3-YEAR DATA UPDATE PRESENTED AT ASH

CSL Behring

HEMGENIX® (etranacogene dezaparvovec-drlb) demonstrates long-term durability, safety, and significant bleed protection vs factor IX prophylaxis

Highlights from a 3-year follow-up analysis of the first FDA-approved gene therapy for hemophilia B

Indication

HEMGENIX 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.

The data presented in this resource and publication are consistent with the statistical plan for the HOPE-B clinical trial. The data were evaluated independently from the Prescribing Information and utilized a different methodology for interpreting the data. Therefore, some differences are present between the data from the published clinical trial and the data contained within the Prescribing Information for HEMGENIX. Please refer to the Prescribing Information when assessing HEMGENIX for clinical practice.

Please see Important Safety Information on page 4 and accompanying full Prescribing Information for HEMGENIX.

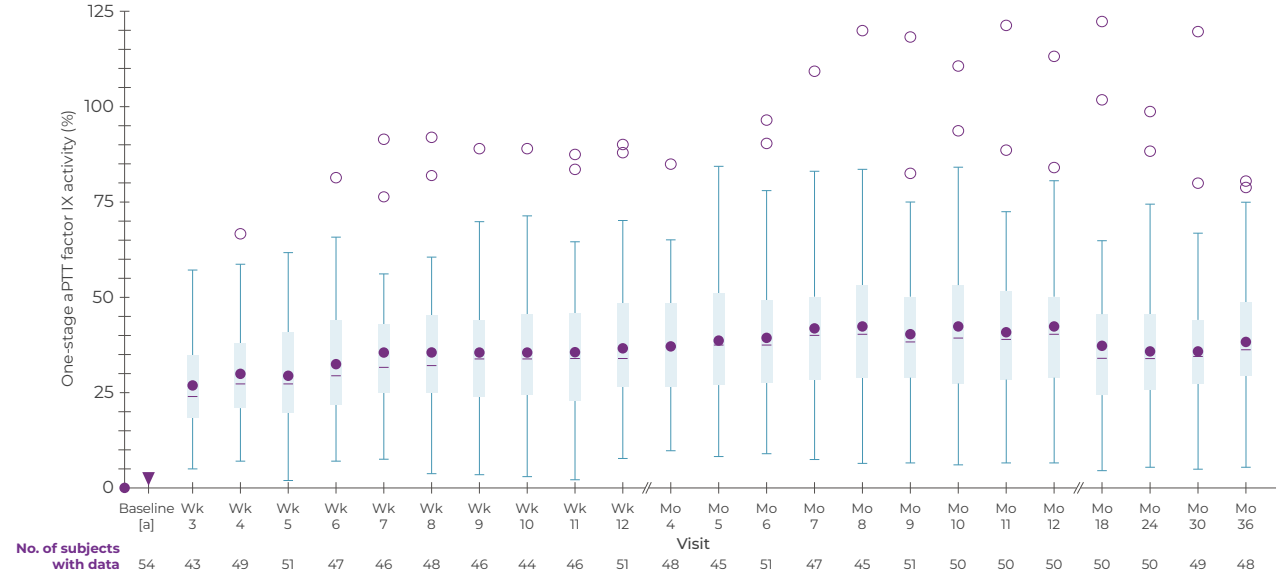
Healthcare Systems

HEMGENIX® etranacogene dezaparvovec-drlb

At 3 years, patient response with HEMGENIX showed sustained factor IX levels and ABR reduction[1]

Elevated and sustained factor IX levels for years after a single infusion[1]

Factor IX activity was sustained over 3 years after dosing[2]



Abbreviations: aPTT, activated partial thromboplastin time; Mo, month; Wk, week.

[a] Baseline factor IX was imputed based on subject's historical hemophilia B severity. If the subject had documented severe factor IX deficiency (factor IX plasma level <1%), their baseline factor IX activity level was imputed as 1%. If the subject had documented moderately severe factor IX deficiency (factor IX plasma level ≥1% and ≤2%), their baseline factor IX activity level was imputed as 2%.[2]

Only uncontaminated samples were included in analysis, ie, blood sampling did not occur within 5 half-lives of exogenous factor IX use. The lower and upper edges of the box correspond to the interquartile range (IQR), the 25th and 75th percentile. The line at the middle of the box corresponds to the median. The whiskers show the lowest and highest observation within 1.5 times the IQR of the bottom and top of the box, respectively. The solid circles represent the arithmetic mean. Any points outside of the whiskers are plotted individually.[2]

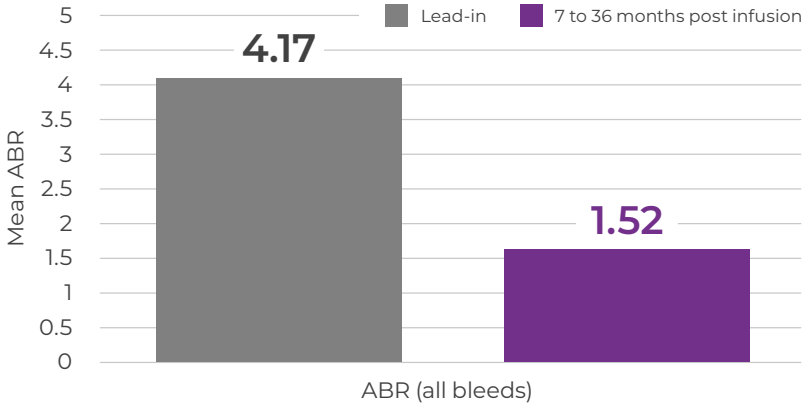
Endogenous factor IX activity levels	At year 2 (n=50)[3]	At year 3 (n=48)[1]
Mean ± SD	36.7% ± 19.0%	38.6% ± 17.8%
Median	33.9%	36.0%
IQR	25.8%-45.5%[4]	29.5%-48.1%
Min-max	4.7%-99.2%	4.8%-80.3%

Abbreviations: AAV5, adeno-associated virus serotype 5; SD, standard deviation.

Pharmacodynamic profile was not significantly different in participants with AAV5 neutralizing antibodies undetected or at a titer ≤1:678.[3]

Significant bleed protection vs factor IX prophylaxis[1]

HEMGENIX ABR vs routine factor IX prophylaxis (N=54)



Mean annualized bleed rate (ABR) for all bleeds during months 7 to 36 post-treatment was significantly reduced by sustaining the same bleed rate reduction that satisfied the primary endpoint during months 7 to 18.[1]

Median bleeds per participant remained at 0 bleeds through year 3 compared with 2 bleeds during the lead-in period.[1]

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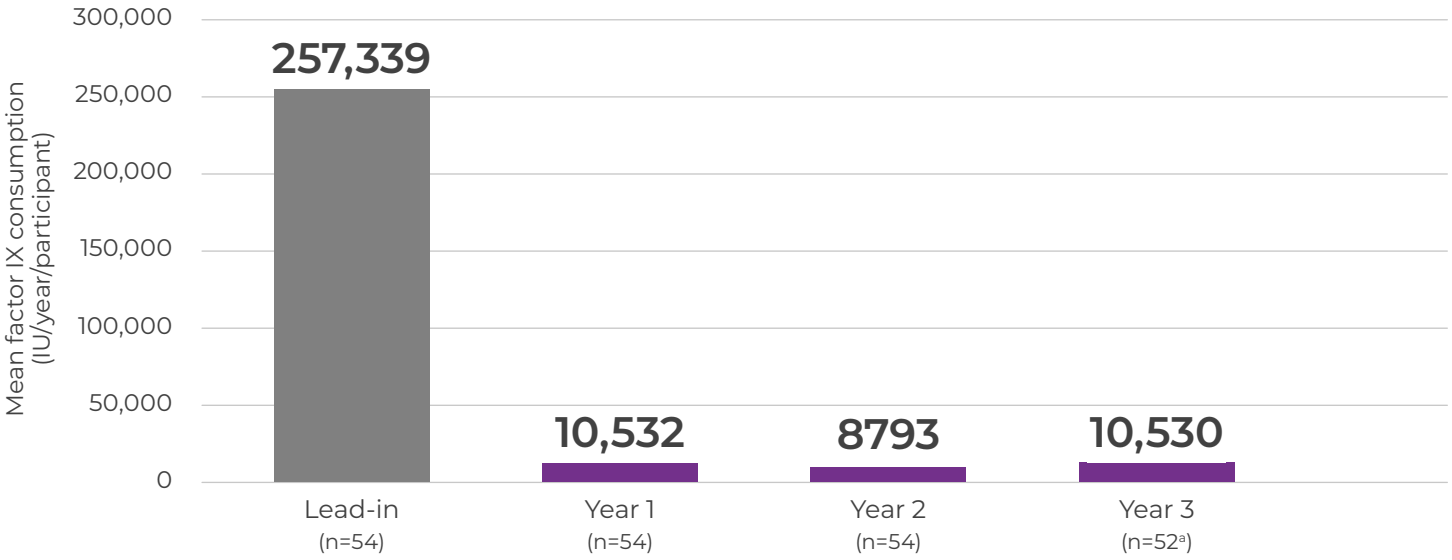
HEMGENIX® etranacogene dezaparvovec-drlb

Annualized mean factor IX consumption decreased 96% from lead-in to 3 years post-treatment[1]



Three patients required continuous prophylaxis after treatment

- One patient only received a partial dose (~10% of the dosage) due to an infusion reaction
- Another patient had a high preexisting neutralizing antibody titer of 3212
- One patient's factor IX levels eventually declined to the 2% to 5% range; the patient's bleeding phenotype returned, and they resumed prophylaxis per protocol at month 30 post treatment
- One additional patient required intermittent prophylaxis for approximately 20 weeks during months 7 to 18

[a]One patient died unrelated to treatment at month 15 (prophylaxis-free). One patient who remained on prophylaxis withdrew consent for efficacy assessment.

Long-term safety profile[1]

There were no serious adverse events (AEs) related to treatment with HEMGENIX

- During the 3 years post-treatment, all participants experienced at least 1 treatment-emergent AE (TEAE): 76% were mild, 19% were moderate, and 4% were severe
- 70% of participants experienced 96 treatment-related TEAEs, of which 95% occurred before 6 months post-treatment
- The most common AE was an increase in alanine transaminase (ALT), for which 9 (16.7%) participants received supportive care with reactive corticosteroids for a mean duration of 81.4 days (SD, 28.6; range, 51 to 130 days)

Please see Important Safety Information on page 4 and accompanying full Prescribing Information for HEMGENIX.

Ensure your eligible members have access to HEMGENIX

Learn more at marketaccess.cslbehring.com

HEMGENIX®
etranacogene dezaparvovec-drlb

Healthcare Systems

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.

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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.

References: 1. Pipe SW, van der Valk P, Verhamme P, et al. Long-term bleeding protection, sustained FIX activity, reduction of FIX consumption and safety of hemophilia B gene therapy: results from the HOPE-B trial 3 years after administration of a single dose of etranacogene dezaparvovec in adult patients with severe or moderately severe hemophilia B. Presented at: 65th American Society of Hematology Annual Meeting; December 9-12, 2023; San Diego, CA. **2.** Data on file. Available from CSL Behring as DOF HGX-005. **3.** Pipe SW, van der Valk P, Verhamme P, et al. Long-term bleeding protection, sustained FIX activity, reduction of FIX consumption and safety of hemophilia B gene therapy: results from the HOPE-B trial 3 years after administration of a single dose of etranacogene dezaparvovec in adult patients with severe or moderately severe hemophilia B. Abstract presented at: 65th American Society of Hematology Annual Meeting; December 9-12, 2023; San Diego, CA. Abstract 1055. **4.** Pipe SW, Castaman G, Miesbach W, et al. Interindividual variability of response to gene therapy in haemophilia B: ranges of factor IX activity levels sustained after 24 months in HOPE-B etranacogene dezaparvovec trial. Abstract presented at: 12th BIC International Conference; September 8-10, 2023; Palermo, Italy.

HEMGENIX is manufactured by uniQure Inc. and distributed by CSL Behring LLC.

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