ICD-10-PCS codes for autologous administration of betibeglogene autotemcel (beti-cel)

LET'S RECODE THE STORY

Background Only
ICD-10 Coordination and Maintenance Committee
8 – 9 March 2022

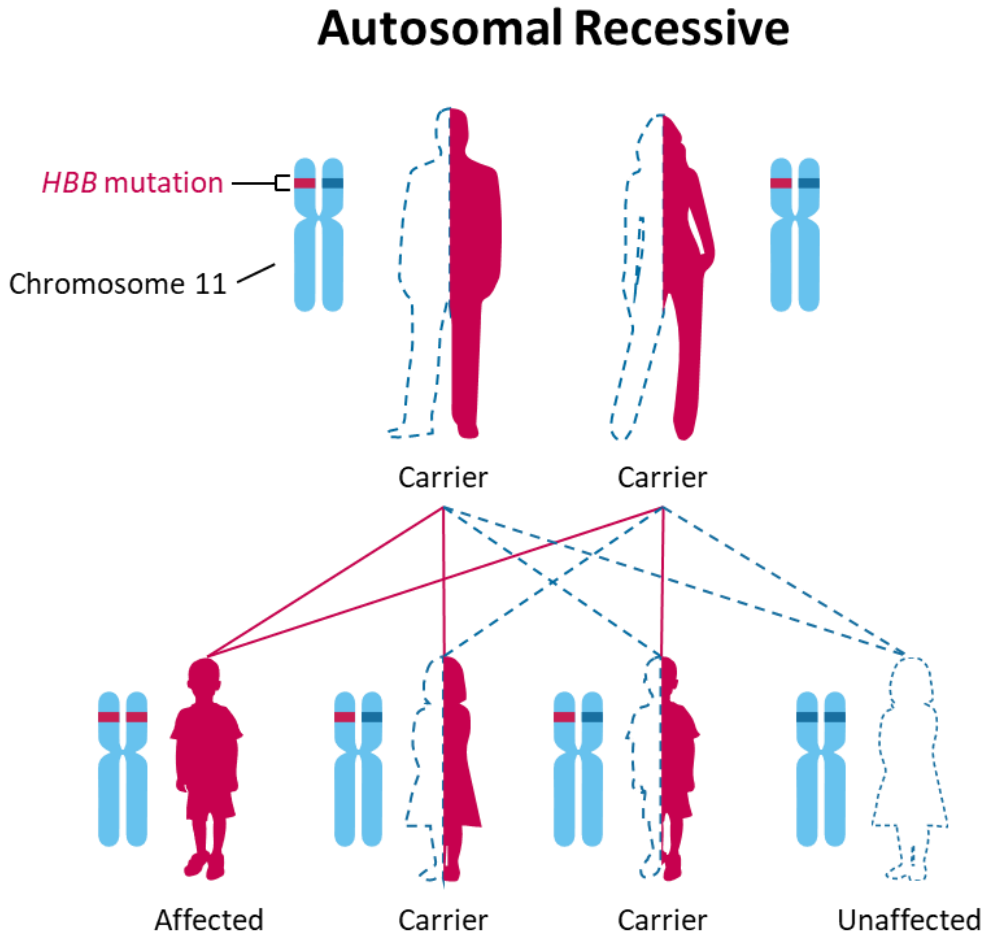
NASDAQ: BLUE

ß-thalassemia is a genetic disease caused by mutations affecting the production of ß-globin

- Patients with ß-thalassemia have reduced or no ß-globin production due to mutations affecting the *HBB* gene on chromosome 11[1]
- Inheritance is typically autosomal recessive[1]
  - A child of 2 carrier parents has a 25% chance of being affected
- Nearly 350 mutations have been identified that may cause ß-thalassemia.[2]
- These mutations are grouped into 3 categories[2-4].

Allele	Phenotype
$ß^0$	No functional ß-globin production[2,3]
$ß^+$	Reduced functional ß-globin production[2,3]
$ß^E$	Reduced functional ß-globin production (primarily found in Southeast Asia)[3,4]

- Red blood cell transfusions correct the anemia and enable survival but lead to iron overload and associated complications.[3,5]
- Available treatment options for TDT include lifelong chronic red blood cell transfusions with iron chelation or allogeneic hematopoietic stem cell transplant (HSCT).[3]



HBB, human ß-globin gene.

References: 1. Cao A, Galanello R. *Genet Med*. 2010;12(2):61-76. **2.**Taher et al., N Engl J Med. 2021;384:727-743. **3.** Cappellini, et al. T*halassaemia International Federation*. 4th ed. 2021. 4. Fucharoen, et al. Cold Spring Harb Perspect Med 2012;2:a011734. **5.** Tubman, et al. *J Pediatr Hematol Oncol* 2015;37:e162-69.

betibeglogene autotemcel (beti-cel) is an investigational product that has not been approved by the FDA

Note: This slide represents a real family impacted by beta thalassemia, but no family member has been treated with beti-cel.

process of *ex vivo* gene therapy with beti-cel for TDT[1]

Collection of cells

Via plerixafor and G-CSF mobilization and apheresis

Mobilization: 5 days; Apheresis: on day 5
(mobilization/apheresis on days 6&7 if needed)

Myeloablative conditioning

Using busulfan

4 days + washout period

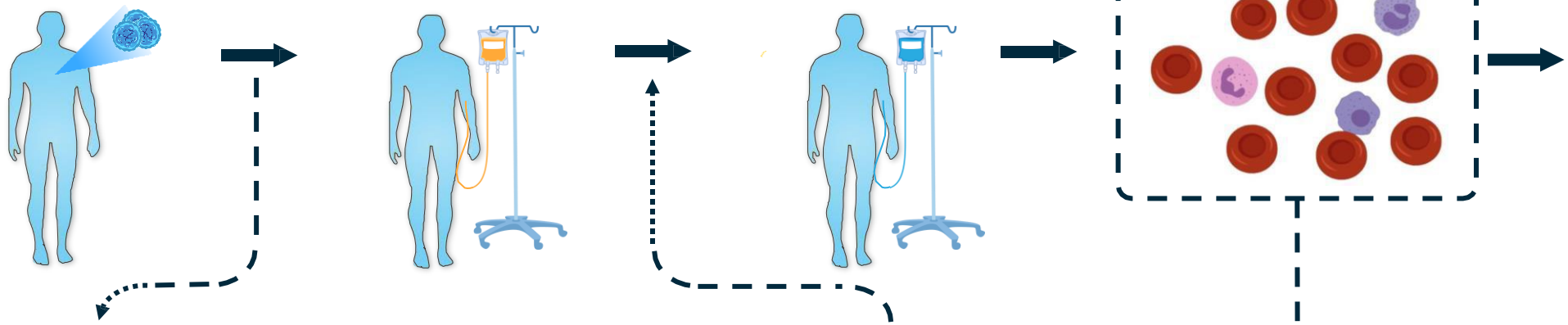
Drug product infusion

Hospitalization median ~6 weeks (includes conditioning)

Engraftment and repopulation

Long-term monitoring

15-yr total follow-up



beti-cel manufacturing

Select CD34+ HSCs

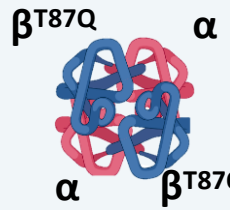
Transduce

Quality testing and safety monitoring

Transgene

Third generation
BB305 lentiviral vector

Modified RBCs express gene therapy-derived HbA^{T87Q}



Measurable by HPLC

HSCs, hematopoietic stem cells; RBCs, red blood cells; HbA, adult hemoglobin; HPLC, high-performance liquid chromatography.

1. Locatelli et al. EHA 2021. Abstract S266.

betibeglogene autotemcel Phase 3 clinical trials overview in pediatric, adolescent, and adult patients with transfusion dependent β-thalassemia (TDT)

(Data presented at the European Hematology Association Annual Congress, June 2021)

HGB-207 (Northstar-2)
non-β^0/β^0 genotypes

Primary Endpoint

Transfusion Independence

Weighted average Hb ≥ 9 g/dL without any pRBC* transfusions for ≥ 12 months

Additional Key Endpoints

Hb over time, $\beta^{A\text{-}T87Q}$-globin expression, assessment of improvement in ineffective erythropoiesis

Enrollment Complete

23 patients infused

Median follow-up: 24.28 months**

(min – max: 13.0 – 27.5 months)

HGB-212 (Northstar-3)
β^0/β^0, $\beta^{+IVS\ I\ 110}/\beta^{+IVS\ I\ 110}$, and $\beta^0/\beta^{+IVS\ I\ 110}$

Primary Endpoint

Transfusion Independence

Weighted average Hb ≥ 9 g/dL without any pRBC transfusions for ≥ 12 months

Additional Key Endpoints

Hb over time, $\beta^{A\text{-}T87Q}$-globin expression, assessment of improvement in ineffective erythropoiesis

Enrollment Complete

18 patients infused

Median follow-up: 22.98 months**

(min – max: 4.1 – 26.8 months)

After completing 2 years of follow-up in HGB-207 and HGB-212, patients are invited to enroll in a 13-year long-term follow-up study, LTF-303

Reference: Locatelli F, et al. EHA 2021. Abstract S266

*pRBC: packed red blood cells

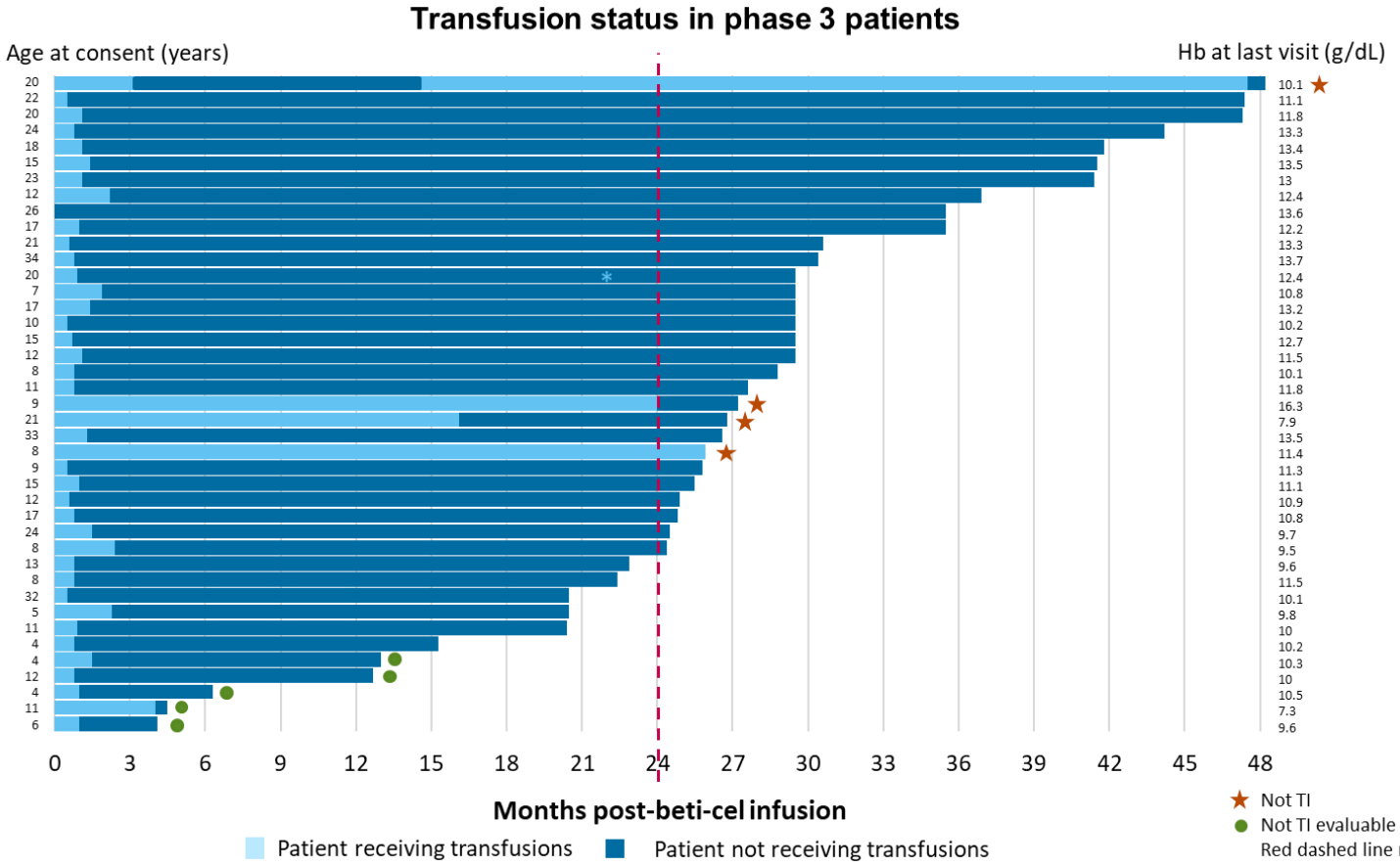
**Median follow-up in parent study.

Data as of March 9, 2021

Updated results from HGB-207 (Northstar-2) and HGB-212 (Northstar-3)

(Data presented at the European Hematology Association Annual Congress, June 2021)

89% (32/36) of evaluable patients across both Phase 3 studies achieved the primary endpoint of transfusion independence



Weighted average Hb during TI: 11.6 (9.3 – 13.7) g/dL

Last pRBC transfusion post-infusion: 0.85 (0.0 – 2.4) months

Duration of ongoing TI: 25 (12.5 – 38.5) months

All patients who achieved TI maintain TI

*Patient's total Hb level at Month 22 was 13.4 g/dL. Following a planned orthopedic surgery, the patient had blood loss, which required 1 pRBC transfusion.
All values are median (min–max). Hb, hemoglobin; RBC, red blood cell; TDT, transfusion-dependent β-thalassemia; TI, transfusion independence (defined as weighted average Hb ≥ 9 g/dL without pRBC transfusions for ≥ 12 months)

Reference: Locatelli F, et al. EHA 2021. Abstract S266

Data as of March 9, 2021

Phase 3 clinical trials safety overview: betibeglogene autotemcel

(Data presented at the European Hematology Association Annual Congress, June 2021)

Non hematologic Grade ≥ 3 AEs* *Post beti cel infusion up to 2 yr follow up in ≥ 3 patients in either study*	Phase 3 N 41 n (%)
Oropharyngeal inflammation	29 (71)
Febrile neutropenia	20 (49)
Epistaxis	8 (20)
Decreased appetite	6 (15)
Pyrexia	5 (12)
Alanine aminotransferase increase	5 (12)
Veno-occlusive liver disease	3 (7)
Serious AEs *Post beti cel infusion Venom up to 2 yr follow up in ≥ 2 patients in either study*	
Pyrexia	4 (10)
Thrombocytopenia	3 (7)
Veno-occlusive liver disease	3 (7)

- Adverse events considered related or possibly related to the drug product were:
  - Thrombocytopenia (n=3), abdominal pain (n=3), leukopenia (n=1), neutropenia (n=1), pain in extremity (n=1), tachycardia (n=1), and autoimmune disorder¥ (n=1). Leukopenia, neutropenia, and one event of thrombocytopenia all occurred in the same patient.
  - All events were grade 1/2 except for grade 3 events of autoimmune disorder and 2 events of thrombocytopenia
- VOD occurred in 10% (4/41) of patients
  - VOD severity: Non-serious (grade 2): n=1; Serious (grade 4): n=3
  - All VODs were attributed to busulfan conditioning
  - All VOD resolved with defibrotide treatment
- One patient developed serious, grade 3 CHF unrelated to drug product, which was downgraded to grade 1 at 5 months and resolved at 12 months
- No graft failure, GVHD, or deaths occurred
- No replication-competent lentivirus, clonal predominance, or malignancy detected in any patient (all patients monitored in at least 6-month intervals)

*Hematologic AEs commonly observed post-transplantation have been excluded. ¥Immune thrombocytopenia with autoantibodies to glycoprotein 2b/3a.
AE, adverse event; CHF, congestive heart failure; VOD, veno-occlusive liver disease; GVHD, graft-versus-host disease

Reference: Locatelli F, et al. EHA 2021. Abstract S266

Data as of March 9, 2021

beti-cel treatment regimen, information record, and current coding

- **Treatment Regimen:** The treatment regimen for patients with beti-cel comprises mobilization/apheresis to collect the patient's own stem cells, myeloablative conditioning, and intravenous infusion of beti-cel into a vein.
  - The myeloablative conditioning and beti-cel infusion are expected to occur in the inpatient setting.
  - In some cases, the mobilization and apheresis procedures may take place in the inpatient setting.
- **Information Record:** Information regarding the comprehensive process by which beti-cel is administered will be documented in the medical record and traceable (e.g., use of a deidentified patient number on physician orders, pharmacy notes, treatment summary)
- **Current ICD-10-PCS codes do not adequately describe the intravenous administration of beti-cel**
  - Without the creation of a specific beti-cel code, providers and coding professionals will resort to reporting other non-specific ICD-10-PCS codes, which can obscure the use of this therapy within Medicare claims, making it more difficult to efficiently track cases for safety and health economic purposes.
  - Long-term follow up is critical, particularly in the case of single administration, potentially curative gene therapies like beti-cel given that the safety profile and clinical durability of such therapies are central issues for providers, patients, and manufacturers.

thank you

bluebirdbio®