

Health-related quality of life improvements following valoctocogene roxaparvovec gene therapy in people without bleeds or target joints at baseline: a post hoc analysis from GENER8-1

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Background

- The primary analysis of GENER8-1 (NCT03370913), a phase 3 trial evaluating the efficacy and safety of valoctocogene roxaparvovec, has identified a sustained benefit following a single dose of valoctocogene roxaparvovec.^{1,2}
- It is recognized that treatment goals in hemophilia can involve a series of treatment milestones leading to “health equity” or “hemophilia-free mind”.^{3,4}
- This analysis aimed to understand how People with Severe Hemophilia-A (PwSHA) who have achieved the treatment milestone of “minimal joint impairment” and “freedom from bleeds”³ can benefit from valoctocogene roxaparvovec based on 3-year data from the GENER8-1 trial.

Methods

- Analysis was conducted with the HIV-negative participants (modified intent-to-treat population [mITT]) in the GENER8-1 trial for two groups achieving clinical milestones at baseline:
 - PwSHA without any treated bleeds at baseline
 - PwSHA without target joints at baseline
- Health-related quality of life (HRQoL) data were collected using the Haemo-QoL-A, a validated hemophilia-specific questionnaire. The Haemo-QoL-A responses are scored on a scale of 0 to 100, where higher scores indicate higher HRQoL⁵. Anchor-based thresholds were used to establish clinically important differences in HRQoL (5.5 for the total score and 6 for the domains⁵).
- Mean change from baseline scores to Week 156 (Year 3) for total and domain scores were calculated, and statistical significance was assessed.

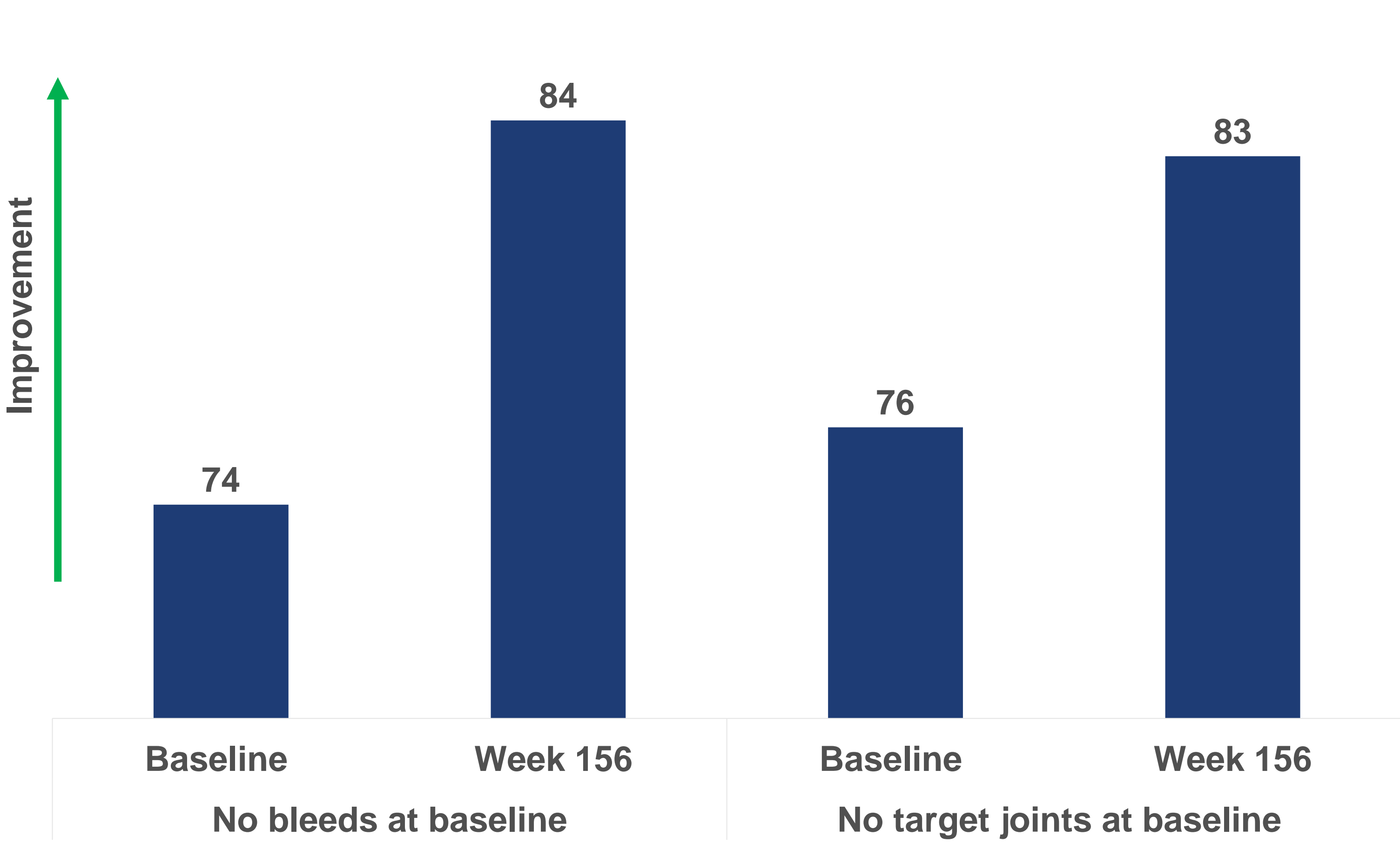
Table 1. Domains and example item for the Haemo-QoL-A

Domain	Example item
Physical functioning	Loss of joint mobility affects how I walk
Role functioning	I feel frustrated because I can't do what I want to do
Worry	I worry about finding or losing a job
Emotional impact	I feel I have the same opportunities to succeed in life as others
Consequences of bleeding	I am afraid to go to crowded places like concerts or bars for fear of being bumped or injured
Treatment concern	I worry about the availability of hemophilia products

Results

- A total of 132 PwSHA participated in the GENER8-1 trial (mITT population). A total of 43 (33%) trial participants had no treated bleeds at baseline, while 95 (72%) of trial participants had no target joints at baseline. As previously reported, for the overall mITT population the Haemo-QoL-A total score improved at Week 156 compared to baseline.⁶
- Absolute scores are presented at baseline and week 156 (Figure 1) for PwSHA who experienced no treated bleeds or had no target joints at baseline.
- Both groups experienced clinically meaningful improvement in Haemo-QoL-A at Week 156 compared to baseline. PwSHA with no treated bleeds at baseline experienced an improvement of 9.98 and PwSHA with no target joints at baseline experienced an improvement of 7.04 (Table 2)**
- For both groups, clinically meaningful change were observed in the following domains: “treatment concern”, “role functioning”, “consequences of bleeding” and “worry”.**

Figure 1. Observed Haemo-QoL-A total score at baseline and at Week 156 for two groups: people with no treated bleeds at baseline (n=38) and people with no target joints at baseline (n=81)



Notes: For patients who return to prophylaxis, data were censored after return to prophylaxis. Data reported for participants who had both baseline and Week 156 data. Haemo-QoL-A total score are on a scale from 0 to 100.

Table 2. Mean change from baseline to Week 156 in Haemo-QoL-A total and domain scores for two groups: people with no treated bleeds at baseline and people with no target joints at baseline

	Zero treated bleeds at baseline			No target joints at baseline		
Haemo-QoL-A scores	n	Mean	95%CI	n	Mean	95%CI
Total score	38	9.98	[5.67, 14.28] ***	81	7.04	[3.94, 10.14] ***
Physical functioning	38	4.85	[0.86, 8.85] *	81	3.93	[0.62, 7.24]*
Role functioning	38	10.67	[5.39, 15.95] ***	81	7.77	[3.89, 11.64] ***
Consequences of bleeding	38	14.59	[9.50, 19.67] ***	81	12.00	[7.57, 16.44] ***
Worry	38	11.05	[5.00, 17.10] **	81	6.96	[2.45, 11.48] **
Emotional impact	38	4.84	[-0.21, 9.90]	81	2.11	[-1.26, 5.47]
Treatment concern	38	13.86	[4.90, 22.82] **	81	9.55	[4.22, 14.87] **

Notes: *p<0.05, **p<0.01, ***p<0.001 are based on paired t-test; CI: confidence interval; Data from participants who returned to prophylaxis were censored after return. Conclusions hold when data are censored after return to prophylaxis as well as when all data are included.

Conclusions

- Even **PwSHA that have achieved the treatment milestone of “minimal joint impairment” and “freedom from bleeds” experienced a sustained clinically meaningful improvement in HRQoL three years post valoctocogene roxaparvovec, with improvement in domains suggesting increased freedom from treatment burden and decreased psychological burden** relating to the condition.
- The results suggest that **there is still a significant unmet need for PwSHA that already achieved significant clinical treatment milestones. Patient-relevant outcomes need to be assessed to demonstrate whether available treatments achieve “health equity” and lead to the ultimate treatment goal of “optimised health and well-being”³.**

References

1. Mahlangu J, et al. N Engl J Med 2023;388(8):694-705. 2. O’Mahony B, et al. J Thromb Haemost 2023;21(12):3450-3462. 3. Skinner MW, et al. Haemophilia 2020;26(1):17-24. 4. Krumb E, Hermans C. Res Pract Thromb Haemost 2021;5(5):e12567. 5. Quinn J, et al. Patient Relat Out Meas 2022;169-180. 6. Mahlangu J, et al. Res Pract Thromb Haemost 2023;7(S2):100459.

Disclosures

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