

Improved quality of life in people with hemophilia A following gene therapy with dirloctocogene samoparvovec (SPK-8011)

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Summary and Conclusions

Quality of life was investigated in participants of the phase I/II trial of dirloctocogene samoparvovec gene therapy using assessments including the Haem-A-QoL, a hemophilia-specific instrument with 10 domains



n=16

Clinically meaningful improvements were reported for Haem-A-QoL Total Score at Years 1, 2, and 3 after dirloctocogene samoparvovec infusion compared with baseline



'Physical Health' and 'Sports and Leisure' Haem-A-QoL domains displayed clinically meaningful improvements at Years 1, 2, and 3 after infusion compared with baseline



These results suggest quality of life benefit accompanies previously reported reductions in bleeds and factor VIII infusions in participants who received dirloctocogene samoparvovec



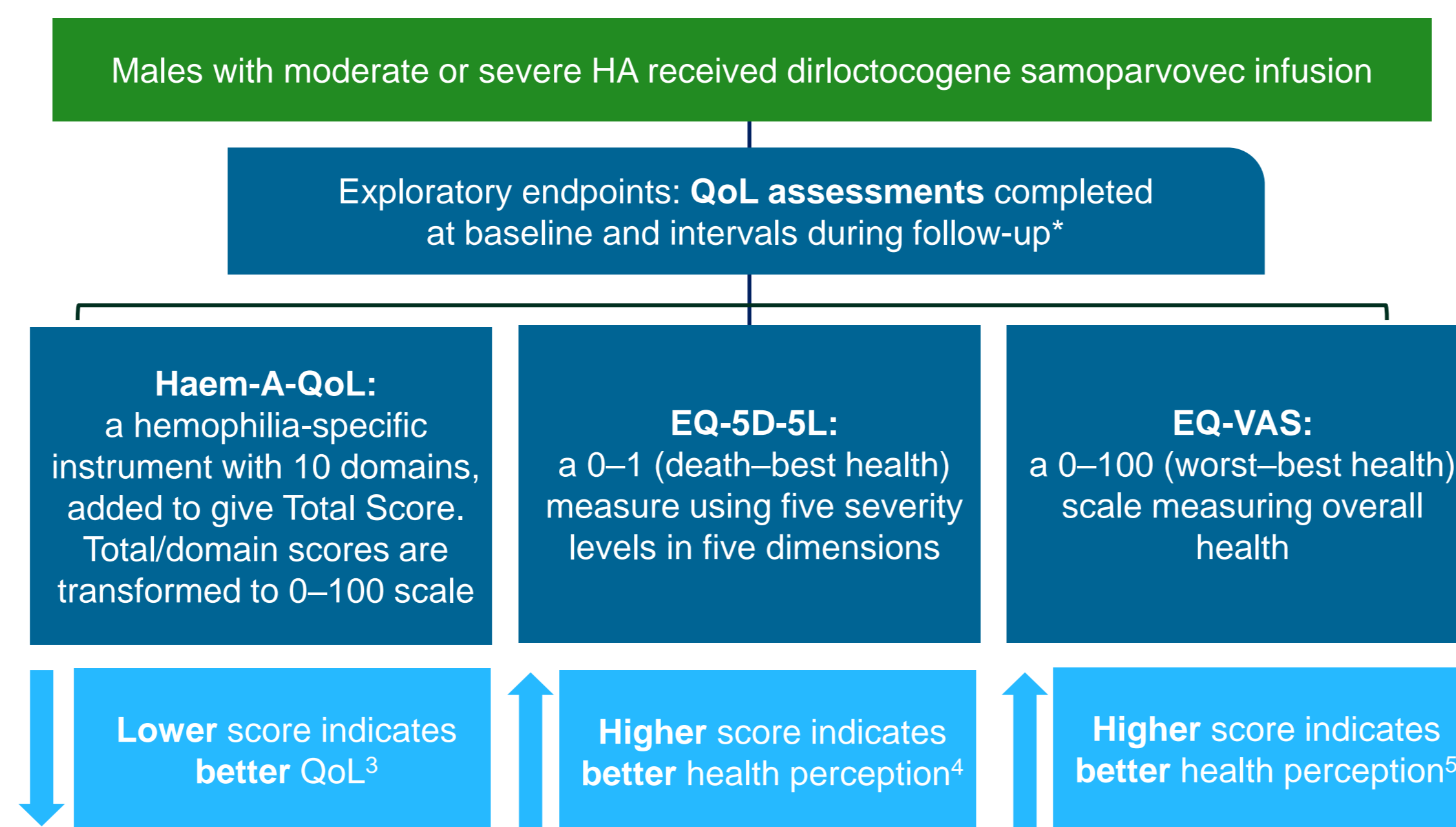
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Background

- Hemophilia A (HA) is a bleeding disorder accompanied by pain, functional impairment, and treatment burden, which substantially impacts quality of life (QoL).¹
- Dirloctocogene samoparvovec (SPK-8011) is an investigational gene therapy for HA that uses a modified adeno-associated viral vector.
- Phase I/II dirloctocogene samoparvovec trial results showed a 92% (95% confidence interval [CI]: 89–94%) reduction in annualized bleed rate and a 96% (95% CI: 96–97%) reduction in annualized factor VIII infusion rate.²
- This analysis aims to report the impact on QoL for people with HA enrolled in this phase I/II trial of dirloctocogene samoparvovec.

Methods

Figure 1. Open-label, multicenter, non-randomized, phase I/II dose-escalation trial of dirloctocogene samoparvovec (NCT03003533/NCT03432520)²

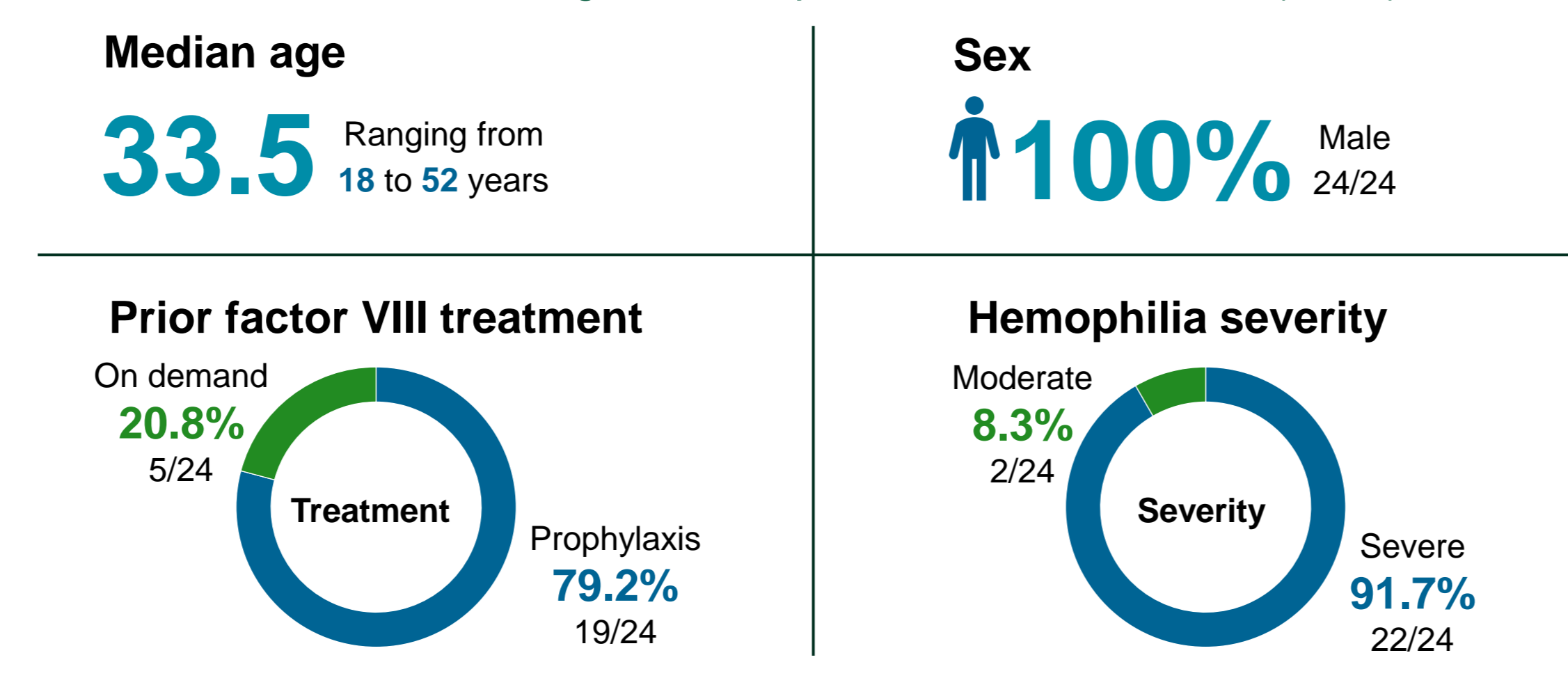


*Baseline assessment completed at screening or Day 0 pre-dose visit. Closest assessments after each time point are used for this analysis. EQ-5D-5L, EuroQoL Group 5-dimension 5-level descriptive system; EQ-VAS, EuroQoL Group visual analog scale; Haem-A-QoL, Haemophilia Quality of Life Questionnaire for Adults.

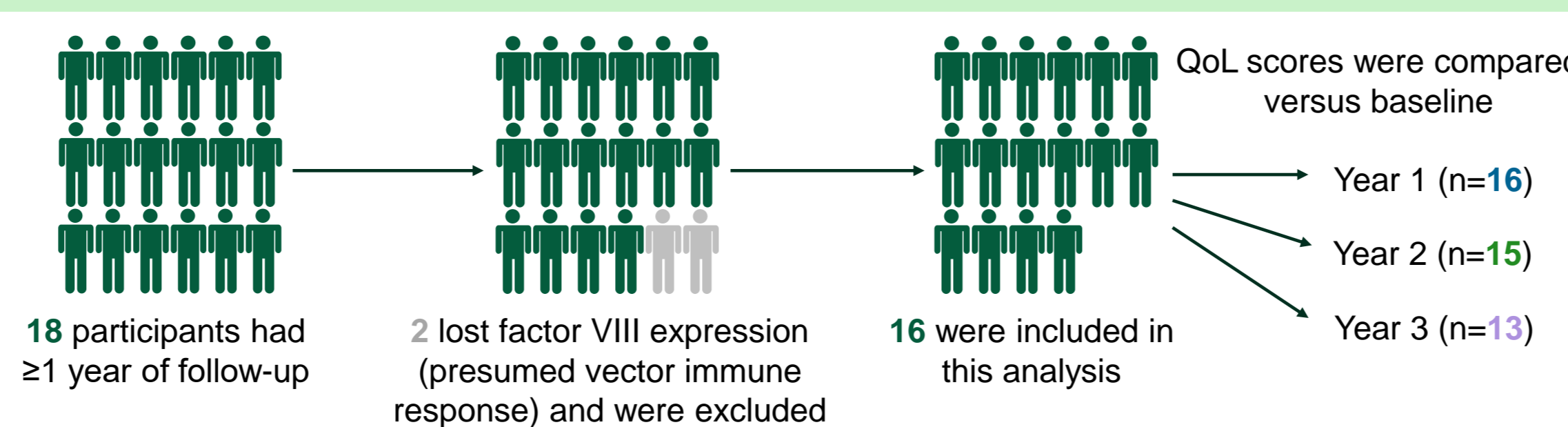
Results (data cut-off: October 4, 2022)

Baseline demographics and characteristics

Figure 2. Baseline demographics and characteristics of participants who had received dirloctocogene samoparvovec at data cut-off (n=24)

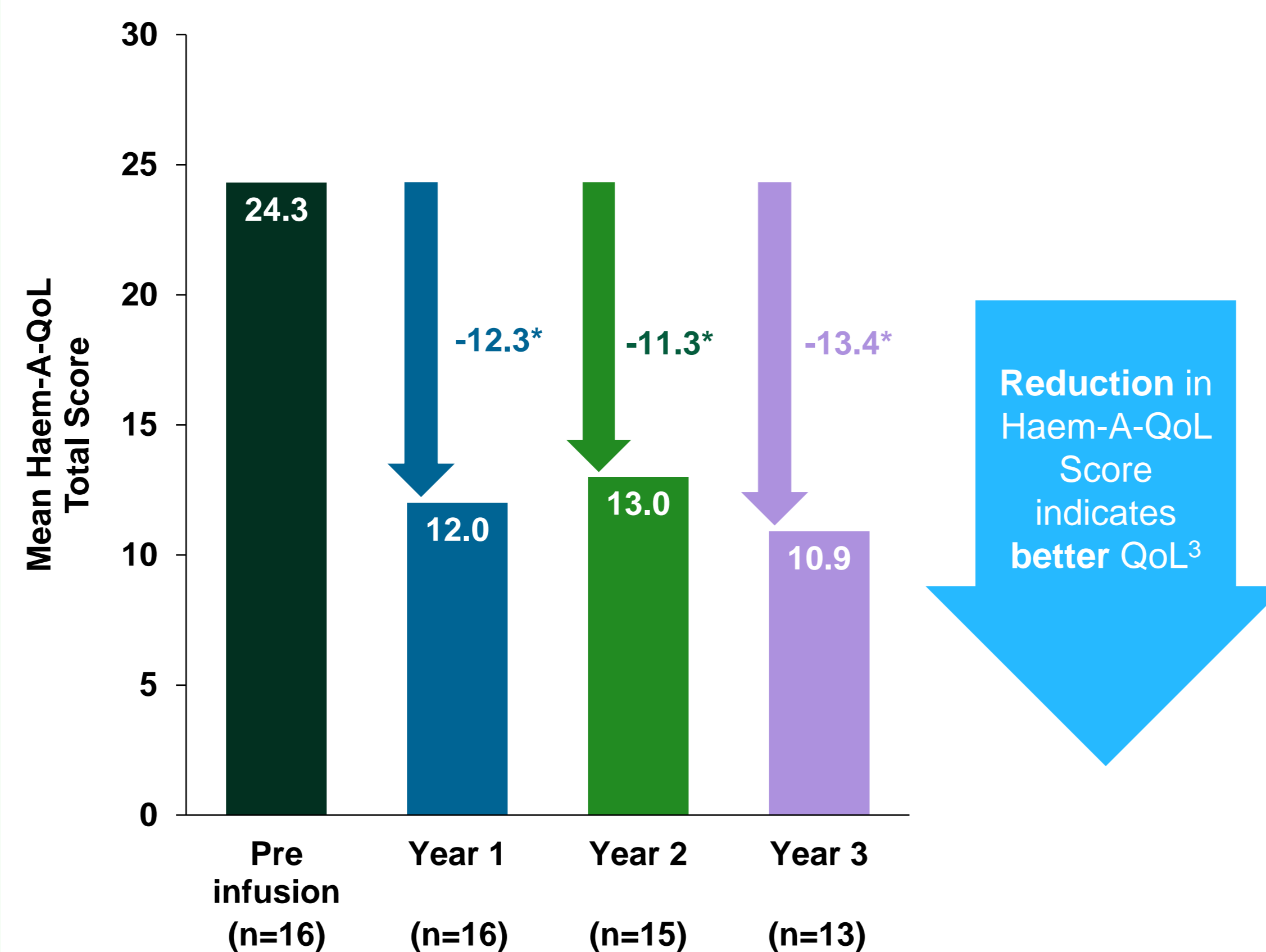


Participants with ≥1 year of follow-up were included in this analysis



Clinically meaningful improvements in Haem-A-QoL Total Score were observed at Years 1, 2, and 3 after infusion compared with baseline

Figure 3. Mean Haem-A-QoL Total Score



*Indicates a clinically meaningful difference, which is a change of ≥7 in Total Score.³

Improvements in Haem-A-QoL scores were observed across almost all domains at Year 3 after infusion compared with baseline, suggesting reduced perception of physical limitations and treatment burden, as well as improvements in mental health and wellbeing

Table 1. Mean change in Haem-A-QoL domain scores from pre dirloctocogene samoparvovec infusion to Year 3 after infusion

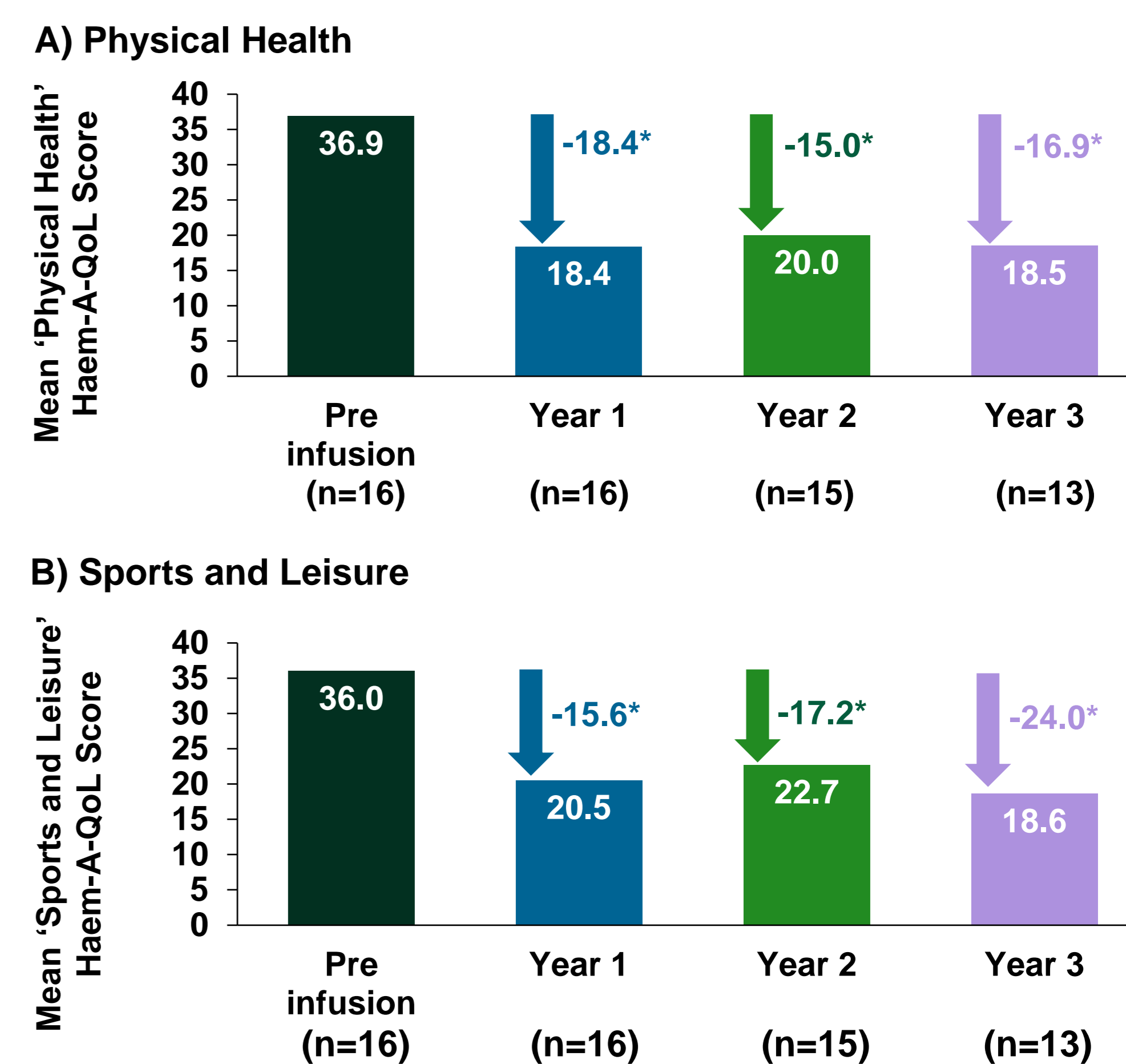
Domain	Pre infusion score (n)	Year 3 score (n)	Change in score (n)	Improvement at Year 3?
Physical Health	36.9 (n=16)	18.5 (n=13)	-16.9* (n=13)	✓
Sports and Leisure	36.0 (n=16)	18.6 (n=12)	-24.0* (n=12)	✓
Feelings	16.0 (n=16)	2.4 (n=13)	-13.0 (n=13)	✓
View of Yourself	29.7 (n=15)	18.5 (n=12)	-12.9 (n=12)	✓
Work and School	13.3 (n=16)	6.9 (n=12)	-7.6 (n=12)	✓
Dealing with Hemophilia	15.6 (n=16)	21.8 (n=13)	5.8† (n=13)	X†
Treatment	26.8 (n=16)	5.3 (n=13)	-21.2 (n=13)	✓
Future	30.3 (n=16)	11.5 (n=13)	-18.1 (n=13)	✓
Family Planning	6.3 (n=13)	3.0 (n=9)	-3.2 (n=9)	✓
Partnership and Sexuality	10.4 (n=16)	1.3 (n=13)	-10.3 (n=13)	✓

Reduction in Haem-A-QoL Score indicates better QoL³

*Change of ≥10 is clinically meaningful in the 'Physical Health' and 'Sports and Leisure' domains.⁶ †Clinically meaningful change in the other domains has not been defined.³ ‡Haem-A-QoL scores for the 'Dealing with Hemophilia' domain improved at Years 1 and 2, with mean changes in score of -6.7 and -8.3, respectively, compared with baseline.

Clinically meaningful improvements (change of ≥10) were reported for 'Physical Health' and 'Sports and Leisure' compared with baseline

Figure 4. Mean Haem-A-QoL scores for A) 'Physical Health' and B) 'Sports and Leisure' domains



Reduction in Haem-A-QoL Score indicates better QoL³

*Indicates a clinically meaningful difference (change of ≥10 in 'Physical Health' and 'Sports and Leisure' domains).⁶

Starting from a high baseline score, mean EQ-5D-5L index score was slightly improved versus baseline at Year 3, suggesting better perception of health after infusion

Table 2. Mean change in EQ-5D-5L index score compared with baseline

Pre infusion score (n)	Year 3 score (n)	Change in score (n)	Improvement at Year 3?
0.85 (n=16)	0.91 (n=13)	0.06 (n=13)	✓

Increase in EQ-5D-5L score indicates better health perception⁴

An improved mean EQ-VAS score was observed at Year 3 after infusion compared with baseline, suggesting better perception of health after infusion

Table 3. Mean change in EQ-VAS score compared with baseline

Pre infusion score (n)	Year 3 score (n)	Change in score (n)	Improvement at Year 3?
84.0 (n=16)	89.0 (n=13)	5.8 (n=13)	✓

Increase in EQ-VAS score indicates better health perception⁵

Change in EQ-VAS at Year 2 did not show improvement compared with baseline mainly due to a single outlier. In one participant, an EQ-VAS score of 0 was recorded at Year 2. This same participant had a score of 70 at baseline and 90 at Year 1 and 3. The study site is closed so data clarification was not possible.

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Disclosures

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