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

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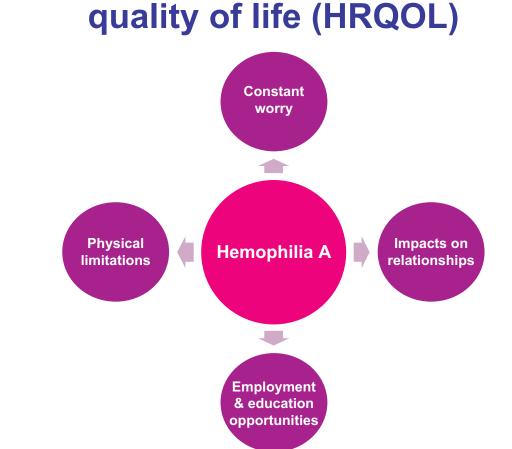
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Introduction

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



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 bleeding³⁻⁵

Potential to reduce disease burden of hemophilia A⁶ Less burder Protection on loved

ones and

Methods

Study design

Endpoints* Eligibility ■ Adult men with severe hemophilia A (FVIII ≤1 IU/dL) Change from baseline - HRQOL

- Previously receiving FVIII prophylaxis No history of FVIII inhibitors or antibodies against the capsid

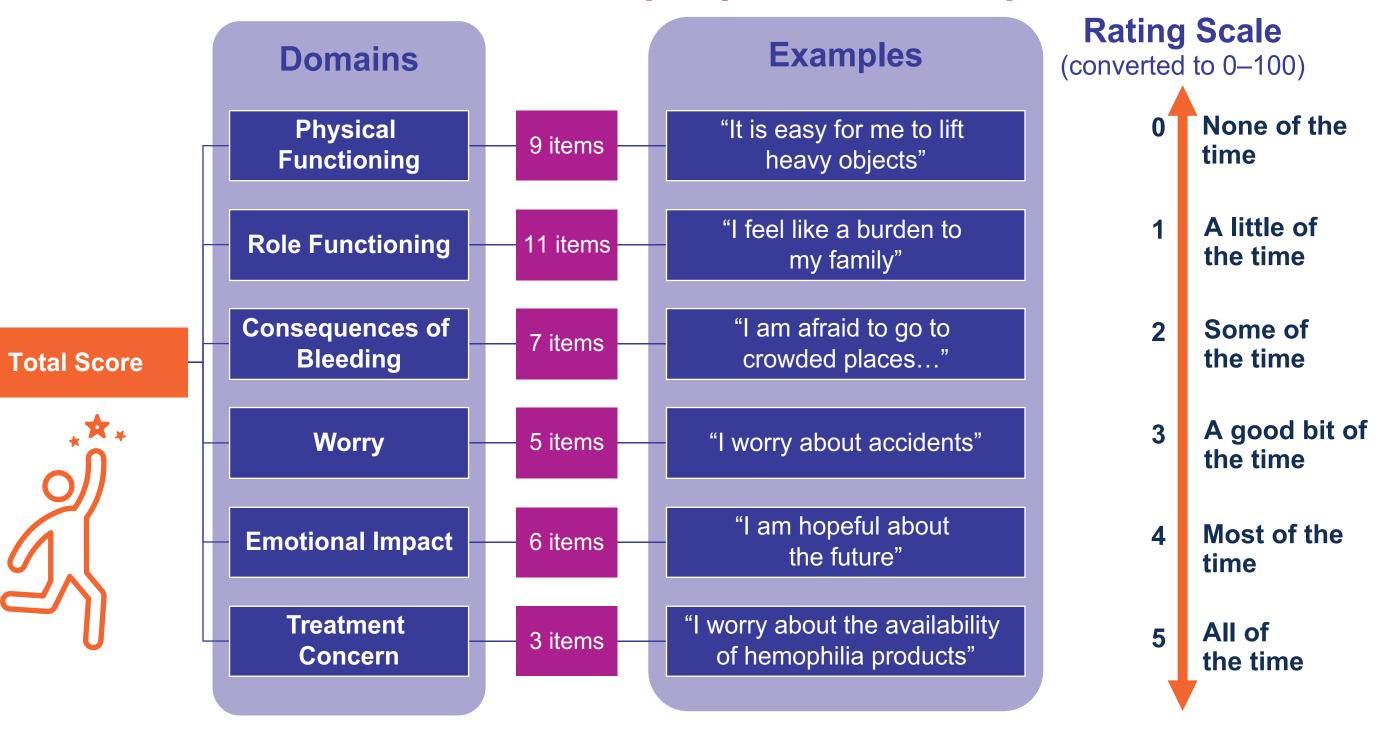
- No significant liver dysfunction

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



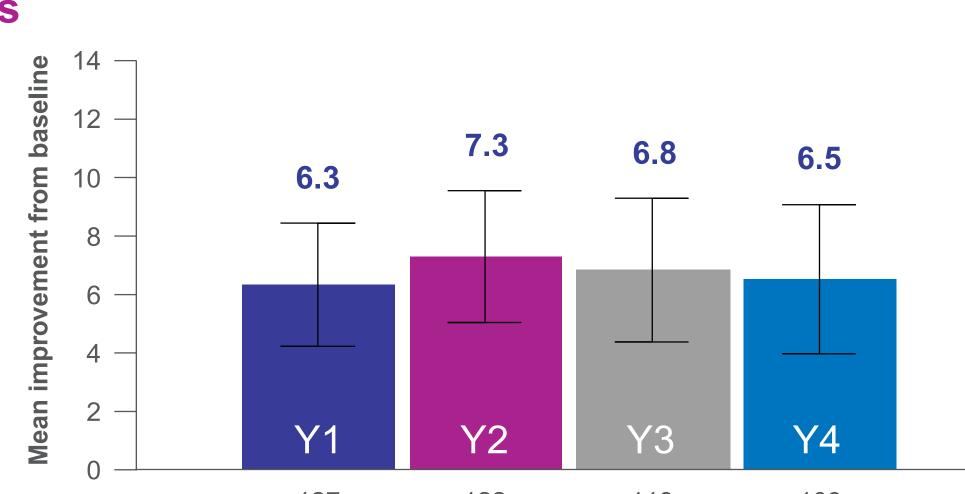
- BL, baseline; FVIII, factor VIII; HRQOL, health-related quality of life; W, week
- 134 participants enrolled and received an infusion of valoctocogene roxaparvovec
- This analysis included the 132 participants who were HIV-negative
- To ensure results are based only on the effects of valoctocogene 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



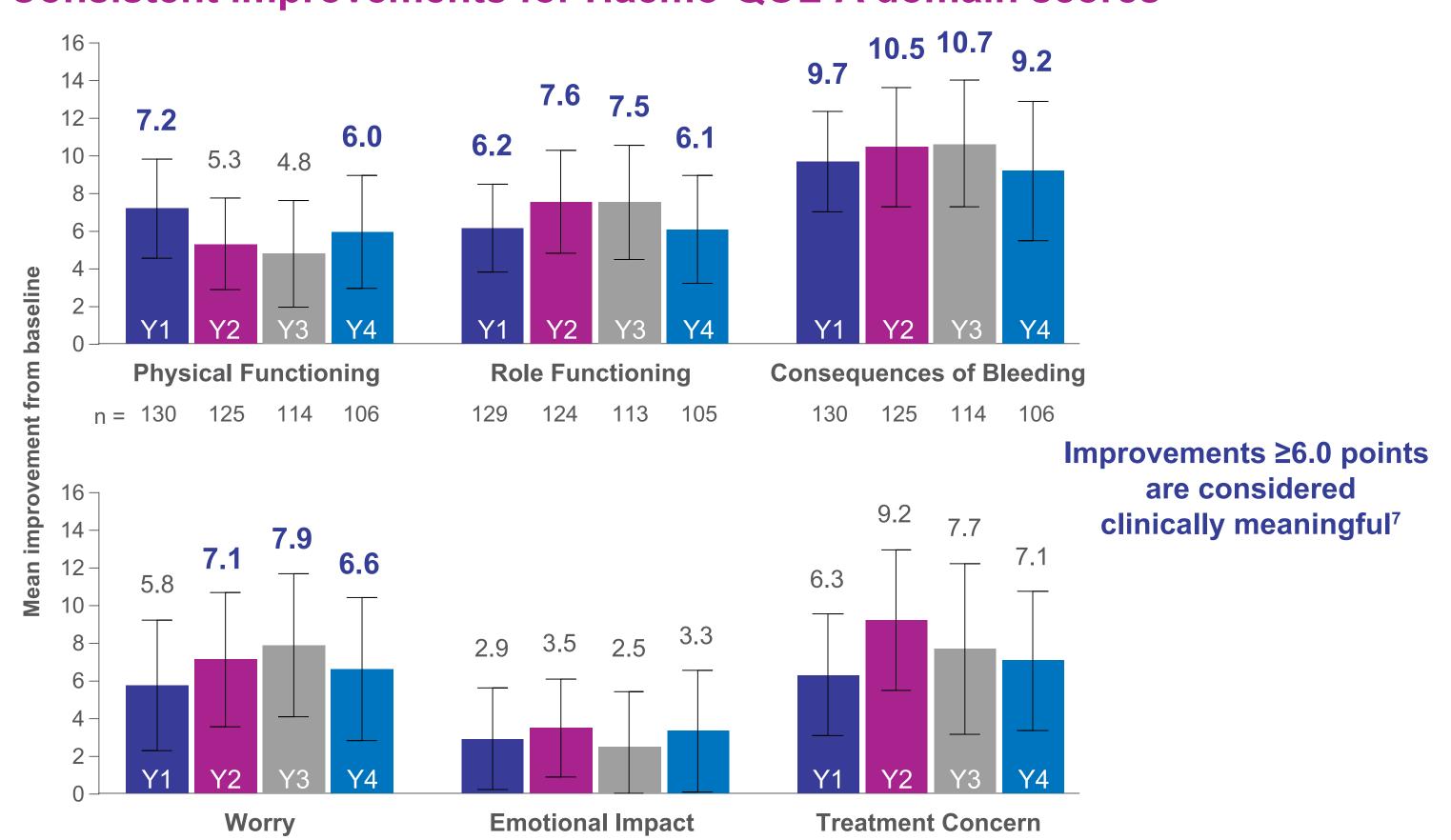
Results

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



127 122 113 The improvements at the end of each year were deemed clinically meaningful⁷ 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.

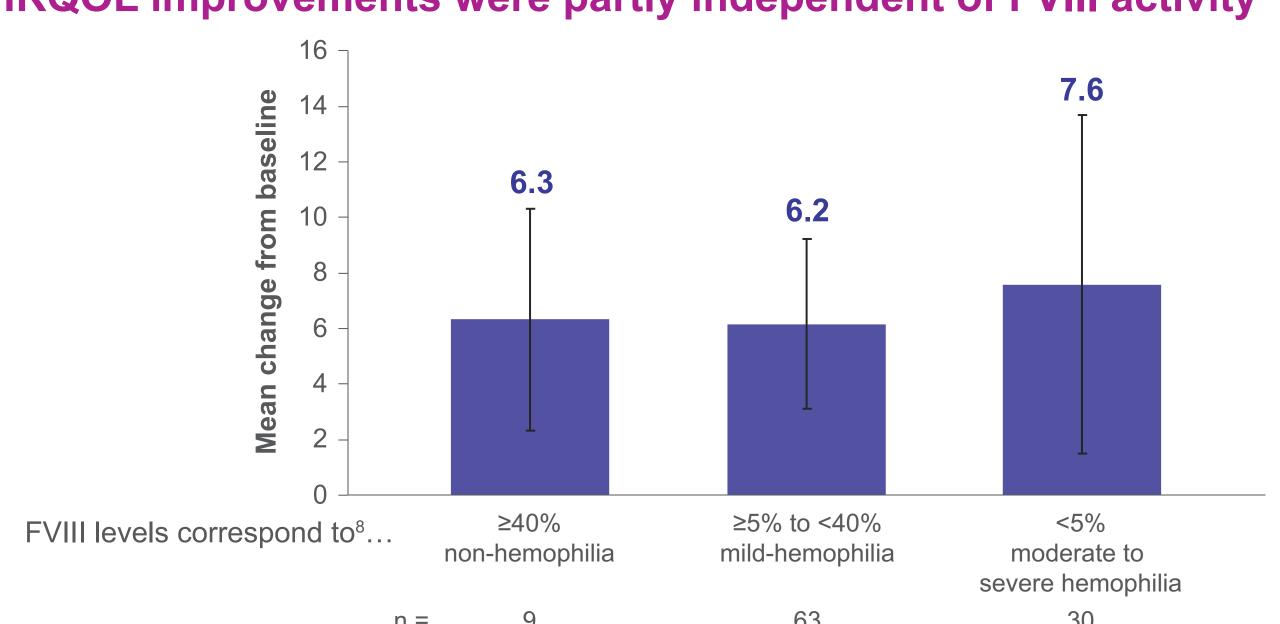
Consistent improvements for Haemo-QOL-A domain scores



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.

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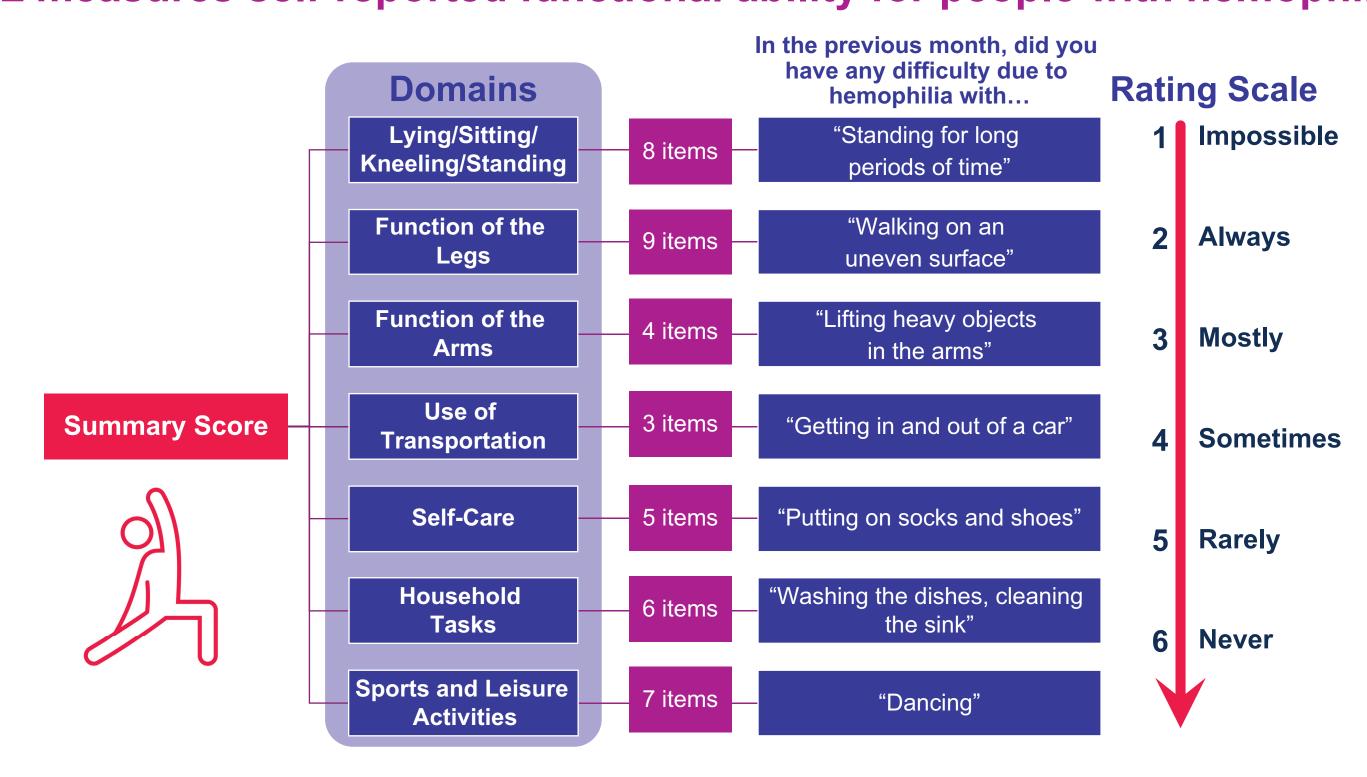
HRQOL improvements were partly independent of FVIII activity



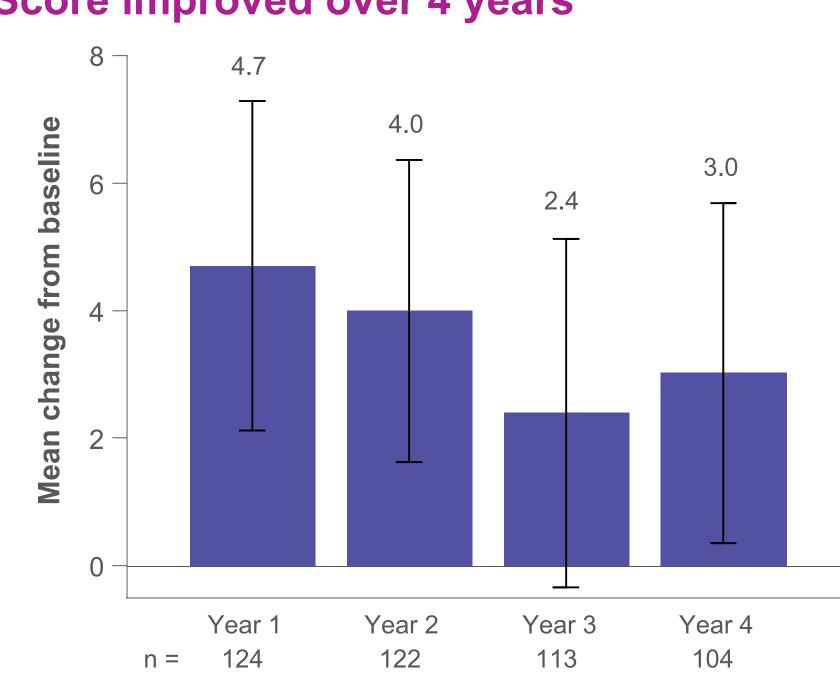
Improvement in Haemo-QOL-A Total Score at the end of year 4 was deemed clinically meaningful for participants with FVIII levels <5%⁷

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

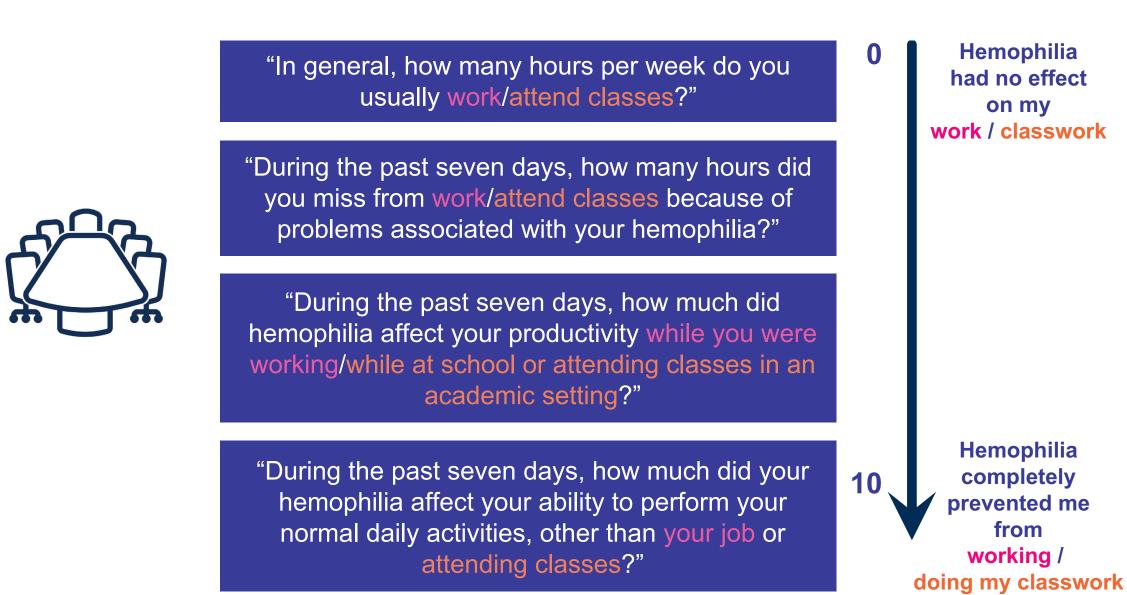


HAL Summary Score improved over 4 years

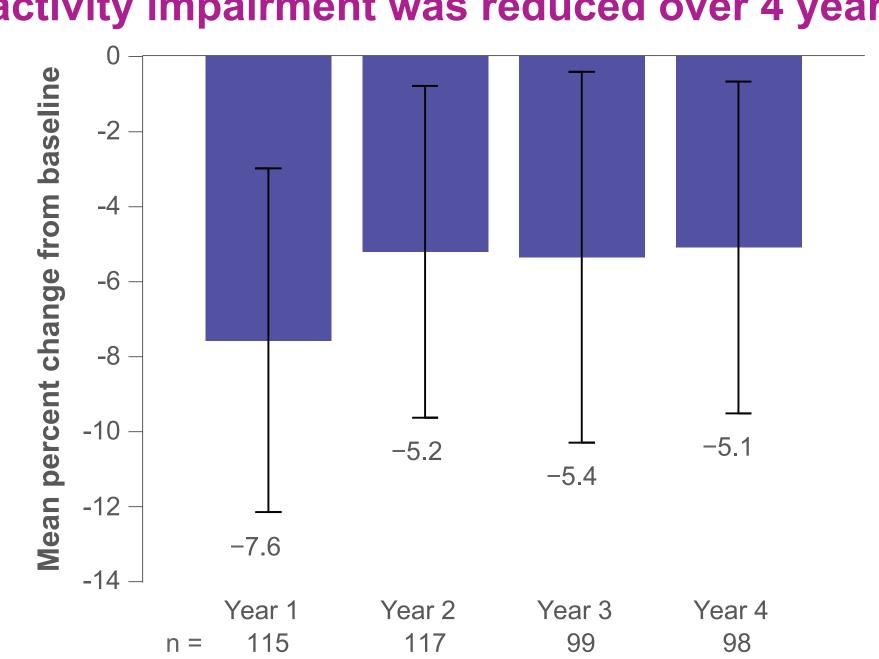


Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.

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

<5% at year 4

Haemo-QOL-A

 Valoctocogene roxaparvovec provides clinically meaningful HRQOL improvements over 4 years

Participants reported improved ability

to perform daily activities over 4 years

Work and school activity impairment

 The meaningful improvements also apply to participants with FVIII activity



WPAI+CIQ:HS

HAL

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

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