

Improvements in health-related quality of life in adults with severe or moderately severe hemophilia B after receiving etranacogene dezaparovec gene therapy

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Introduction

- Etranacogene dezaparovec: Investigational gene therapy for people with hemophilia B
- Recombinant adeno-associated virus 5 vector incorporating an expression cassette containing a codon-optimized Padua variant of factor IX (FIX) with a liver-specific promoter^{1,2}
- Aims to provide long-term circulating FIX activity after a single injection, adequate to ameliorate the severe bleeding phenotype of HB and eliminate the requirement for continuous prophylaxis
- Breakthrough bleeding and the need for frequent infusions of FIX replacement products may negatively impact health-related quality of life (HRQoL)
- In the Phase 3 HOPE B trial, etranacogene dezaparovec demonstrated sustained FIX activity and bleeding protection superior to standard of care FIX prophylaxis used during the lead-in period³

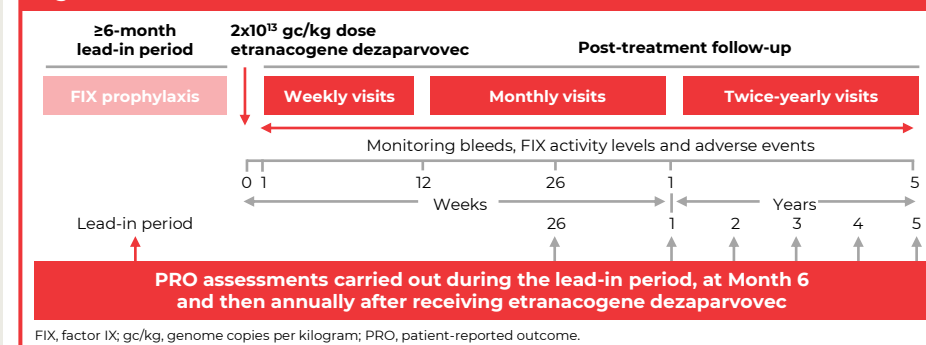
Aims

- Patient-reported outcome (PRO) assessment tools included in the HOPE-B trial evaluate the impact of gene therapy from the participant's perspective
- This poster describes the impact of etranacogene dezaparovec gene therapy on HRQoL in the first 2 years after treatment

Methods

- Secondary PRO endpoints in the HOPE-B trial included:
 - International Physical Activity Questionnaire (iPAQ)** total scores in the first 12 months post-treatment
 - EQ-5D-5L Visual Analog Scale (VAS)** scores in the first 12 months post-treatment
- Exploratory PRO endpoints in the HOPE-B trial included:
 - iPAQ** total scores beyond the first 12 months post-treatment
 - EQ-5D-5L VAS** scores beyond the first 12 months post-treatment
 - EQ-5D-5L Index** scores
 - Hemophilia Specific Quality of Life Questionnaire (Hem-A-QoL)** total and domain scores
 - Hemophilia Activities List (HAL)** total scores
 - Work Productivity and Activity Impairment (WPAI)** domain scores
 - Brief Pain Inventory (BPI)** domain scores
- Hem-A-QoL and HAL are specific for hemophilia; other PRO measures are disease non-specific
- PROs are assessed at various timepoints throughout the HOPE-B clinical trial (**Figure 1**)

Figure 1. PRO assessments in the HOPE-B Phase 3 trial³



Acknowledgments

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- Repeated measures linear mixed models were used to estimate the difference in PROs before and after receiving etranacogene dezaparovec for the first and second years after administration
- P-values for secondary endpoints were controlled for multiplicity but the nominal p values for the exploratory endpoints were not controlled
- A one-sided p-value of ≤ 0.025 for the post-treatment versus lead-in period was considered statistically significant for the prespecified secondary endpoints and nominally statistically significant for all other endpoints

Results

- EQ-5D-5L VAS:** Nominally statistically significant improvement during Year 2 post-treatment versus lead-in (least squares [LS] mean increase: 2.8; $p=0.0244$) (**Figure 2**)
 - No significant improvement during the first 12 months post-treatment versus lead-in
- EQ-5D-5L Index score:** Nominally statistically significant improvement during Year 2 post-treatment versus lead-in (LS mean increase: 0.0439; $p=0.0132$)
 - Primarily due to improvements in pain, mobility and usual activities domains (**Table 1**)
- Hem-A-QoL total:** Nominally statistically significant improvement post-treatment versus lead-in (**Table 2 and 3**)
 - Significant improvements observed during the first 12 months post-treatment were maintained at 24 months
- iPAQ:** No statistically significant difference between lead-in and the post-treatment period
- BPI, WPAI or HAL:** No statistically significant difference between the first 24 months post-treatment and lead-in period

Figure 2. Mean EQ-5D-5L VAS scores by visit

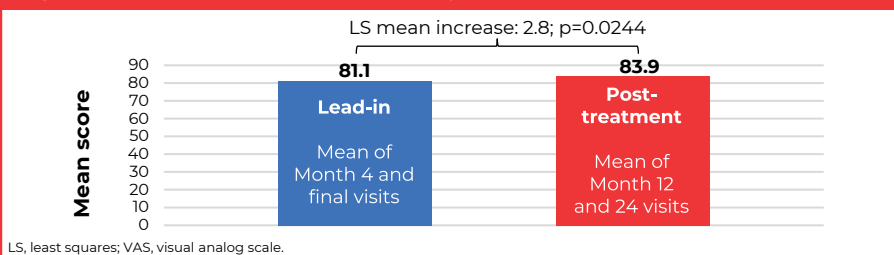


Table 1. EQ-5D-5L categorical response for pain, mobility and usual activities

Domain and visit	No/slight, n (%)	Moderate, n (%)	Severe/extreme, n (%)
Pain			
Lead-in (n=44)	32 (72.7)	7 (15.9)	5 (11.4)
Post-treatment Month 12 (n=49)	37 (75.5)	10 (20.4)	2 (4.1)
Post-treatment Month 24 (n=49)	39 (79.6)	10 (20.4)	0
Mobility			
Lead-in (n=44)	34 (77.3)	6 (13.6)	2 (4.5)
Post-treatment Month 12 (n=49)	41 (83.7)	7 (14.3)	1 (2.0)
Post-treatment Month 24 (n=49)	40 (81.6)	9 (18.4)	0
Usual activities			
Lead-in (n=44)	37 (84.1)	4 (9.1)	3 (6.8)
Post-treatment Month 12 (n=49)	43 (87.8)	5 (10.2)	1 (2.0)
Post-treatment Month 24 (n=49)	43 (87.8)	6 (12.2)	0

Table 2. Hem-A-QoL: Improvements observed after 12 months⁴

Domain	Mean: Lead-in*	Mean: 12-month post-treatment*	Mean (SE) difference*	p-value†	Improvement, %
Total	25.56	20.06	-5.50 (0.972)	<0.0001	21.5
Feelings	20.61	11.19	-9.42 (1.938)	<0.0001	45.7
Treatment	25.24	10.36	-14.88 (1.789)	<0.0001	59.0
Work/school	17.34	12.35	-4.99 (1.825)	0.0036	28.8
Future	30.94	25.92	-5.02 (1.736)	0.0023	16.3

Hem-A-QoL domains that did not reach nominal significance after 12 months included physical health, view of self, sports, dealing with hemophilia, family planning and relationships/sexuality

* Scores range from 0 to 100; higher scores indicate lower quality of life. The mean difference was derived from the repeated measures linear mixed models.
† These are exploratory endpoints not adjusted for multiplicity and the p-values should be considered nominally significant.
Hem-A-QoL, Hemophilia Quality of Life Questionnaire for Adults; SE, standard error.

Table 3. Hem-A-QoL: Improvements maintained at 24 months⁴

Domain	Mean: Lead-in*†	Mean: 24-month post-treatment*	Mean (SE) difference*	p-value‡	Improvement, %
Total	26.20	20.0	-6.2 (1.19)	<0.0001	23.7
Feelings	20.32	11.22	-9.10 (1.96)	<0.0001	44.8
Treatment	25.78	11.54	-14.24 (2.10)	<0.0001	55.2
Work/school	17.31	12.07	-5.24 (2.19)	0.0102	30.3
Future	31.2	24.63	-6.57 (1.83)	0.0004	21.1

Hem-A-QoL domains that did not reach nominal significance after 24 months included physical health, view of self, sports, dealing with hemophilia, family planning and relationships/sexuality

* Scores range from 0 to 100; higher scores indicate lower quality of life. The mean difference was derived from the repeated measures linear mixed models.
† Mean lead-in values for Year 2 were different from Year 1 because the repeated measures analysis was applied in a somewhat different manner.
‡ These are exploratory endpoints not adjusted for multiplicity and the p-values should be considered nominally significant.
Hem-A-QoL, Hemophilia Quality of Life Questionnaire for Adults; SE, standard error.

Conclusions

- Improvements in HRQoL measures observed in the HOPE-B clinical trial suggest that etranacogene dezaparovec can reduce the burden associated with hemophilia and FIX prophylaxis
- This may contribute to how people with hemophilia B view their work or school performance as well as providing a sense of optimism for the future

References

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