QUARTO EVENTO NAZIONALE

# SIE incontra i pazienti

26 maggio 2025

Bologna, Royal Hotel Carlton

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# SIE incontra i pazienti

## Nuovi farmaci nella talassemia.

26 maggio 2025

Bologna, Royal Hotel Carlton

Società Italiana di Ematologia

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
*Istituto di Ricovero e Cura a Carattere Scientifico*

# SIE incontra i pazienti

## Disclosures of Emanuele Angelucci

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
|---|---|---|---|---|---|---|---|
| Vertex | | | | | | | **DMC** |
| BMS | | | | | | | **DMC** |
| Menarini-Stemline | | | **X** | | | | |
| Sanofi | | | | | **X** | **X** | |
| Johson & Johnson | | | **X** | | | | |

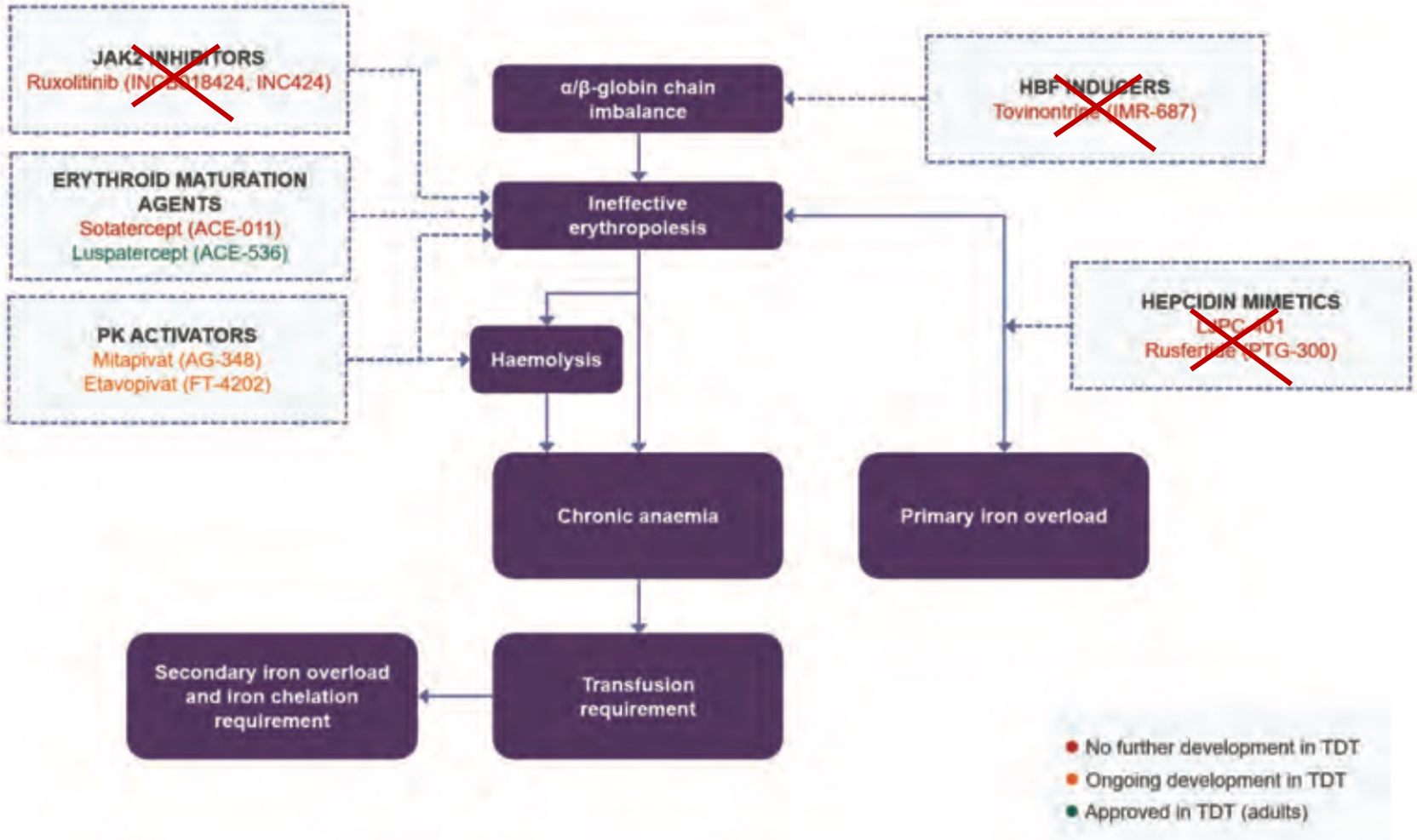
## SIE incontra i pazienti

- Farmaci con effetto sulla eritropoiesi
- Chelanti del ferro
- Trapianto allogenico e terapia genica

## SIE incontra i pazienti

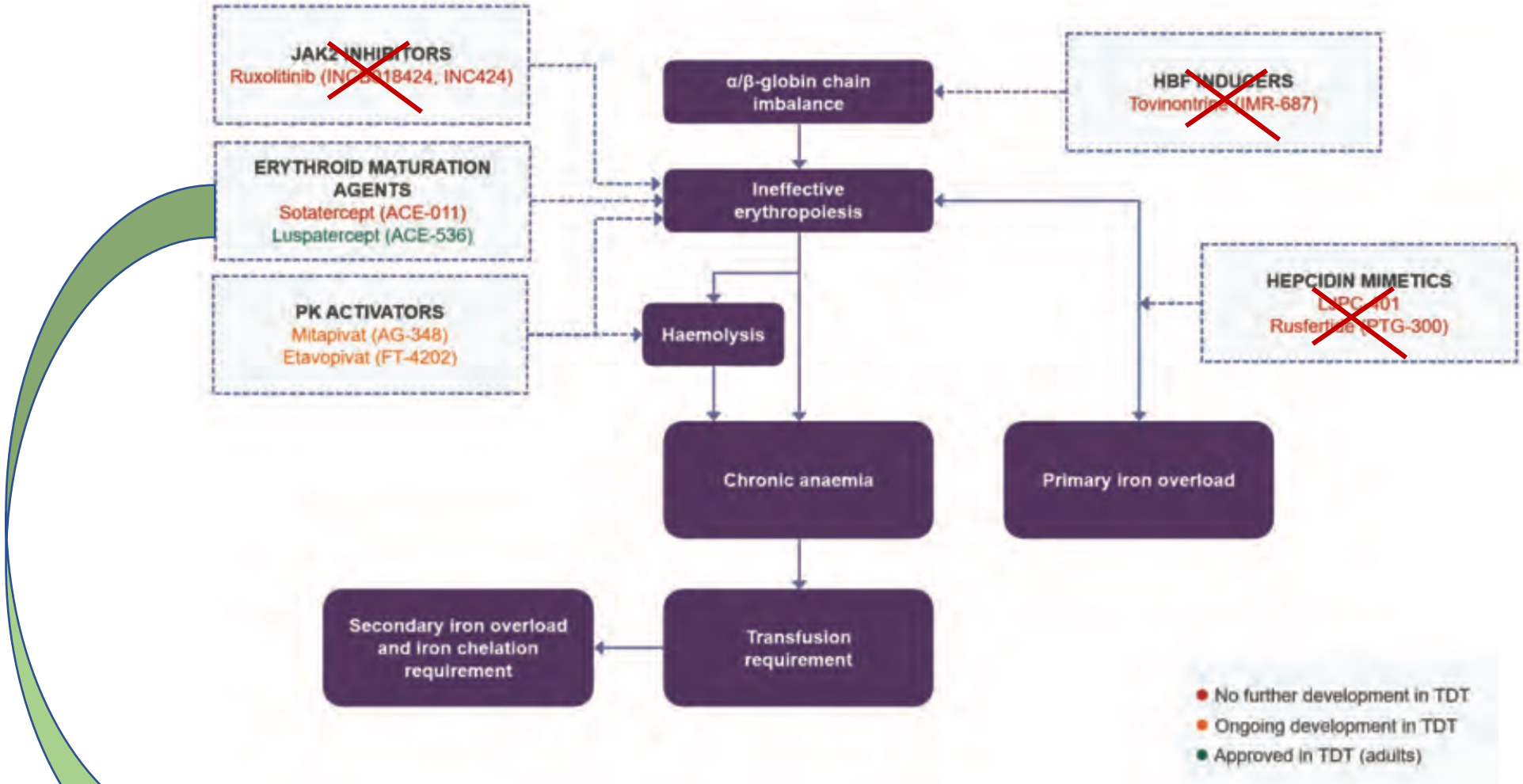
- **Farmaci con effetto sulla eritropoiesi**
- Chelanti del ferro
- Trapianto allogenico e terapia genica

# Novel disease-modifying therapies that have been recently developed or approved in transfusion-dependent β-thalassaemia




5th Edition GUIDELINES FOR THE MANAGEMENT OF TRANSFUSION-DEPENDENT β-THALASSAEMIA

# Novel disease-modifying therapies that have been recently developed or approved in transfusion-dependent β-thalassaemia




5th Edition GUIDELINES FOR THE MANAGEMENT OF TRANSFUSION-DEPENDENT β-THALASSAEMIA

**Luspatercept is FDA and EU approved for adult patients with β-TDT**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# A Phase 3 Trial of Luspatercept in Patients with Transfusion-Dependent β-Thalassemia

M.D. Cappellini, V. Viprakasit, A.T. Taher, P. Georgiev, K.H.M. Kuo, T. Coates, E. Voskaridou, H.-K. Liew, I. Pazgal-Kobrowski, G.L. Forni, S. Perrotta, A. Khelif, A. Lal, A. Kattamis, E. Vlachaki, R. Origa, Y. Aydinok, M. Bejaoui, P.J. Ho, L.-P. Chew, P.-C. Bee, S.-M. Lim, M.-Y. Lu, A. Tantiworawit, P. Ganeva, L. Gercheva, F. Shah, E.J. Neufeld, A. Thompson, A. Laadem, J.K. Shetty, J. Zou, J. Zhang, D. Miteva, T. Zinger, P.G. Linde, M.L. Sherman, O. Hermine, J. Porter, and A. Piga, for the BELIEVE Investigators*

N ENGL J MED 382;13 NEJM.ORG MARCH 26, 2020

The NEW ENGLAND JOURNAL of MEDICINE

## Phase 3 Trial of Luspatercept for Transfusion-Dependent β-Thalassemia

MULTINATIONAL, DOUBLE-BLIND, RANDOMIZED, CONTROLLED PHASE 3 TRIAL


| ≥33% Reduction in transfusion burden, weeks 13–24 | Luspatercept | Placebo |
|---|---|---|
| | 21.4% (48/224) | 4.5% (5/112) |

OR, 5.79; 95% CI, 2.24–14.97; P<0.001

Transient bone pain, arthralgia, dizziness, hypertension, and hyperuricemia were more frequent with luspatercept

M.D. Cappellini et al. 10.1056/NEJMoa1910182



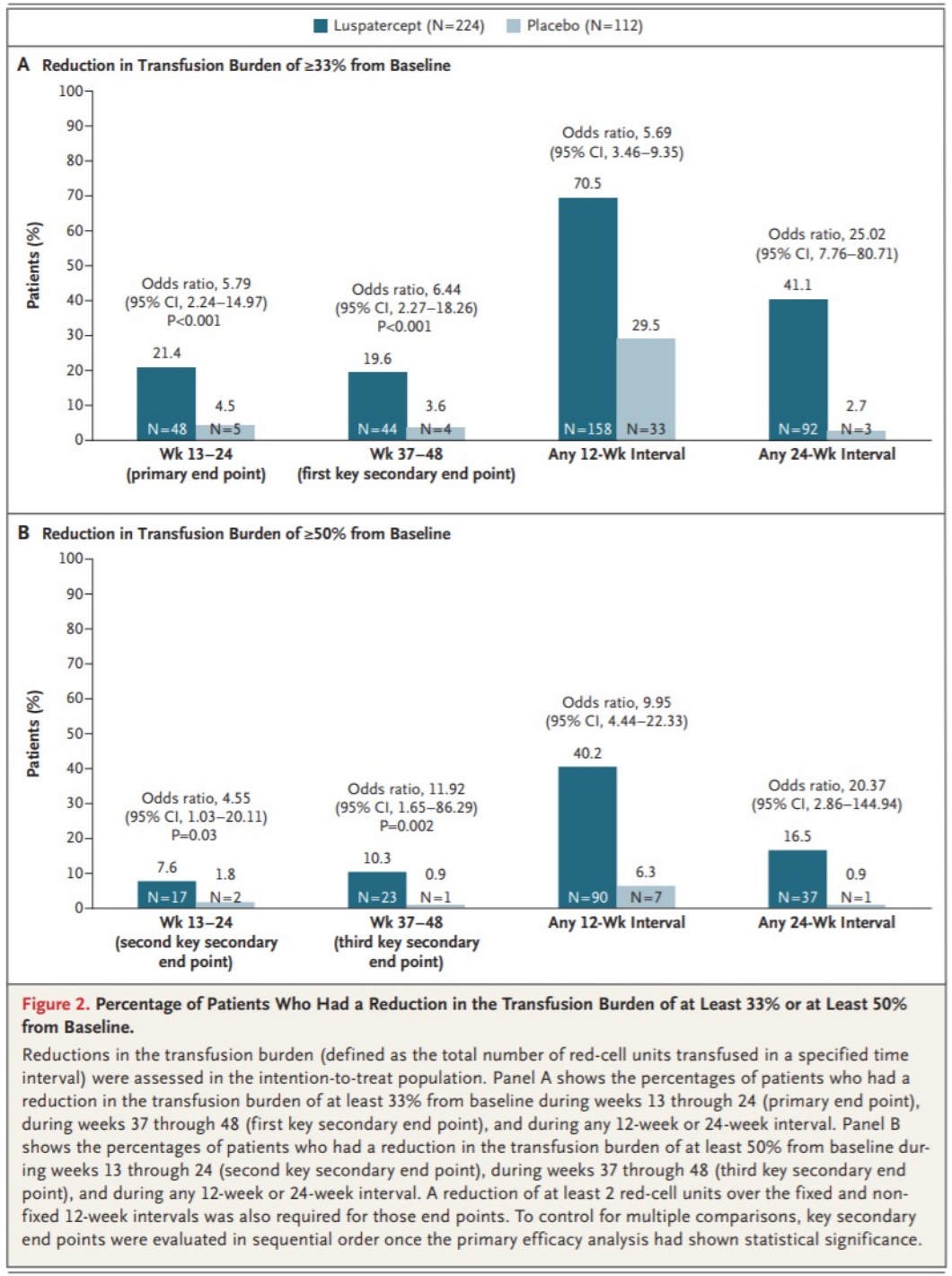



**Figure 2. Percentage of Patients Who Had a Reduction in the Transfusion Burden of at Least 33% or at Least 50% from Baseline.**

Reductions in the transfusion burden (defined as the total number of red-cell units transfused in a specified time interval) were assessed in the intention-to-treat population. Panel A shows the percentages of patients who had a reduction in the transfusion burden of at least 33% from baseline during weeks 13 through 24 (primary end point), during weeks 37 through 48 (first key secondary end point), and during any 12-week or 24-week interval. Panel B shows the percentages of patients who had a reduction in the transfusion burden of at least 50% from baseline during weeks 13 through 24 (second key secondary end point), during weeks 37 through 48 (third key secondary end point), and during any 12-week or 24-week interval. A reduction of at least 2 red-cell units over the fixed and non-fixed 12-week intervals was also required for those end points. To control for multiple comparisons, key secondary end points were evaluated in sequential order once the primary efficacy analysis had shown statistical significance.

# Luspatercept for Non-Transfusion Dependent β-thalassemia

## BEYOND trial

- Randomized phase 2 trial

**Adults with non-transfusion-dependent β-thalassaemia or HbE/β-thalassaemia received**:

- ≤ 5 RBC units within the 24 weeks before randomization
- No RBC transfusion within 8 weeks before randomization
- Hb ≤ 10 g/dL (planned N = 150)

*Randomized 2:1*

Week 48

**Luspatercept** 1 mg/kg[a] s.c. q21d + **BSC**

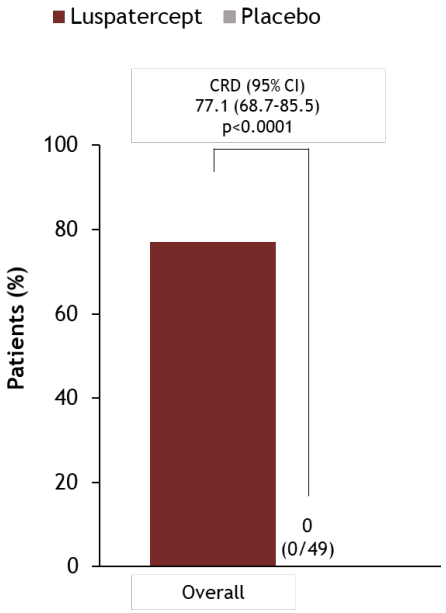
**Placebo** s.c. q21d + **BSC**

**Primary endpoint**

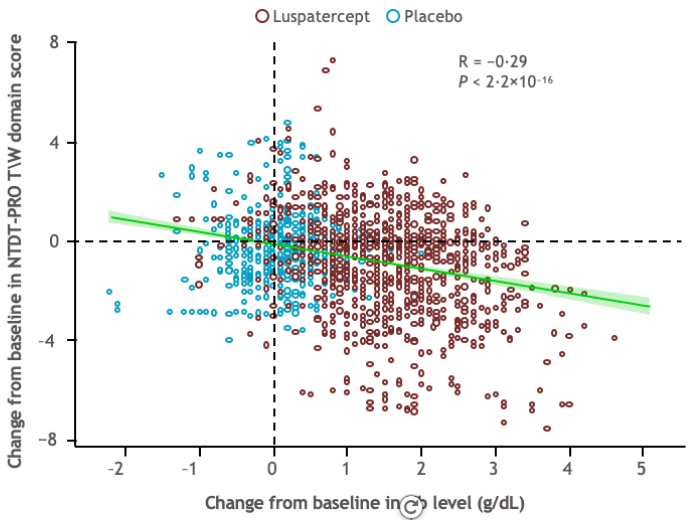
Proportion of patients with increase in mean Hb concentration of ≥ 1 g/dL in absence of RBC transfusion from Week 13 to 24 vs baseline[b]

**Secondary endpoint**

Patient-reported β-thalassaemia symptoms (NTDT-PRO), functional and health-related QoL (FACIT-F score, SF-36), physical activity (6MWT); iron chelation therapy daily dose, LIC, serum ferritin; PK; AEs




Significantly more patients in the luspatercept group than in the placebo group (74/96 [77.1%] vs none) had a mean hemoglobin level increase of ≥ 1.0 g/dL from baseline over a continuous 12-week interval (weeks 13–24) in the absence of RBC transfusions.




The correlation analysis showed that as hemoglobin levels increased, NTDT-PRO T/W domain scores decreased, suggesting improvement in patient-reported tiredness and weakness (R = −0.29; *P* < 0.0001)

Taher AT, et al. *Lancet Haematol 2022*

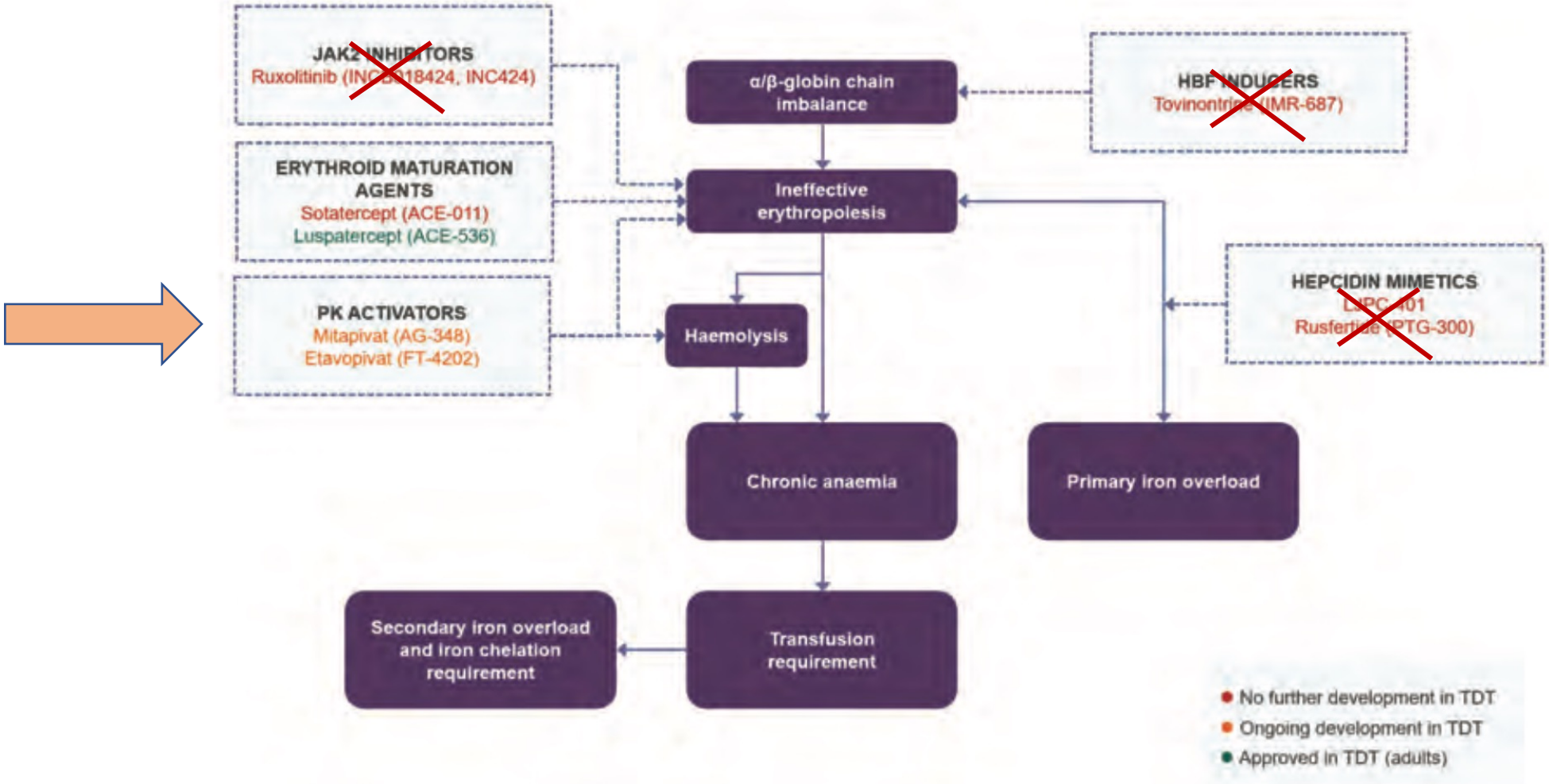
# Studies ongoing

- Luspatercept in pediatric patients with transfusion-dependent β-thalassemia: design and eligibility criteria of a phase 2a study evaluating safety and pharmacokinetics of luspatercept in children

- A Phase 2, Double-blind, Randomized, Placebo-controlled, Multicenter Study to Determine the Efficacy and Safety of Luspatercept for the Treatment of Anemia in Adults with Alpha (α)-thalassemia

http://clinicaltrials.gov

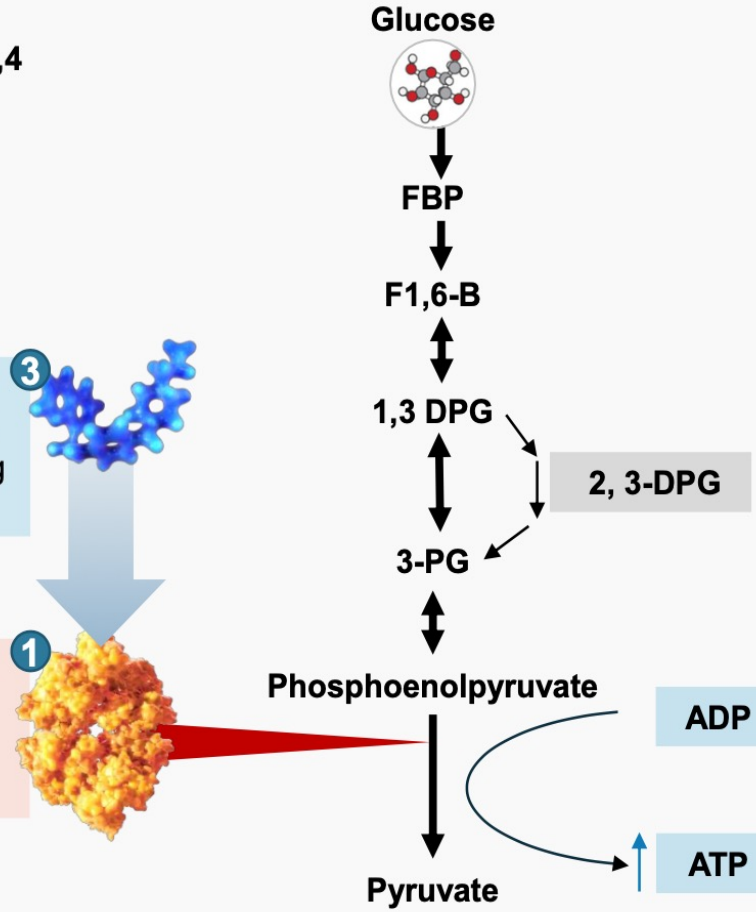
# Novel disease-modifying therapies that have been recently developed or approved in transfusion-dependent β-thalassaemia




5th Edition GUIDELINES FOR THE MANAGEMENT OF TRANSFUSION-DEPENDENT β-THALASSAEMIA

# Mitapivat is a first-in-class, oral, small-molecule allosteric activator of mutant and wild-type pyruvate kinase

## Mitapivat Mechanism of Action[1,3,4]




**Mitapivat**
activates both wild-type and mutant forms of RBC PK (PKR) enzymes *in vitro*, leading to increased production of ATP for RBCs

**Pyruvate kinase**
catalyzes the final step of the glycolytic pathway; it is crucial for generating ATP and maintaining healthy RBCs

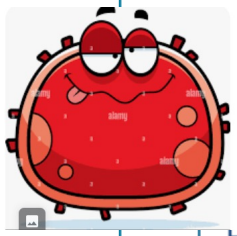
**Efficient generation of ATP**
is essential for maintaining function of RBCs and integrity of cell membranes. Thalassemic RBCs have increased demand for ATP but insufficient production of ATP to meet that demand.

ATP, adenosine triphosphate; DPG, 2,3-diphosphoglycerate; FBP, fructose bisphosphate; FDA, US Food and Drug Administration; NTDT, non–transfusion dependent thalassemia; PK, pyruvate kinase; PKR, protein kinase R; RBC, red blood cell.

1. Kung C, et al. *Blood*. 2017;130(11):1347-1356. 2. PYRUKYND. Package insert. , Inc.; 2022. 3. Rab MAE, et al. *Haematologica*. 2021;106(1):238-249. 4. Cappellini MD, et al. *Blood Rev*. 2018;32(4):300-311.

# Mitapivat mechanisms in thalassemia

## Pathophysiology



Imbalanced α- to β-globin ratio

↓

Globin precipitates and aggregates

↓

Oxidative damage ← Dysregulated iron metabolism

↓

Hemolysis; Ineffective erythropoiesis

↓

**Anemia**; **Iron overload**

## Mechanism of Action

**Mitapivat**

↓

**Enhanced glycolysis and ↑ ATP**

Imbalanced α- to β-globin ratio

↓

Globin precipitates and aggregates

Oxidative damage ← Dysregulated iron metabolism

↓

Hemolysis; Ineffective erythropoiesis

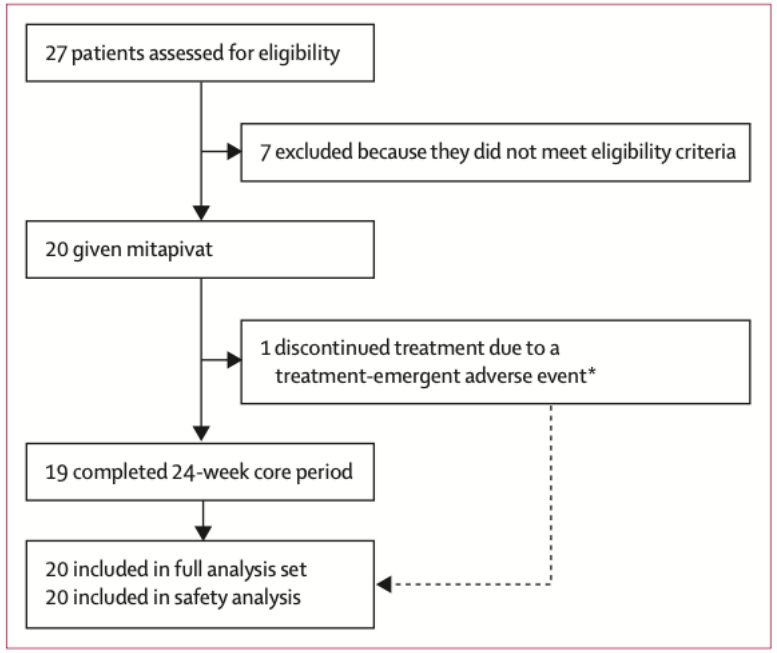
↓

**Anemia**; **Iron overload**

ATP, adenosina trifosfato.

# Safety and efficacy of mitapivat, an oral pyruvate kinase activator, in adults with non-transfusion dependent α-thalassaemia or β-thalassaemia: an open-label, multicentre, phase 2 study

*Kevin H M Kuo, D Mark Layton, Ashutosh Lal, Hanny Al-Samkari, Joy Bhatia, Penelope A Kosinski, Bo Tong, Megan Lynch, Katrin Uhlig, Elliott P Vichinsky*




| | Patients with α-thalassaemia (n=5) | Patients with β-thalassaemia (n=15)* | All patients (N=20) |
|---|---|---|---|
| Sex | | | |
| Female | 4 (80%) | 11 (73%) | 15 (75%) |
| Male | 1 (20%) | 4 (27%) | 5 (25%) |
| Age, years | 35 (35–37) | 52 (35–57) | 44 (35–56) |
| Race and ethnicity | | | |
| Asian | 5 (100%) | 5 (33%) | 10 (50%) |
| White | 0 | 4 (27%) | 4 (20%) |
| Black or African | 0 | 1 (7%) | 1 (5%) |
| American | 0 | 0 | 0 |
| Native Hawaiian or other | 0 | 1 (7%) | 1 (5%) |
| Other | 0 | 3 (20%) | 3 (15%) |
| Not reported | 0 | 1 (7%) | 1 (5%) |
| Baseline haemoglobin, g/dL | 8·37 (7·57–8·80) | 8·50 (6·57–9·13) | 8·43 (6·78–8·98) |
| <85 g/L (8·5 g/dL) | 3 (60%) | 7 (47%) | 10 (50%) |
| ≥85 g/L (8·5 g/dL) | 2 (40%) | 8 (53%) | 10 (50%) |
| Indirect bilirubin, μmol/L | 62·1 (33·6–87·2) | 18·0 (14·5–23·0) | 21·0 (15·5–36·1) |
| Previous splenectomy | | | |
| Yes | 0 | 2 (13%) | 2 (10%) |
| No | 5 (100%) | 13 (87%) | 18 (90%) |
| Previous chelation status | | | |
| Yes | 1 (20%) | 2 (13%) | 3 (15%) |
| No | 4 (80%) | 13 (87%) | 17 (85%) |
| LDH, IU/L | 263·0 (202·0–313·0) | 245·0 (175·0–380·0) | 249·0 (176·5–368·0) |
| Erythropoietin, IU/L | 45·0 (29·0–79·0) | 95·5 (30·0–141·0) | 79·0 (29·0–137·0) |
| Reticulocyte, $10^9$/L | 196·0 (180·0–351·5) | 86·0 (51·5–169·0) | 145·8 (63·8–188·0) |

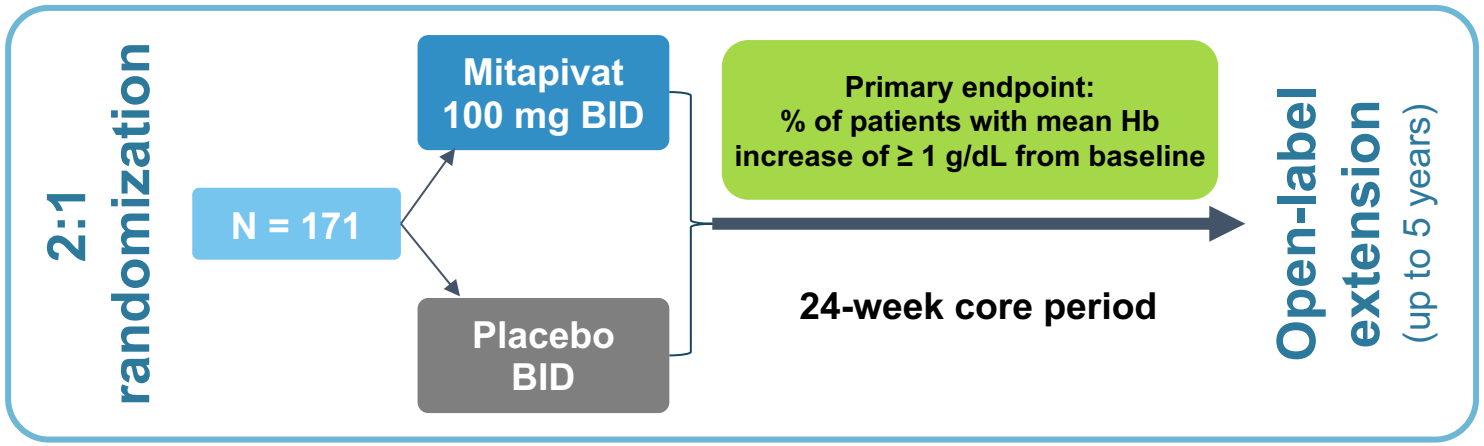
Data are n (%) or median (IQR). LDH=lactate dehydrogenase. *Includes two patients with haemoglobin E β-thalassemia.

***Table 1:*** **Patient demographics and baseline characteristics**

*Lancet* 2022; 400: 493–501

# Two Phase 3, global, randomized, controlled trials of mitapivat in adults with α- or β-thalassemia

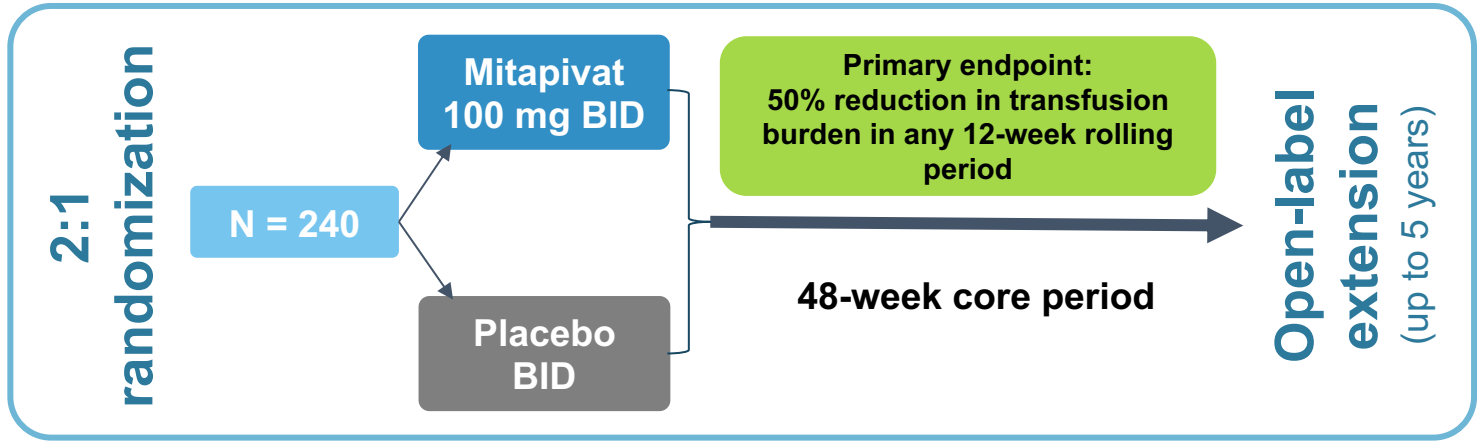
## ENERGIZE




**Key inclusion criteria**

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Non-transfusion-dependent (≤ 5 RBC units during the 24-week period before randomization and no RBC transfusions ≤ 8 weeks prior)
- Hb ≤ 10.0 g/dL

## ENERGIZE-T




**Key inclusion criteria**

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Transfusion-dependent (6–20 RBC units transfused and ≤ 6-week transfusion-free period during the 24-week period before randomization)

BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H; RBC = red blood cell.
ClinicalTrials.gov: ENERGIZE (NCT04770753); ClinicalTrials.gov: ENERGIZE-T (NCT04770779).

# ENERGIZE T RESULTS

## Mitapivat demonstrated a statistically significant reduction in transfusion burden vs placebo

**Primary endpoint**

ELSEVIER

Blood 144 (2024) 409–411

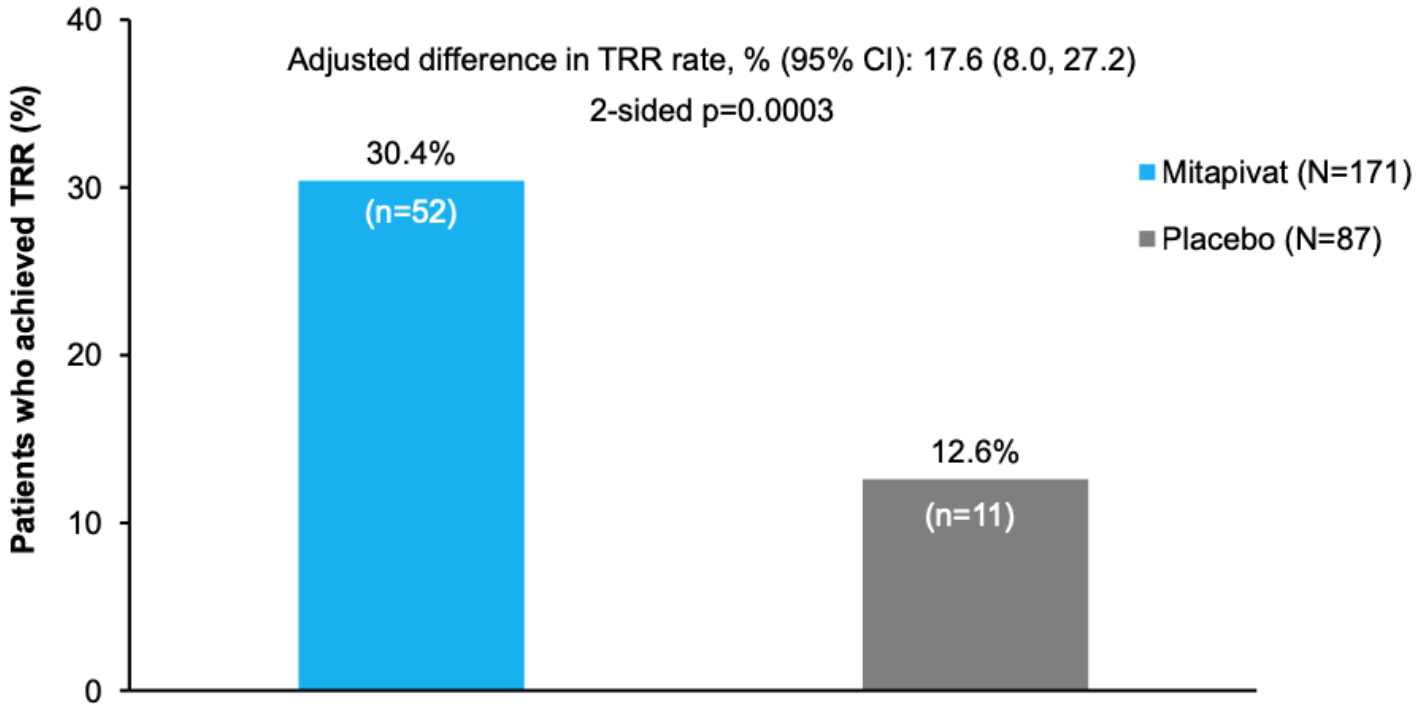
The 66th ASH Annual Meeting Abstracts

**ORAL ABSTRACTS**

**112.THALASSEMIA AND GLOBIN GENE REGULATION**

**ENERGIZE-T: A Global, Phase 3, Double-Blind, Randomized, Placebo-Controlled Study of Mitapivat in Adults with Transfusion-Dependent Alpha- or Beta-Thalassemia**

*Maria Domenica Cappellini, MD [1], Sujit Sheth, MD [2], Ali T. Taher, MD FRCP [3], Hanny Al-Samkari, MD [4], Ali Bülent Antmen, MD PhD [5], David Beneitez, MD [6], Giovanna Cannas, MD [7], Thomas D. Coates, MD [8], Lauren Czapla, ANP [9], Jayme L. Dahlin, MD PhD [10], Jeremie H. Estepp, MD [11], Elizabeth Feenstra, MD [7], Pencho Georgiev, MD PhD [11], Sarah Gheuens, MDPhDMMSc [7], Keely S Gilroy, PhD [7], Andreas Glenthøj, MD PhD [12], Khaled Musallam, MDPhD [13], Kareem Osman, MD [9], John B. Porter [14], Hui Shao, PhD [7], Katrin Uhlig, MD MS [9], Eduard J. Van Beers, MD PhD [15], Vip Viprakasit, MD DPhil(Oxon) [16], Kevin H.M. Kuo, MDMSc,FRCPC [17], Antonis Kattamis, MD [18]*

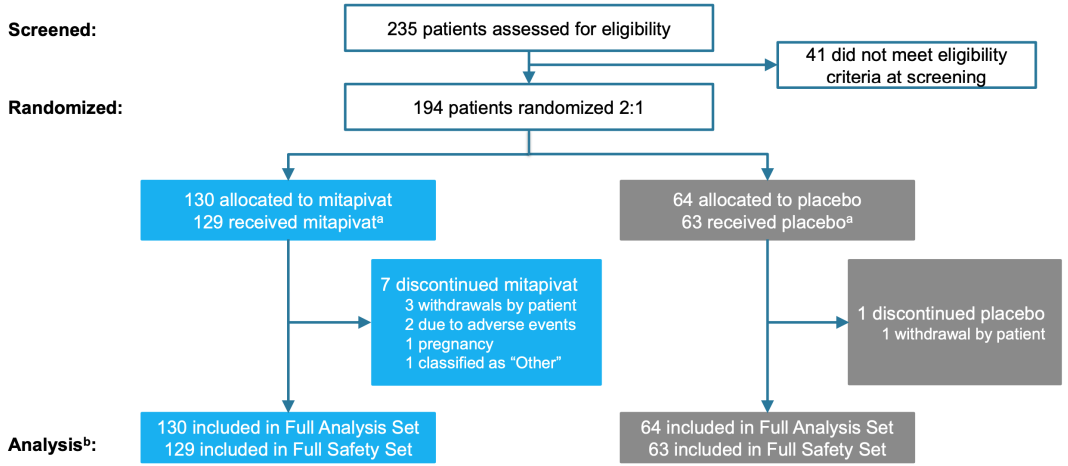



**Transfusion reduction response (TRR) was defined as a ≥50% reduction in transfused RBC units and a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through Week 48 compared with baseline**

Analysis conducted on Full Analysis Set. Baseline transfusion burden standardized to 12 weeks=total number of RBC units transfused during the 24-week period (168 days) before "reference date"×12/24, where "reference date" is the randomization date for subjects randomized and not dosed or the start of study treatment for subjects randomized and dosed. Subjects withdrawn from the study before Week 12 (Day 85) are considered non-responders. CI, confidence interval; RBC, red blood cell; TRR, transfusion reduction response.

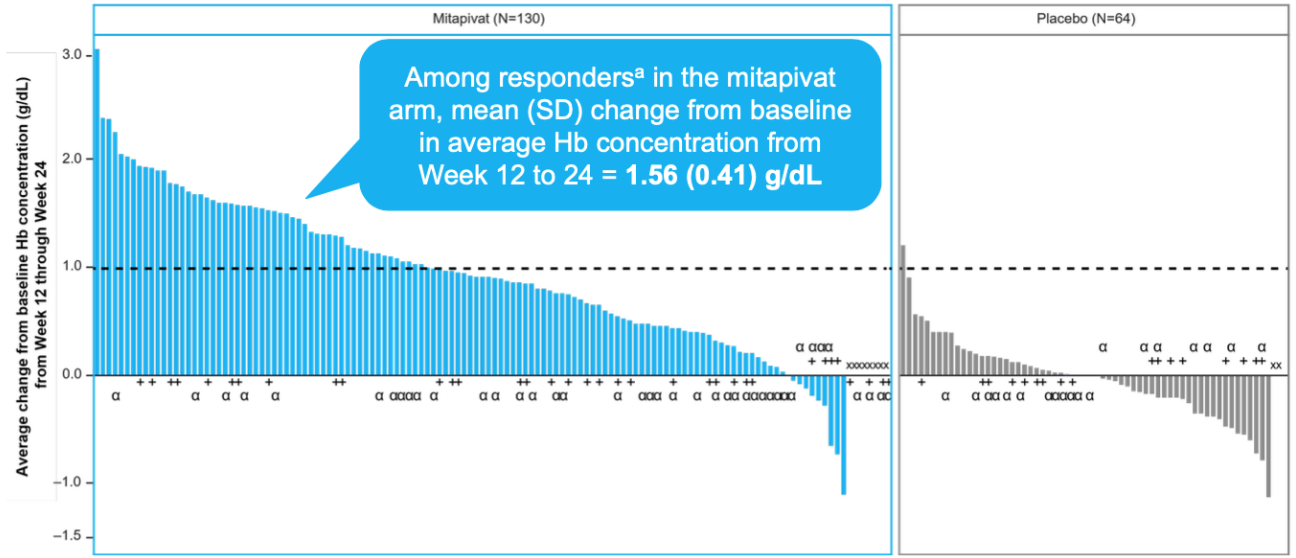
# ENERGIZE – population NTDT

## Patient flowchart: 194 patients were randomized in the study




[a]1 patient in each treatment arm was randomized but not dosed. [b]Full Analysis Set: All patients randomized. Patients are classified according to the randomized treatment group. Full Safety Set: All patients who received ≥1 dose of study treatment. If a patient randomized to placebo received ≥1 dose of mitapivat in the double-blind period, then the patient was classified to the mitapivat arm

| | Mitapivat N=130 | Placebo N=64 | 2-sided p-value |
|---|---|---|---|
| Hb response,[a] n (%) | 55 (42.3) | 1 (1.6) | p<0.0001 |




α = α-thalassemia/HbH disease

\+ = Baseline Hb category: 9.1–10 g/dL

x = Patient with missing baseline or with no assessments from Week 12 through Week 24

ASH abstract 2025

## SIE incontra i pazienti

- Farmaci con effetto sulla eritropoiesi
- **Chelanti del ferro**
- Trapianto allogenico e terapia genica

# Iron chelation therapy: oral ferroportin inhibitor

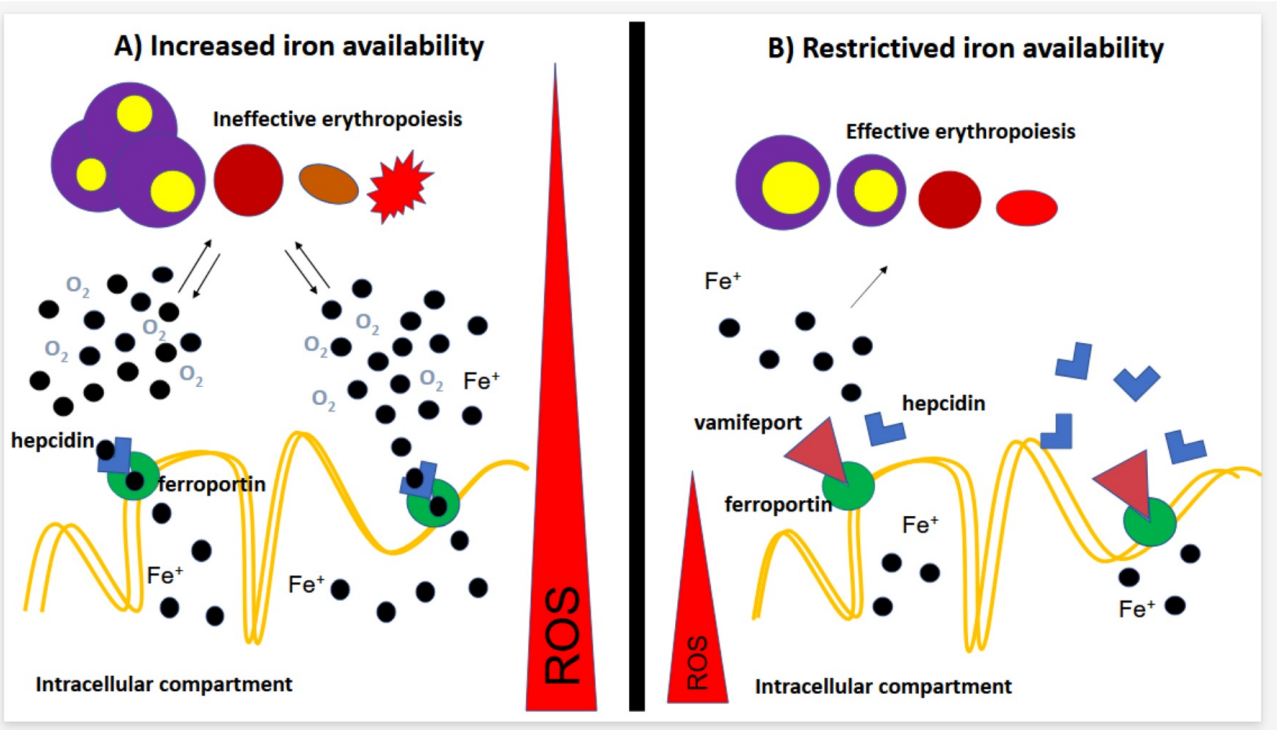



**Table 1.** Completed and ongoing studies.

| Trial | Phase | Target Population | Objectives | Clinicaltrial.gov ID | Status |
|---|---|---|---|---|---|
| VITHAL | Phase 2a, double-blind, randomized, placebo-controlled, parallel group, multicenter study on safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of multiple doses of VIT-2763 in subjects with non-transfusion-dependent β-thalassemia | People aged 18 and older with NTDT 12 years to 65 years | Tolerability and safety. | NCT04364269 | Completed |
| VIT-2763-THAL-203 | Phase 2b multiple-dose, double-blind, randomized, placebo-controlled, parallel-group, multicenter trial | TDT | The main purpose of this study is to evaluate the efficacy of 3 multiple doses of VIT-2763 as measured by the reduction in red blood cell (RBC) transfusion burden from week 13 to week 24, to identify the most efficacious and safe dose. | NCT04938635 | Withdrawn (strategic reasons) |
| VIT-2763-SCD-202 | Phase 2a, double-blind, randomized, placebo-controlled, efficacy, and safety study of multiple doses of VIT-2763 in subjects with sickle cell disease | SCD | The purpose of this study is to investigate the effect of VIT-2763 on markers of hemolysis (breakdown in red blood cells) in sickle cell disease (SCD). The safety, tolerability and clinical beneficial effects of VIT-2763 for the treatment of SCD are also explored. | NCT04817670 | Ongoing |

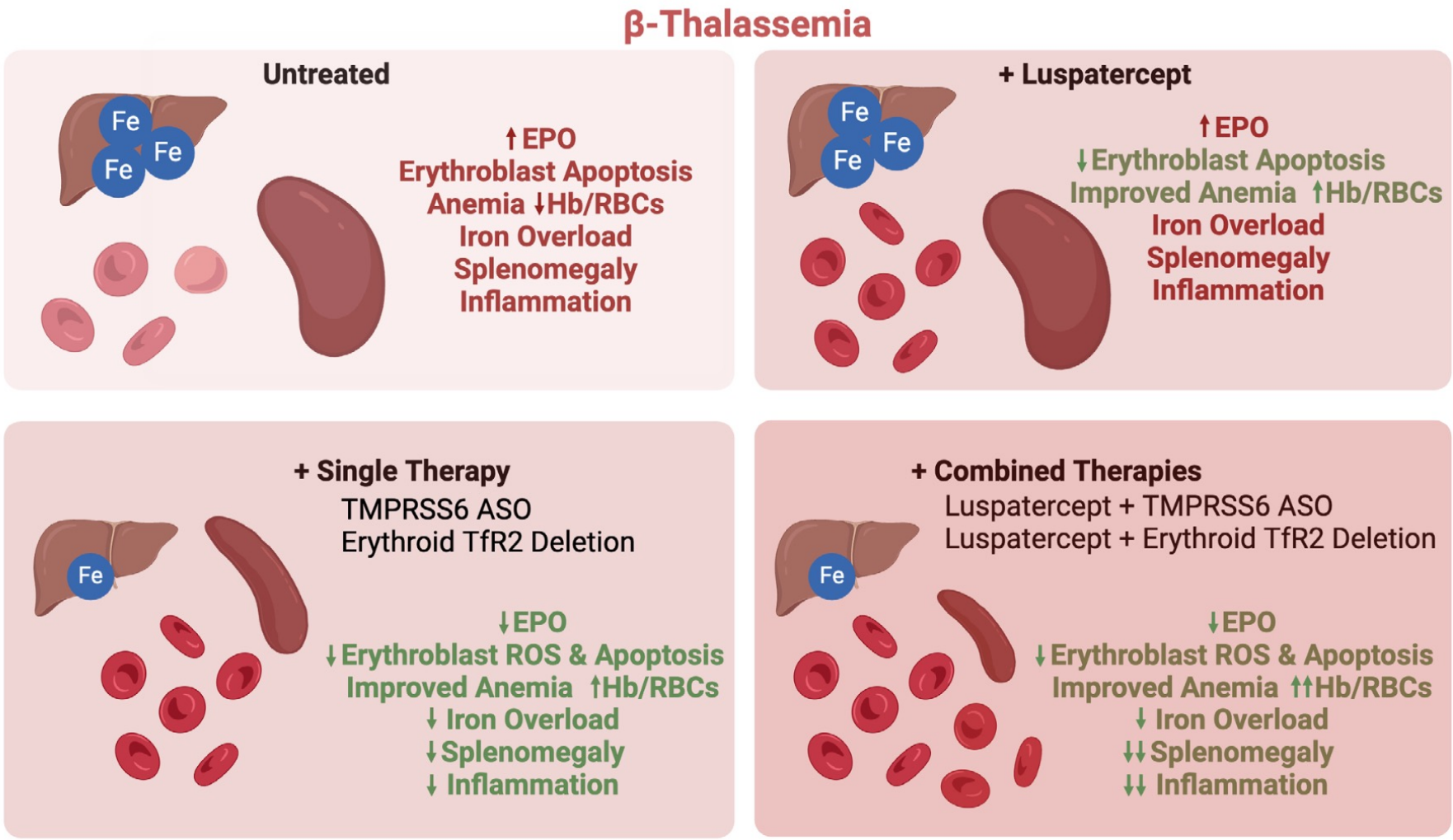
**Table 2.** Summary of preclinical and clinical results for vamifeport.

| | Preclinical Results | Clinical Results |
|---|---|---|
| Thalassemia | • Reduced organ iron levels.<br>• Reduced the level of reactive oxygen species (ROS).<br>• Reduced the amount of early erythroid precursors in the bone marrow and spleen, and increased the number of mature erythrocytes.<br>• Ameliorated hematological parameters. | • Safety and tolerability (revealed no differences between groups in adverse events rates (vamifeport, QD = 66%, BID = 58%; placebo, 75%)).<br>• All AEs were mild or moderate intensity.<br>• No deaths or serious AEs were reported.<br>• Decreased serum iron concentrations.<br>• Hematological markers do not report significant changes. |

Pilo, F.; Angelucci, E. J. Clin. Med.2024,13,5524. https:// doi.org/10.3390/jcm13185524

- Protocol P-SP420-THAL-01 An open-label, dose-escalation, dose-finding, and proof-of-concept trial of SP-420 in subjects with transfusion-dependent α- or β- thalassemia or low-risk myelodysplastic syndromes EU trial number 2023-507396-21-00

# Next future….Combined therapy?



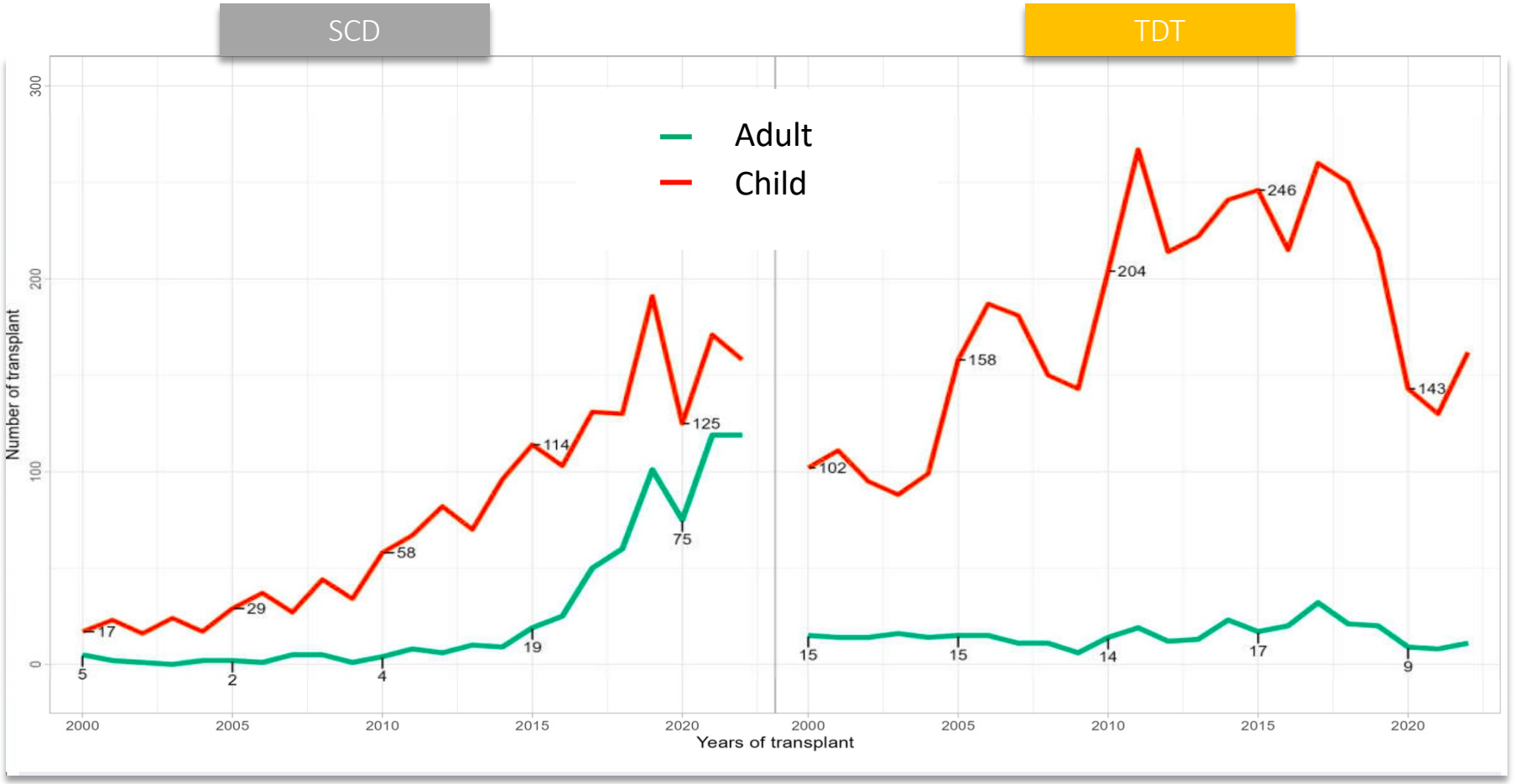

Vinchi F. New partners for Luspatercept in β-thalassemia. Am J Hematol. 2024 Jul;99(7):1217-1219. doi: 10.1002/ajh.27362.

## SIE incontra i pazienti

- Farmaci con effetto sulla eritropoiesi
- Chelanti del ferro
- **Trapianto allogenico e terapia genica**

# EBMT Hemoglobinopathy Registry: TDT-SCD

## Number of transplants (2000-2022) according to age




EBMT, European Society for Blood and Marrow Transplantation; SCD, sickle cell disease; TDT, transfusion-dependent thalassemia.
Slide provided by Emanuele Angelucci from the EBMT Haemoglobinopathies Working Party data.

EBMT
European Society
for Blood and Marrow Transplantation

Real world data

# EBMT Hemoglobinopathy Working Party

## 2891 TDT Patients: Donor and Outcome

| Donor | MSD | Match Related | MM Related | UD 10/10 | UD<10/10 |
|---|---|---|---|---|---|
| OS | 91.8 % | 88.3 % | 85.3% | 93.2% | 81.4% |
| PFS | 83 % | 79.5 % | 62.4% | 85.7% | 68 % |
| Rejection | 8.8% | 8.8% | 22.9% | 7.5% | 13.4% |
| NRM | 8.1% | 11.6% | 14.6% | 6.7% | 18.5% |
| Ac GVHD >2 | 6.6% | 9,3% | 3,1% | 12,7% | 14.2% |
| Cr GVHD | 13.1% | 15.9% | 9.3% | 15% | 17.8% |

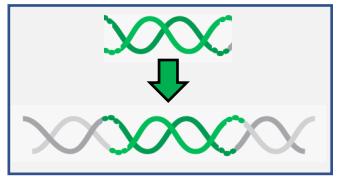
There is a need to increase the pool of donors

Ac, acute; Cr, chronic; EBMT, European Group for Blood and Marrow Transplantation; GVHD, graft-versus-host disease; MM, mismatch; MSD, matched sibling donor; NRM, non-relapse mortality; OS, overall survival; PFS, progression-free survival; TDT, transfusion-dependent β-thalassemia; UD, unrelated donor.

EBMT 2020 Analysis: Data provided by speaker.

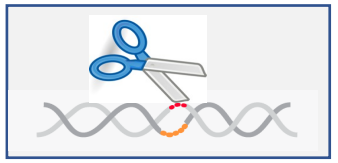
# Potential Methods for Permanently Modifying HSCs for Long-Term Effect

- **Gene Addition (using viral vectors)**



  - Adding a copy of β–globin (for example, $HbA^{T87Q}$)
  - Fetal globin (a β-like anti-sickling globin) activation via transcriptional regulation

- **Genome Editing (using engineered / programmable nucleases)**



  - Gene correction: fixing the mutation itself (HbS)
  - Generating de novo mutations that result in Hereditary Persistence of Fetal Hemoglobin (HPFH)

Gregory. ASH Educational Lecture. Dec 2017.

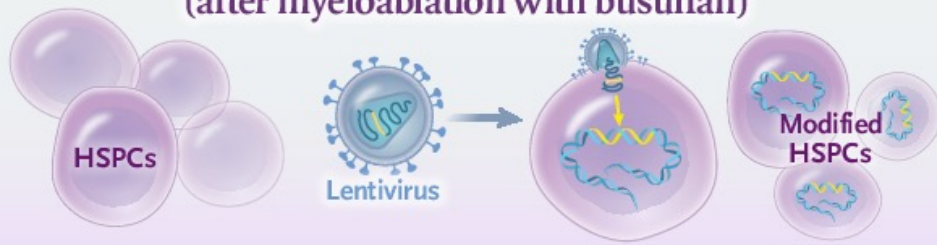
The NEW ENGLAND JOURNAL of MEDICINE

# Betibeglogene Autotemcel Gene Therapy for Non–$\beta^0/\beta^0$ Genotype $\beta$-Thalassemia

**OPEN-LABEL, PHASE 3 STUDY**

**23**
Adult and pediatric patients with transfusion-dependent $\beta$-thalassemia and a non–$\beta^0/\beta^0$ genotype


**Beti-cel gene therapy**
(after myeloablation with busulfan)




| | |
|---|---|
| Transfusion independence (median follow-up, 29.5 mo) | 20 of 22 patients |
| Average hemoglobin level during transfusion independence | 11.7 g/dl (range, 9.5–12.8) |
| Median gene therapy–derived adult hemoglobin level at 12 mo | 8.7 g/dl (range, 5.2–10.6) |

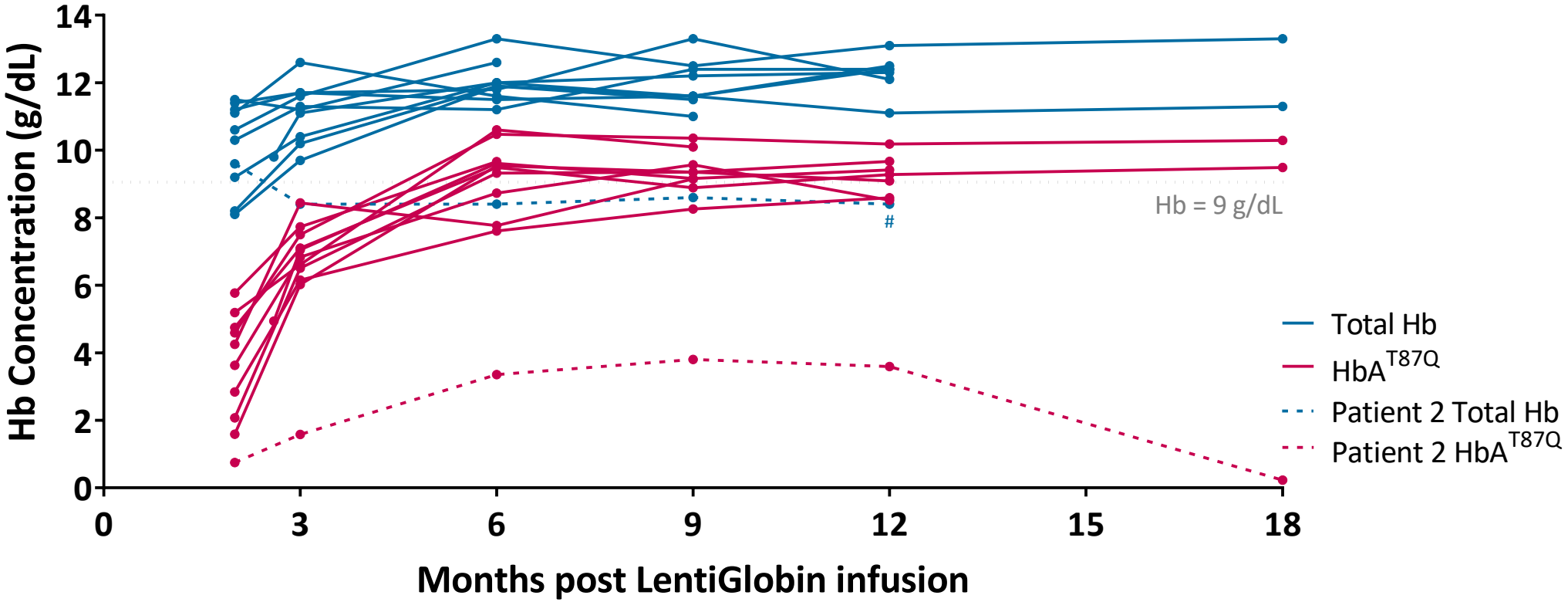
**Beti-cel treatment resulted in transfusion independence in most patients.**

F. Locatelli et al. 10.1056/NEJMoa2113206

# HGB-207: Stable total Hb and gene therapy-derived $HbA^{T87Q}$ in 10/11 patients with ≥ 6 months follow-up

**Median Hb in patients free from transfusions at last study visit (g/dL)**

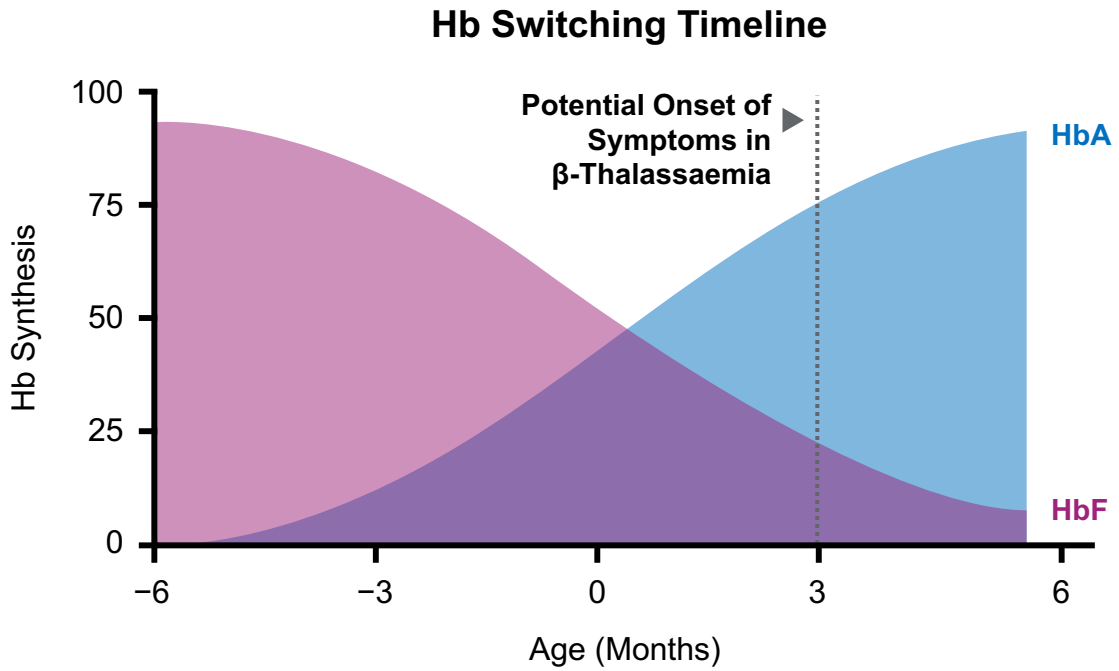
| | M6 (n=10) | M9 (n=9) | M12 (n=7) | M18 (n=2) |
|---|---|---|---|---|
| **Total Hb** | **11.9** | **11.6** | **12.4** | **12.3** |




#Last Hb before

# Disease Symptoms Arise as Haemoglobin (Hb) Switches From Foetal to Adult[1,2]

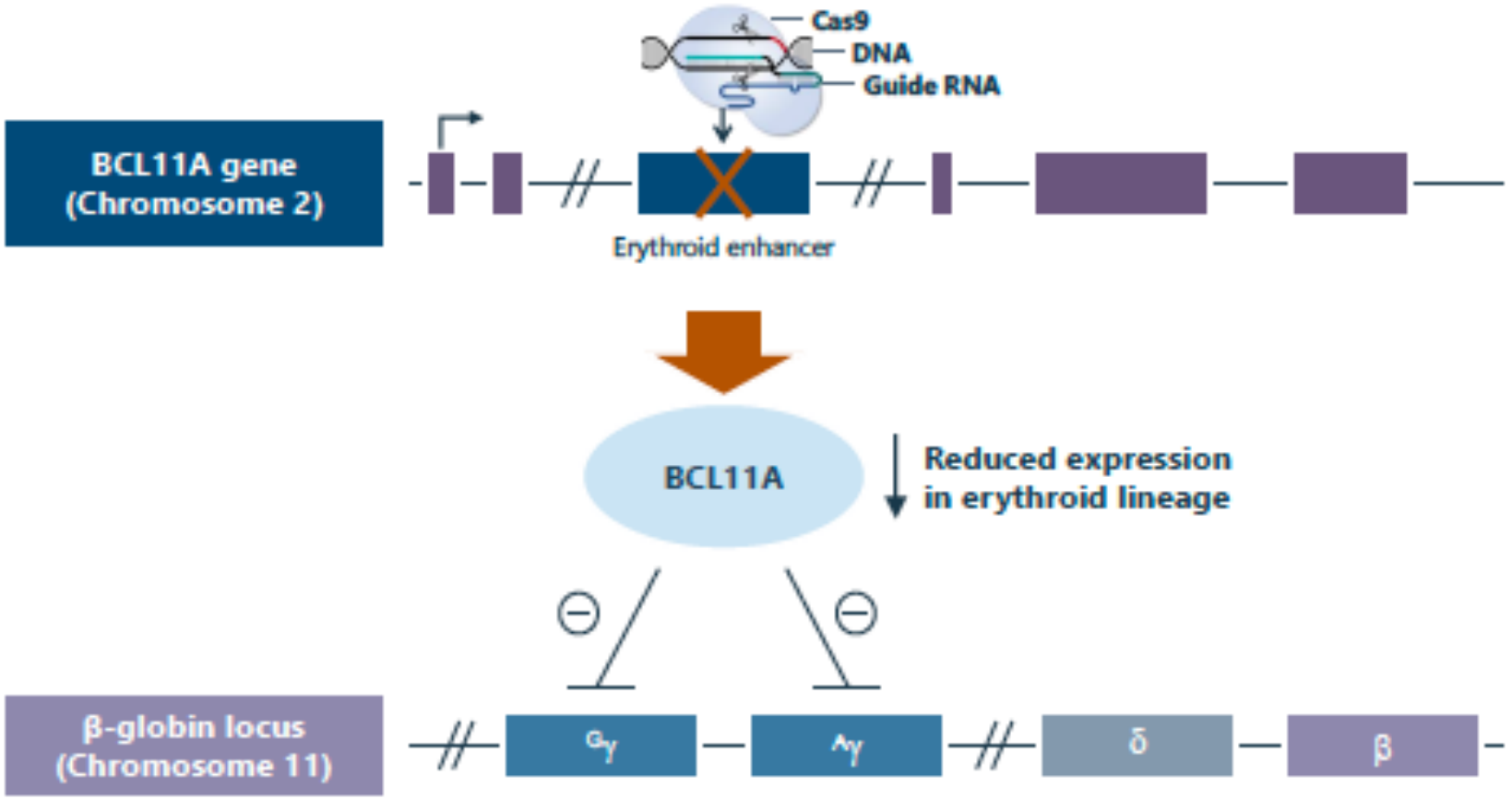
- Various combinations of globin subunits generate different types of Hb, which are expressed at different stages of life[1]
  - Foetal haemoglobin (HbF) consists of 2 α-globin and 2 γ-globin chains[2]
  - Adult haemoglobin (HbA) consists of 2 α-globin and 2 β-globin chains[2]
- Shortly after birth, the predominant Hb switches from HbF to HbA as levels of γ-globin decrease and β-globin increase[2]




This chart is for illustrative purposes only and is not representative of all people with β-thalassaemia.

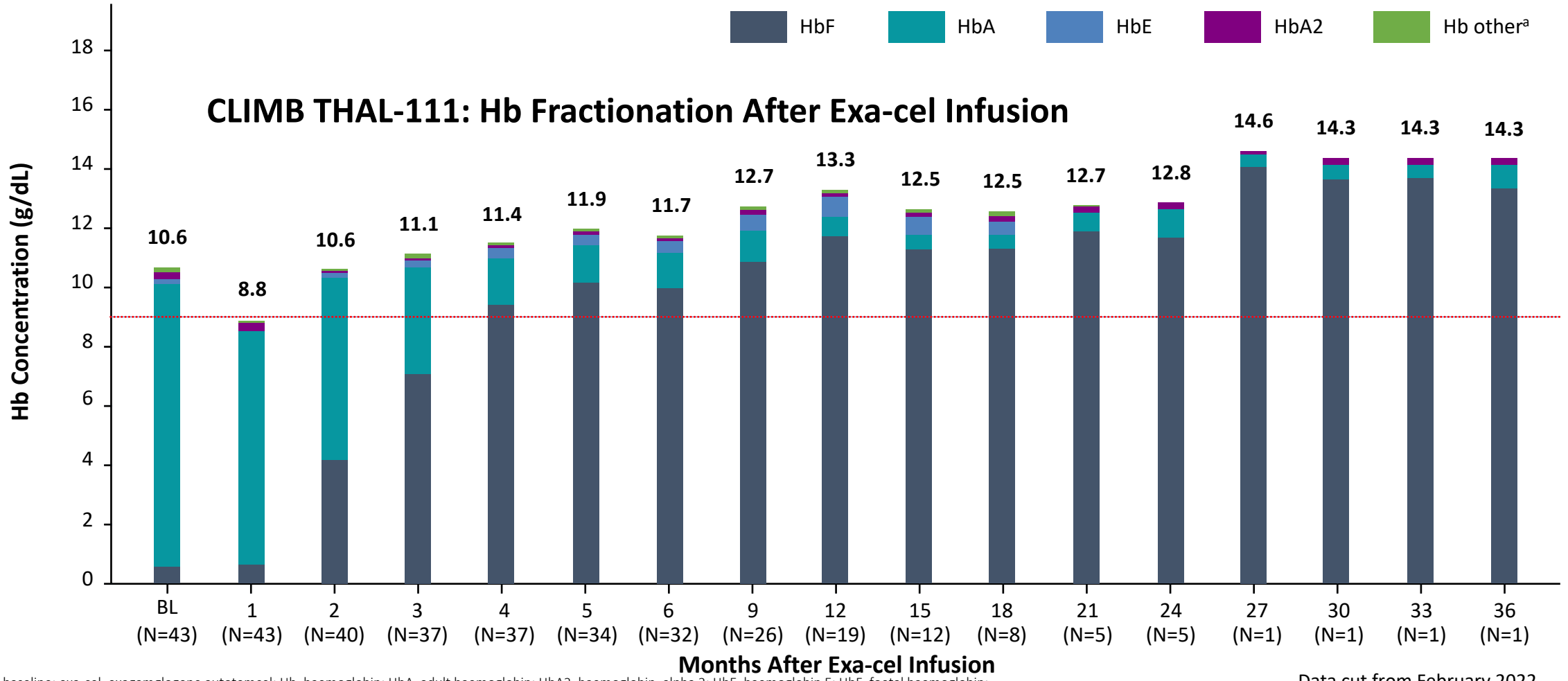

1. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010.
2. Sankaran VG, et al. *Cold Spring Harb Perspect Med*. 2013;3(1):a011643.

# Our approach disrupts the BCL11A erythroid enhancer




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

**The information on this slide is about an investigational approach that is not approved by any Health Authority. Safety and efficacy have not been established.**



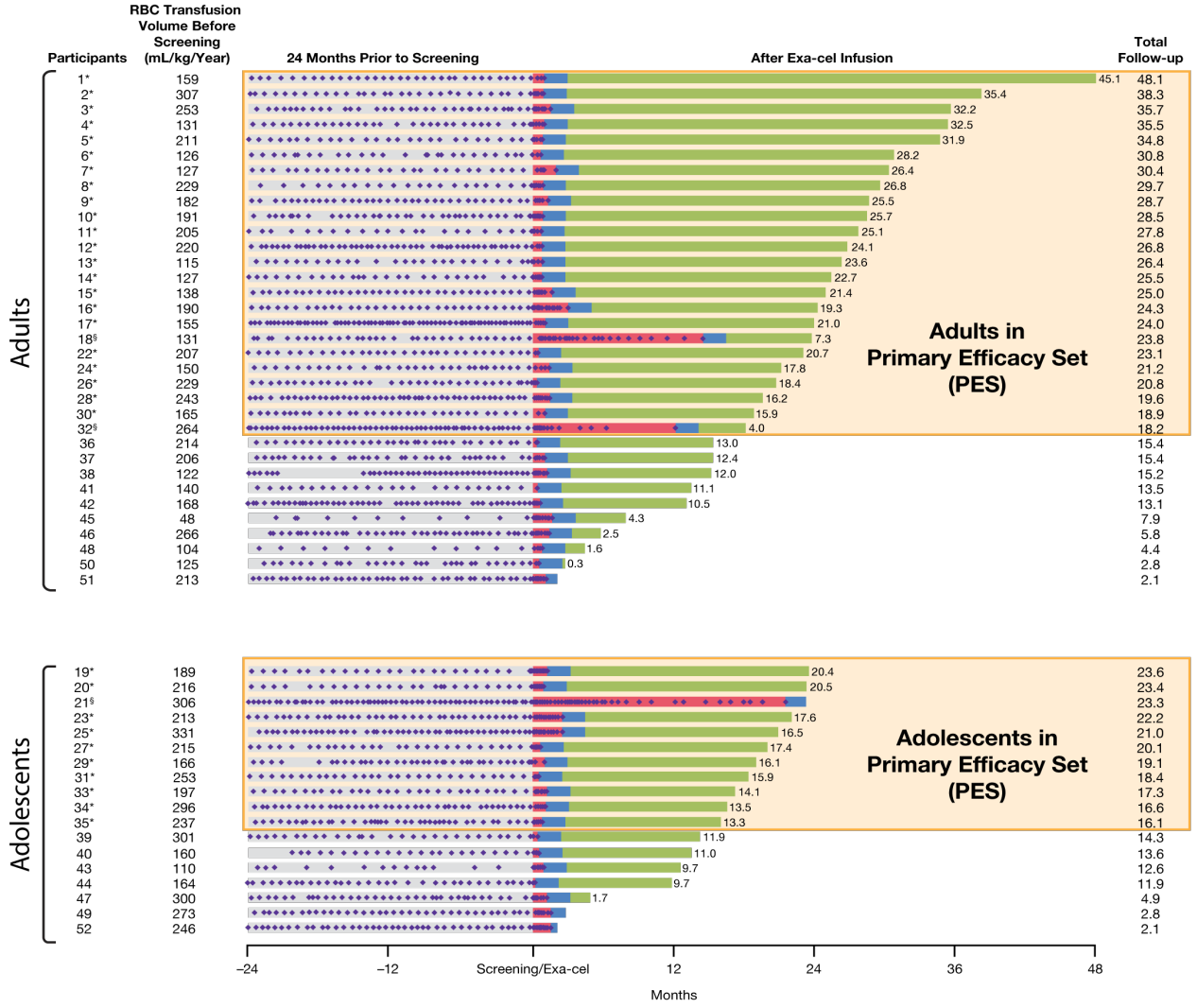

BL, baseline; exa-cel, exagamglogene autotemcel; Hb, haemoglobin; HbA, adult haemoglobin; HbA2, haemoglobin, alpha 2; HbE, haemoglobin E; HbF, foetal haemoglobin; TDT, transfusion-dependent β-thalassaemia.

Mean total Hb concentrations are shown directly above bars. [a]Hb adducts and other variants.

1. Locatelli F, et al. Oral presentation. Presented at the 27th Annual European Hematology Association; 12 June 2022

Data cut from February 2022.
Adapted from Locatelli F, et al. Presented at the 27th Annual European Hematology Association; 12 June 2022.

# Clinically Meaningful Benefit and Consistent Efficacy Between Adults and Adolescents in TDT




- Baseline period
- Time from exa-cel to last adjudicated RBC transfusion for post-transplant support or TDT disease management
- 60-day washout period after last RBC transfusion
- Time without RBC transfusions starting from end of washout period to data cut
- RBC transfusion

F Locatelli Courtesy

*participants who achieved TI12; §participants who did not achieve TI12

**exa-cel,** exagamglogene autotemcel; **RBC,** red blood cell; **TDT,** transfusion dependent β-thalassemia; **TI12;** proportion of participants transfusion independent for ≥12 consecutive months while maintaining a weighted average hemoglobin ≥9 g/dL.

# Hurdles to the Adoption of Gene Therapy as a Curative Option for Transfusion-Dependent Thalassemia

Isabelle Thuret, Annalisa Ruggeri ,*, Emanuele Angelucci, Christian Chabannon

Long term adverse events (insertional mutagenesis)

Pricing and additional costs

Production issues

**COST –** The wholesale acquisition cost (WAC) of a single dose of gene therapy range from $2.2 million to $2.8 million.
The Medical Letter May 13, 2024

*MEDICINES CAN CURE DISEASES BUT ONLY DOCTORS CAN CURE PATIENTS.*

C. G. Jung

*Buricrats neither*
*Emanueele Angelucci*