CR13

Health-related quality-of-life outcomes 4 years after treatment with valoctocogene roxaparvovec

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Introduction

Hemophilia A

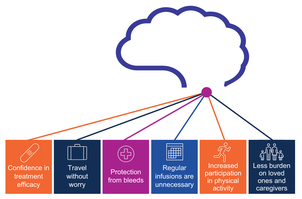
- People with hemophilia A lack the blood clotting protein factor VIII (FVIII) because **the gene is faulty**
- Low FVIII levels cause **excessive bleeding** or bleeding with no apparent cause
- Current treatments are regular injections with clotting FVIII concentrate or non-factor therapies (emicizumab)
- Hemophilia A can **negatively affect mental health, relationships, employment, and overall well-being**[1,2]

Hemophilia A negatively affects health-related quality of life (HRQOL)

Valoctocogene roxaparvovec and HRQOL

- Valoctocogene roxaparvovec is a **gene therapy for severe hemophilia A** that delivers functional genetic instructions for producing FVIII
- Valoctocogene roxaparvovec provides **protection from bleeding with a single infusion**, with the potential to reduce the burden and consequences of living with hemophilia A
- GENEr8-1 is a phase 3 trial to test how safe valoctocogene roxaparvovec treatment is and how well it protects against bleeding[3-5]

Potential to reduce disease burden of hemophilia A[6]



Methods

Study design

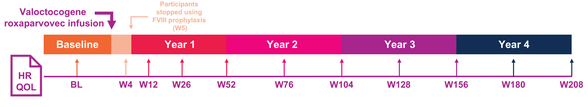
Eligibility

- Adult men with severe hemophilia A (FVIII ≤1 IU/dL)
- Previously receiving FVIII prophylaxis
- No history of FVIII inhibitors or antibodies against the capsid
- No significant liver dysfunction

Endpoints*

- Change from baseline
  - **HRQOL**

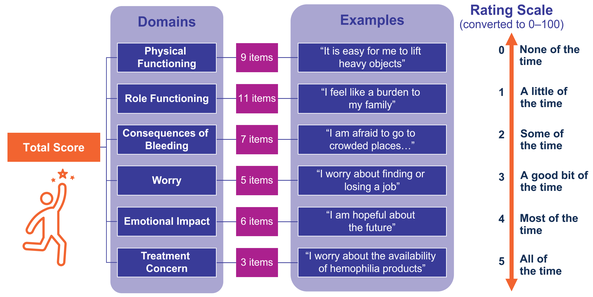
*FVIII activity levels, safety outcomes, and change from baseline in annualized bleeding rate and annualized FVIII infusion rate are reported in a separate poster.



BL, baseline; FVIII, factor VIII; HRQOL, health-related quality of life; W, week.

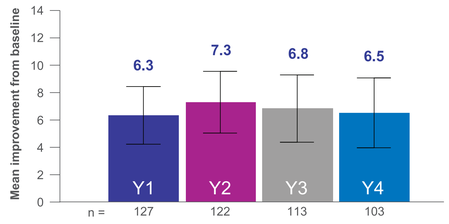
- 134 participants enrolled and received an infusion of valoctocogene roxaparvovec
- This analysis included the **132 participants** who were HIV-negative
- To ensure results are based only on the effects of valoctocogene roxaparvovec, **HRQOL data were analyzed by excluding data after participants restarted prophylaxis** with FVIII or emicizumab; results with those data included were similar
- HRQOL instruments included the Haemophilia-Specific Quality of Life Questionnaire for Adults (**Haemo-QOL-A**), the Haemophilia Activities List (**HAL**), and the Work Productivity and Impairment plus Classroom Impairment Questions: Hemophilia Specific (**WPAI+CIQ:HS**)

Haemo-QOL-A measures HRQOL in people with hemophilia



Results

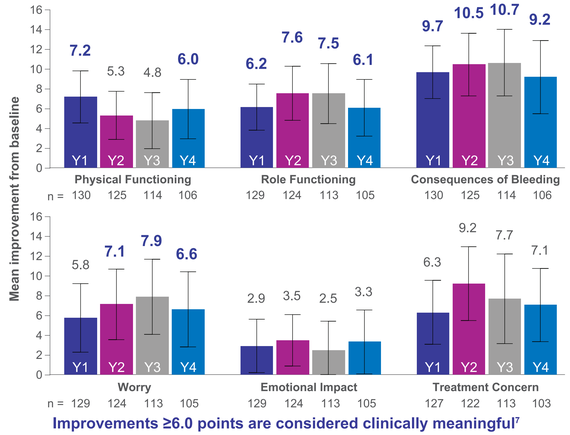
Valoctocogene roxaparvovec improved Haemo-QOL-A Total Score across 4 years



The improvements at the end of each year were deemed clinically meaningful[7]

The clinically important difference (CID) for Total Score is 5.5 points. Change from baseline results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included. Y, year.

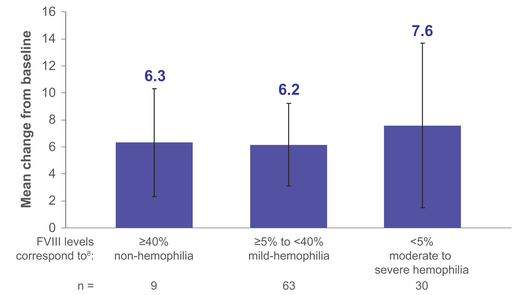
Consistent improvements for Haemo-QOL-A domain scores



Improvements ≥6.0 points are considered clinically meaningful[7]

A clinically important difference (CID) for the Treatment Concern domain has not yet been estimated. Change from baseline results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included. Y, year.

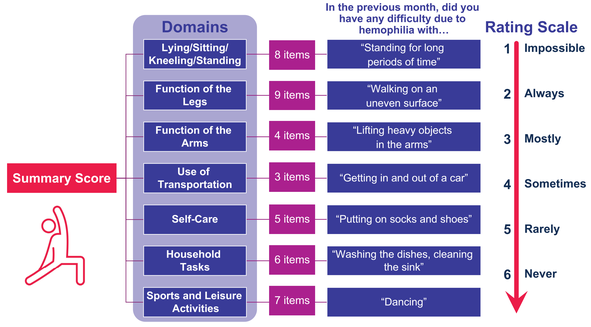
HRQOL improvements were partly independent of FVIII activity



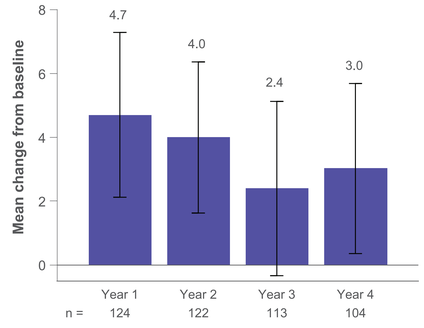
Improvement in Haemo-QOL-A Total Score at the end of year 4 was deemed clinically meaningful for participants with FVIII levels <5%[7]

Results are based on available data at each time point. Error bars represent 95% confidence intervals. Participants who resumed prophylaxis were excluded.

HAL measures self-reported functional ability for people with hemophilia

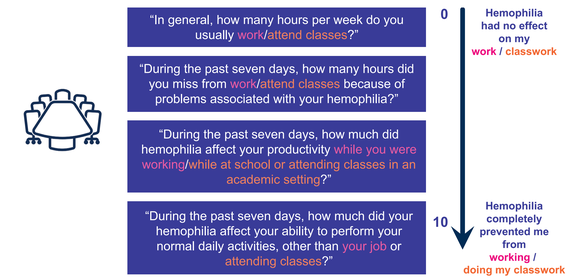


HAL Summary Score improved over 4 years

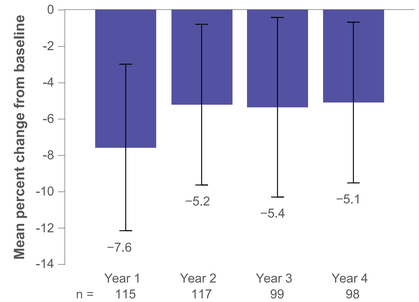


Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.

The WPAI+CIQ:HS measures impairment at work and school due to hemophilia



WPAI+CIQ:HS activity impairment was reduced over 4 years



Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.

Conclusions

Haemo-QOL-A

- Valoctocogene roxaparvovec provides **clinically meaningful HRQOL improvements** over 4 years
- The meaningful improvements also apply to **participants with FVIII activity <5%** at year 4

HAL

- Participants reported **improved ability to perform daily activities** over 4 years

WPAI+CIQ:HS

- Work and school **activity impairment scores were reduced** over 4 years

- In general, HRQOL questionnaires try to capture the **highly individual experiences of each person** — as with any study, average values do not necessarily reflect the results of all participants

References

1. Wiley RE, et al. *Haemophilia.* 2019;25:433-40. **2.** O'Hara S, et al. *Haemophilia.* 2021;27:113-9. **3.** Ozelo M, et al. *N Engl J Med.* 2022;386(11):1013-25. **4.** Mahlangu J, et al. *N Engl J Med.* 2023;388:694-705. **5.** Madan B, et al. *J Thromb Haemost.* 2024;22(7):1880-1893. **6.** Krumb E, et al. *Res Pract Thromb Haemost.* 2021;5:e12567. **7.** Quinn J, et al. *Patient Relat Outcome Meas.* 2022;13:169-80. **8.** Srivastava A, et al. *Haemophilia.* 2020;26:1-158.

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