pediatric Participants Similar to Adolescent and Adult Participants

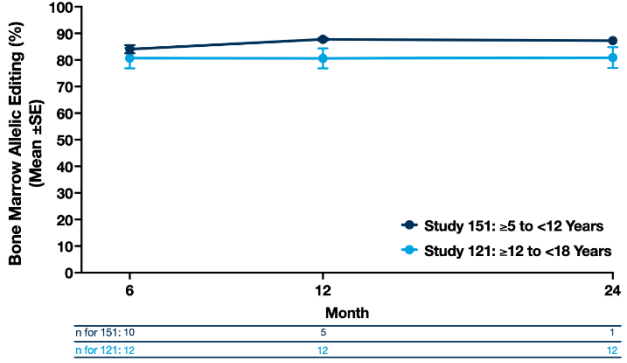
Successful Editing of Long-term HSCs Across Age Groups Consistent With Durable Clinical Benefit

Bone Marrow Allelic Editing (%)

TDT

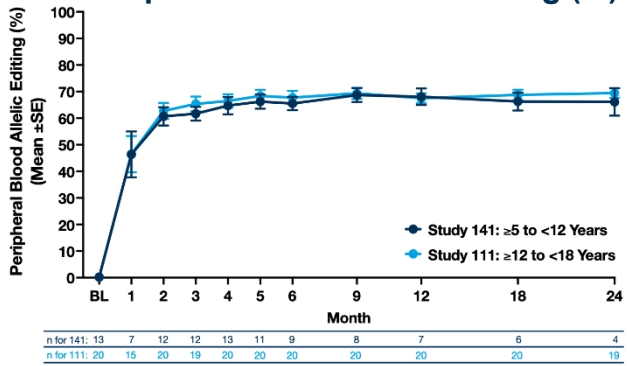


SCD

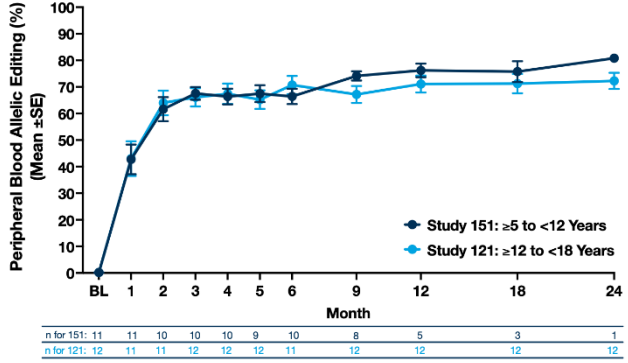


Peripheral Blood Allelic Editing (%)

TDT



SCD

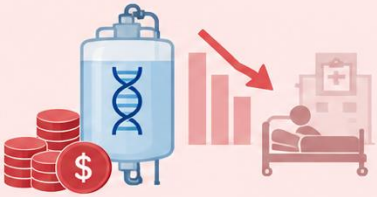


American Society of Hematology

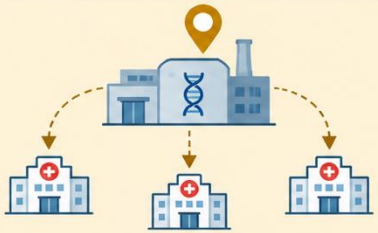
Data are shown as of July 2025 for participants in CLIMB TDT-141 (5-11 years) compared with adolescent (≥12 to <18 years) participants in CLIMB THAL-111 and for participants in CLIMB SCD-151 (5-11 years) compared with adolescent (≥12 to <18 years) participants in CLIMB SCD-121

HSCs, hematopoietic stem cells; **SCD**, sickle cell disease; **TDT**, transfusion-dependent β-thalassemia

Democratizing gene therapy for β-thalassemia



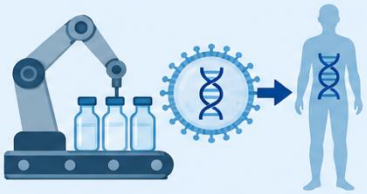
Current gene therapies remain inaccessible to most patients due to high costs, manufacturing complexity, and infrastructure requirements.



Regional manufacturing and hub-and-spoke models could reduce costs, logistics, and dependence on overseas facilities.



Local innovation is emerging with new development and regulatory models in countries such as China and Thailand.



Simpler technologies are needed, including automation, optimized manufacturing, and ultimately *in vivo* gene therapy to enable more scalable and less complex treatment pathways.



Regulatory harmonization and context-specific pathways could accelerate access while maintaining robust safety and quality standards.



More than cheaper products are needed: technology transfer, workforce development, quality systems, governance, and long-term surveillance are essential.

Al-Samkari H *et al*. *Lancet Haematol* 2026; Online ahead of print.

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The placement of gene therapy and allogeneic HSCT in patients with TDT or SCD?

- Gene therapy is associated with a more favorable safety profile.
- There is no risk of bidirectional alloreactivity leading to acute/chronic GvHD or graft rejection.
- Its application is not limited by the availability of a suitable donor.
- The success rate in the clinical trials is at least as good as (indeed better…) than that of allogeneic HSCT.
- The first gene editing therapy has been approved by FDA for children above the age of 2 years.
- A proportion of patients (mainly those with SCD) do not mobilize enough HSC.
- Rarely, drug product manufacturing may fail either for contamination or because of excessive cell loss.
- Equity of access to a costly treatment.