HOPE-B Pivotal Trial: 4-Year Update

Health Outcomes with the Padua Gene: Evaluation in Hemophilia B

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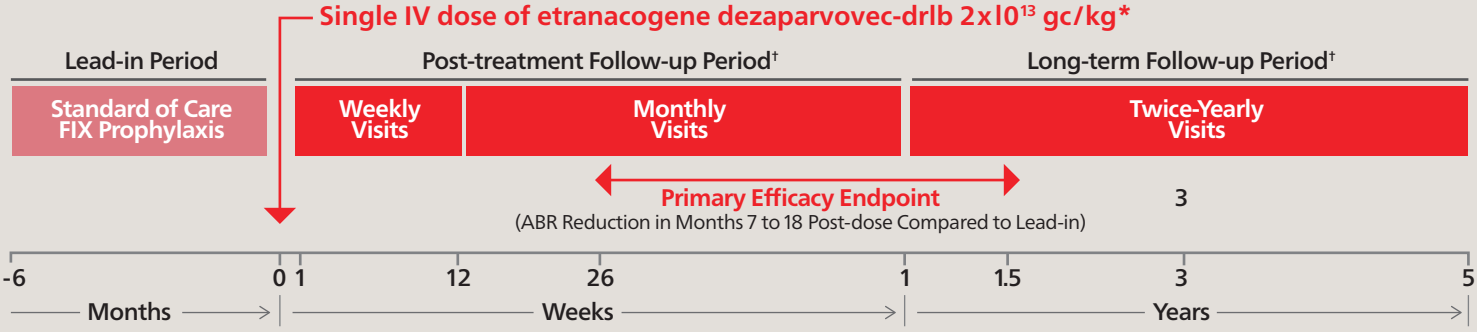
4 years following a single IV dose of etranacogene dezaparvovec-drlb, participants experienced[1]:

- **Stable and durable increase in FIX activity**
- **Significant reductions in ABR compared to lead-in FIX prophylaxis period**
- **No new treatment-related safety events; safety profile remained favorable**

HOPE-B Clinical Trial Information[1,2]

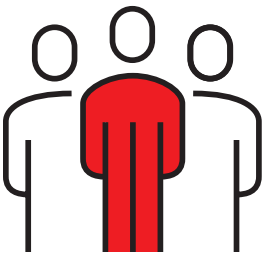
HOPE-B Clinical Trial Design:

A phase 3, open-label, single-dose, multicenter study of etranacogene dezaparvovec-drlb, a liver-directed recombinant AAV5 vector expressing the Padua factor IX variant



*No prophylactic immunosuppression required. †At least quarterly contact (± 2 weeks) between site staff and participants to monitor occurrence of AEs. ‡For this update, 53/54 patients reached 4 years of follow-up for safety.

Enrollment Criteria



Adult male ≥ 18 years

- Severe or moderately severe hemophilia B (FIX activity ≤ 2%)
- Receiving routine prophylaxis (≥ 2 months)
- With or without neutralizing antibodies to AAV5
- No FIX inhibitors, active HBV/HCV, uncontrolled HIV infection, advanced liver disease

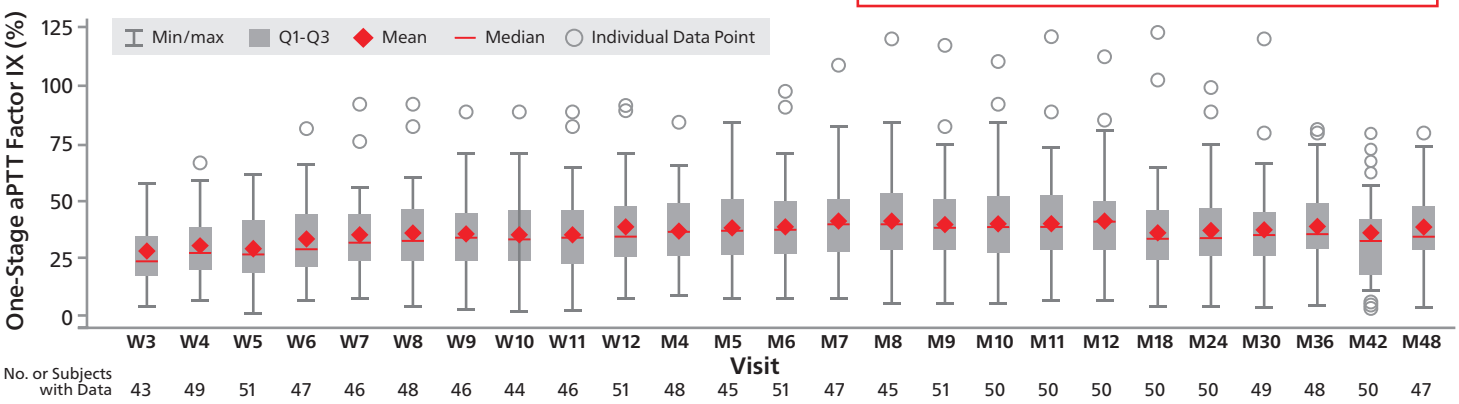
Baseline Characteristics

Characteristic	Full Analysis Set (N = 54)
Average age, y (range)	41.5 (19-75)
NAb status at baseline, n (%)	
Negative	33 (61)
Positive	21 (39)
HIV+, n (%)	3 (6)
Previous HBV, n (%)	9 (17)
Previous HCV, n (%)	31 (57)

Clinical Study Results After 4 Years[1]

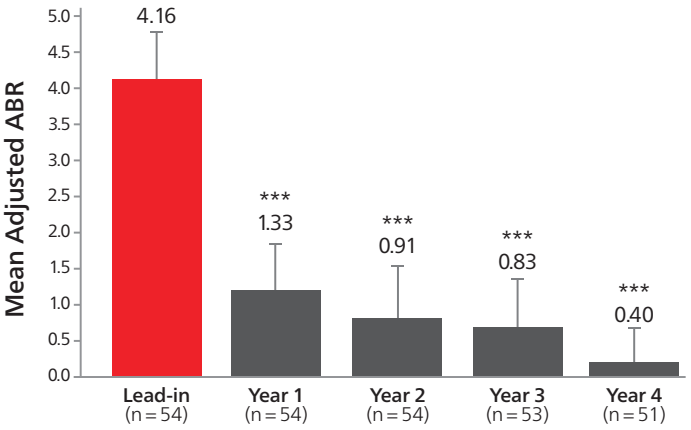
FIX activity was sustained over 4 years post-treatment[3]

- 46/47 (98%) evaluable participants with FIX activity levels ≥5%
- 16/47 (34%) evaluable participants with FIX activity levels ≥40%



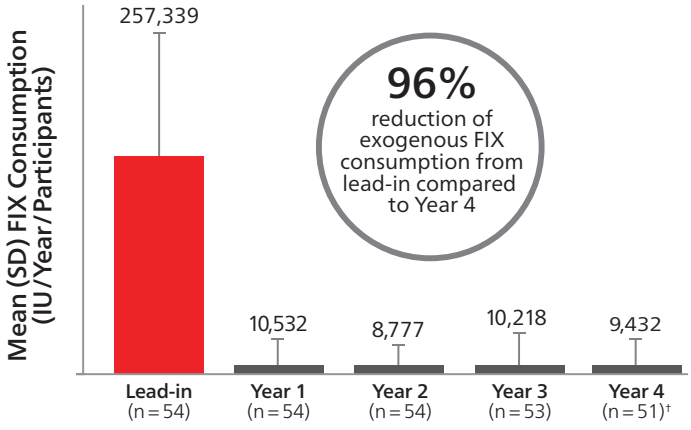
Clinical Study Results After 4 Years[1] *(continued)*

Annualized Bleeding Rates During ≥ 6-month Lead-in Through to Year 4 Post-Treatment



ABR=annualized bleeding rate.
Full analysis set, N=54.
***p<0.0001.

94% (51/54) of participants discontinued FIX prophylaxis and remained prophylaxis-free*



*Two patients experienced lack of efficacy. One patient had the highest NAb titer of 1:3212, and 1 patient received ~10% of the planned dose. One patient returned to factor IX prophylaxis at month 30.
†One patient died (prophylaxis free and was also not included in Year 3). One patient who remained on prophylaxis withdrew consent for efficacy assessment. One patient had a liver transplant (prophylaxis free).

Etranacogene dezaparvovec-drlb remains safe and well-tolerated

TRAEs by MedDRA PT*	Participants, n (%)	Events, n
At least 1 TRAE	**39 (72.2)**	**96**
ALT increased	10 (18.5)	11
Headache	8 (14.8)	9
Influenza-like illness	7 (13.0)	8
AST increased	6 (11.1)	7
CPK increased	4 (7.4)	6
Dizziness	4 (7.4)	4
Fatigue	4 (7.4)	4
Nausea	4 (7.4)	4
Arthralgia	3 (5.6)	3

- 92 of 96 (95.8%) TRAEs occurred in the first 6 months
- IRR† occurred in 7 (13.0%) participants
- 1 death and 1 instance of hepatocellular carcinoma, reported, unrelated to treatment
- 1 instance of schwannoma and 1 instance of myelodysplastic syndrome, reported, unrelated to treatment
- No FIX inhibitors, no thrombotic events

*MedDRA Version 26.0 was used for coding. †IRR: Infusion-related reaction were defined as any adverse events related to the investigation medical product administration procedure or unexpected reactions. They were any treatment-emergent adverse event occuring within 24 hours of infusion, qualifying for special notification, assessed as related or possibly related by the investigator and considered as an infusion-related reaction during the safety assessment. They were infusion-site reaction, hypersensitivity (ie, urticaria), facial flushing, itching, also headache, dizziness, etc.

Abbreviations: AAV, adeno-associated virus; AAV5, adeno-associated virus serotype 5; ABR, annualized bleed rate; AE, adverse event; ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CPK, creatine phosphokinase; FIX, factor IX; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; IRR, infusion-related reaction; IU, international unit; IV, intravenous; MedDRA PT, Medical Dictionary for Regulatory Activities Preferred Term; NAb, neutralizing antibodies; Q, quartile; SAE, serious adverse event; SD, standard deviation; TRAE, treatment-related adverse event.

References: 1. Leebeek FW, et al. Oral Presentation at EAHAD Annual Meeting, February 7, 2025. **2.** Pipe SW, et al. *N Engl J Med.* 2023;388:706-718. **3.** Data on file. Available from CSL Behring as DOF HGX-010.

IMPORTANT SAFETY INFORMATION

Warning and Precautions

Infusion Reactions

Infusion reactions, including hypersensitivity reactions and anaphylaxis, may occur. Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.

Hepatotoxicity/Hepatocellular Carcinoma

Post-dose, monitor for elevated transaminase levels. Consider corticosteroid treatment should elevations occur. The integration of liver-targeting AAV vector DNA into the genome may carry the theoretical risk of hepatocellular carcinoma development. For patients with preexisting risk factors for hepatocellular carcinogenicity, perform regular (eg, annual) abdominal ultrasound and alpha-fetoprotein testing following administration.

Immune-mediated neutralization of the AAV5 vector capsid

Preexisting neutralizing anti-AAV antibodies may impede transgene expression at desired levels.

Monitoring Laboratory Tests

In addition to monitoring liver function, monitor for Factor IX activity and Factor IX inhibitors after administration.

Adverse Reactions

The most common adverse reactions (incidence ≥5%) were elevated ALT, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, nausea, malaise, and elevated AST.

Indication

HEMGENIX®, etranacogene dezaparvovec-drlb, is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:

- Currently use Factor IX prophylaxis therapy, or
- Have current or historical life-threatening hemorrhage, or
- Have repeated, serious spontaneous bleeding episodes.

HEMGENIX is for single use intravenous infusion only.

Contraindications: None.

Please see accompanying full prescribing information for HEMGENIX.

To report SUSPECTED ADVERSE REACTIONS, contact the CSL Behring Pharmacovigilance Department at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Scan here to learn more about gene therapy in hemophilia B

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