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

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Disclosures

- I have received speaker fees from BioMarin Pharmaceutical Inc.

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Hemophilia A

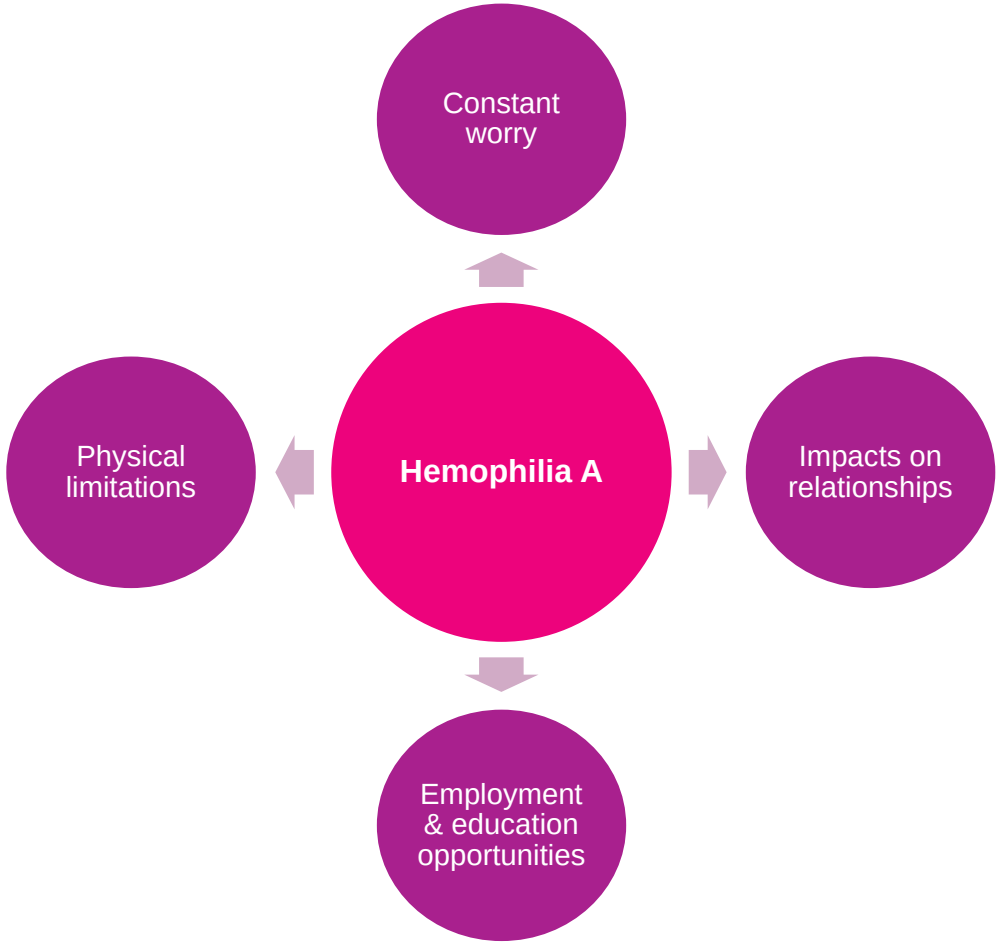
People with hemophilia A lack the blood clotting protein FVIII because **the gene is faulty**

Low factor VIII (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)



1. Wiley RE, et al. *Haemophilia.* 2019;25:433-40. 2. O'Hara S, et al. *Haemophilia.* 2021;27:113-9.

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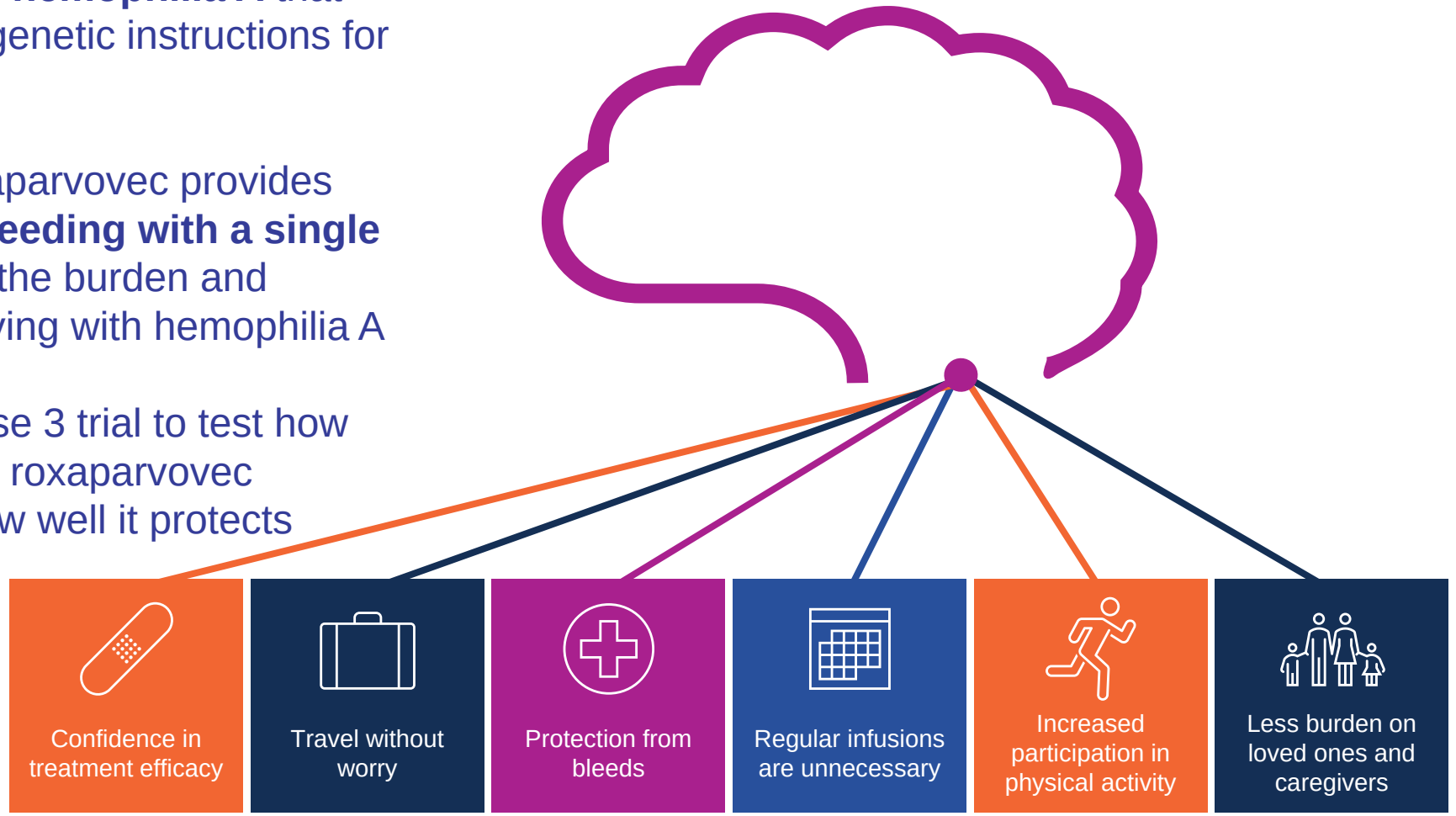
Valoctocogene roxaparvovec and HRQOL outcomes

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**, reducing 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[1-3]

Reduced disease burden of hemophilia A[4]



1. Ozelo M, et al. *N Engl J Med.* 2022;386(11):1013-25. 2. Mahlangu J, et al. *N Engl J Med.* 2023;388:694-705. 3. Madan B, et al. *J Thromb Haemost*. 2024; in press.
4. Krumb E, et al. *Res Pract Thromb Haemost.* 2021;5:e12567.

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GENEr8-1 study design

Eligibility:

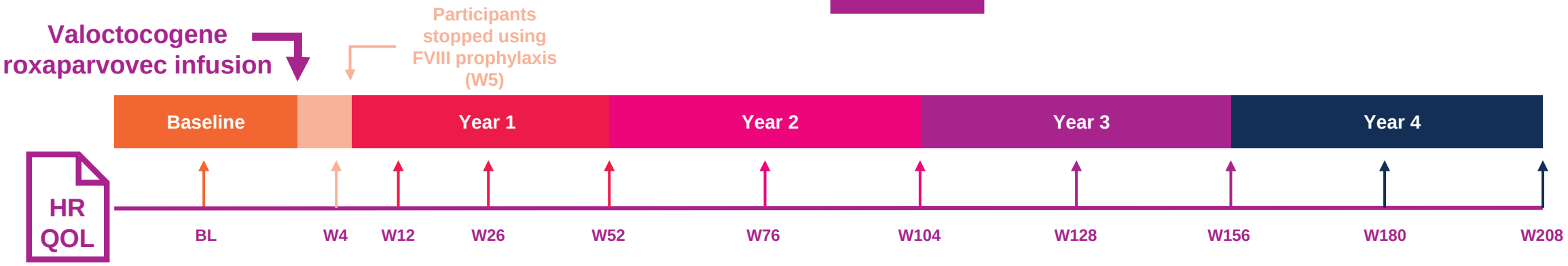
- Adult men with severe hemophilia A (FVIII ≤1 IU/dL)
- Previously receiving FVIII prophylaxis
- No history of FVIII inhibitors or antibodies against the capsid
- No significant liver dysfunction

134 participants enrolled and received an infusion of valoctocogene roxaparvovec

The modified intention-to-treat (mITT) population 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



FVIII, factor VIII; HIV, human immunodeficiency virus; HRQOL, health-related quality of life; W, week.

Haemo-QOL-A measures HRQOL in people with hemophilia

Total Score

Domains		Examples
Physical Functioning	9 items	"It is easy for me to lift heavy objects"
Role Functioning	11 items	"I feel like a burden to my family"
Consequences of Bleeding	7 items	"I am afraid to go to crowded places…"
Worry	5 items	"I worry about accidents"
Emotional Impact	6 items	"I am hopeful about the future"
Treatment Concern	3 items	"I worry about the availability of hemophilia products"

Rating Scale
(converted to 0–100)

0	None of the time
1	A little of the time
2	Some of the time
3	A good bit of the time
4	Most of the time
5	All of the time

Haemo-QOL-A, Haemophilia-Specific Quality of Life Questionnaire for Adults; HRQOL, health-related quality of life.

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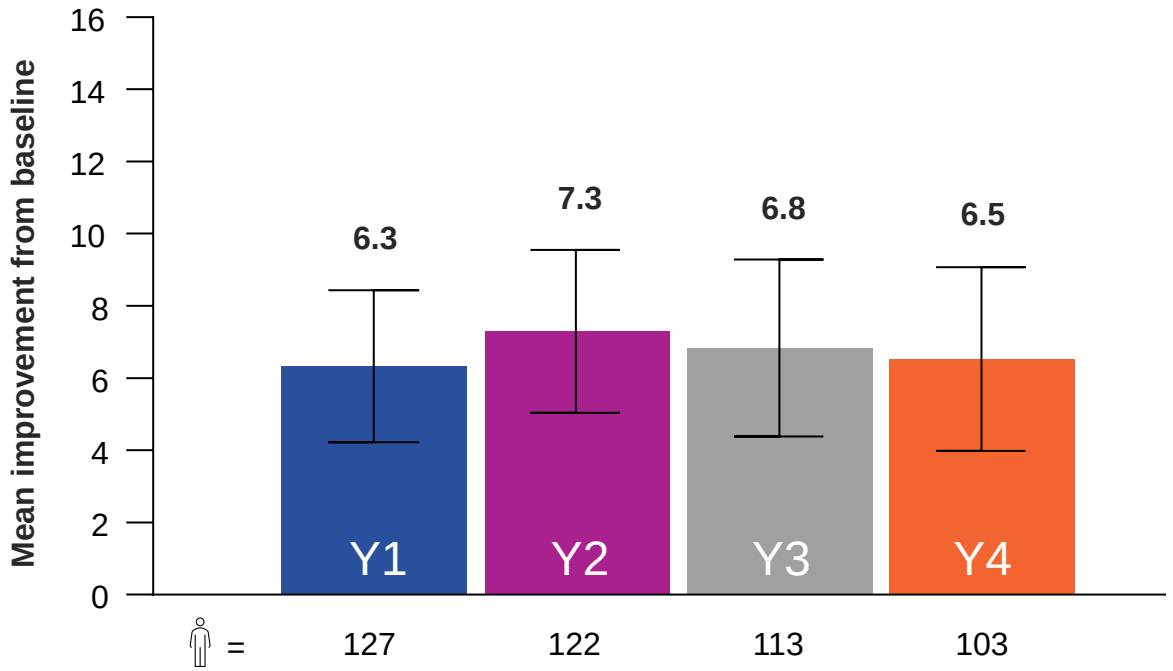
Valoctocogene roxaparvovec improved Haemo-QOL-A Total Score across 4 years

mITT population

The improvements at the end of each year were deemed clinically meaningful[1]



1. Quinn J, et al. *Patient Relat Outcome Meas*. 2022;13:169-80.

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.

Haemo-QOL-A, Haemophilia-Specific Quality of Life Questionnaire for Adults; mITT, modified intention-to-treat; Y, year.

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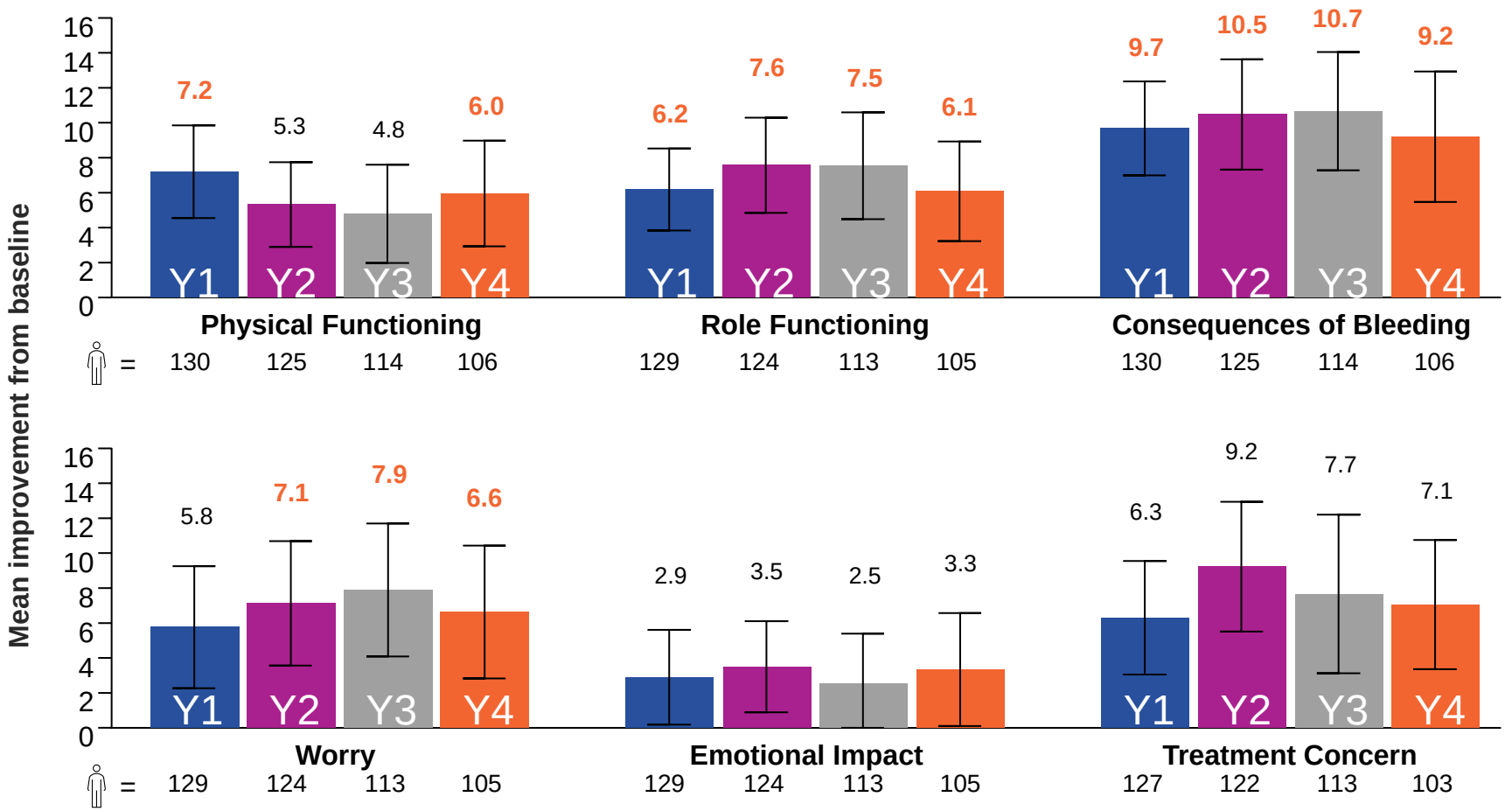
Consistent improvements for Haemo-QOL-A domain scores

mITT population



Improvements ≥6.0 points are considered **clinically meaningful**[1]

1. Quinn J, et al. *Patient Relat Outcome Meas*. 2022;13:169-80.

A 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.

CID, clinically important difference; Haemo-QOL-A, Haemophilia-Specific Quality of Life Questionnaire for Adults; mITT, modified intention-to-treat; Y, year.

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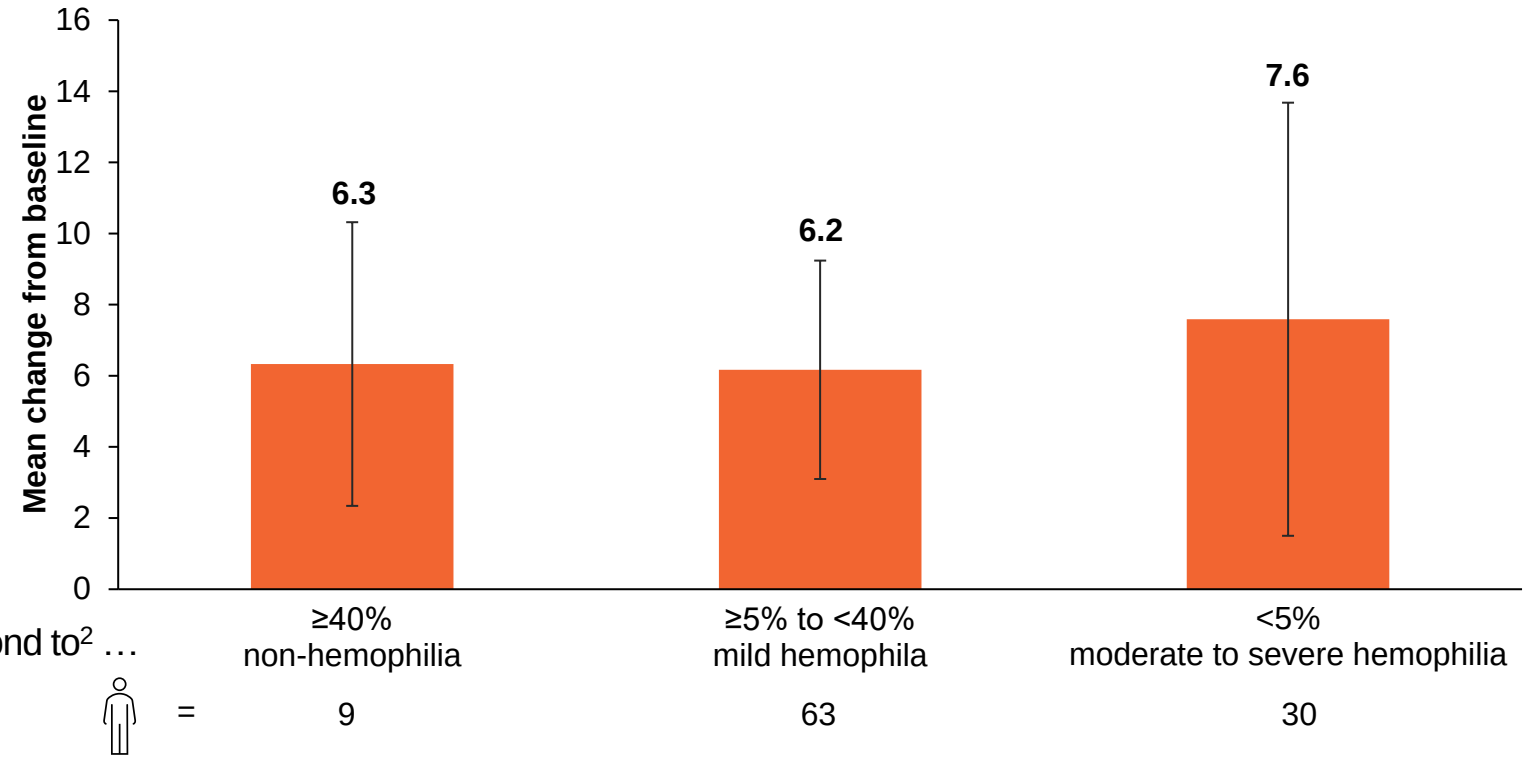
HRQOL improvements were partly independent of FVIII activity

mITT population

Improvement in Haemo-QOL-A Total Score at the end of year 4 was deemed clinically meaningful for participants with FVIII levels below 5%[1]



1. Quinn J, et al. *Patient Relat Outcome Meas*. 2022;13:169-80. 2. Srivastava A, et al. *Haemophilia.* 2020;26:1-158.
Results are based on available data at each time point. Error bars represent 95% confidence intervals. Participants who resumed prophylaxis were excluded.
FVIII, factor VIII; Haemo-QOL-A, Haemophilia-Specific Quality of Life Questionnaire for Adults; mITT, modified intention-to-treat.

HAL measures self-reported functional ability for people with hemophilia

Summary Score

Domains		In the previous month, did you have any difficulty due to hemophilia with…
Lying/Sitting/ Kneeling/Standing	8 items	"Standing for long periods of time"
Function of the Legs	9 items	"Walking on an uneven surface"
Function of the Arms	4 items	"Lifting heavy objects in the arms"
Use of Transportation	3 items	"Getting in and out of a car"
Self-Care	5 items	"Putting on socks and shoes"
Household Tasks	6 items	"Washing the dishes, cleaning the sink"
Sports and Leisure Activities	7 items	"Dancing"

Rating Scale

1 Impossible
2 Always
3 Mostly
4 Sometimes
5 Rarely
6 Never

HAL, Haemophilia Activities List.

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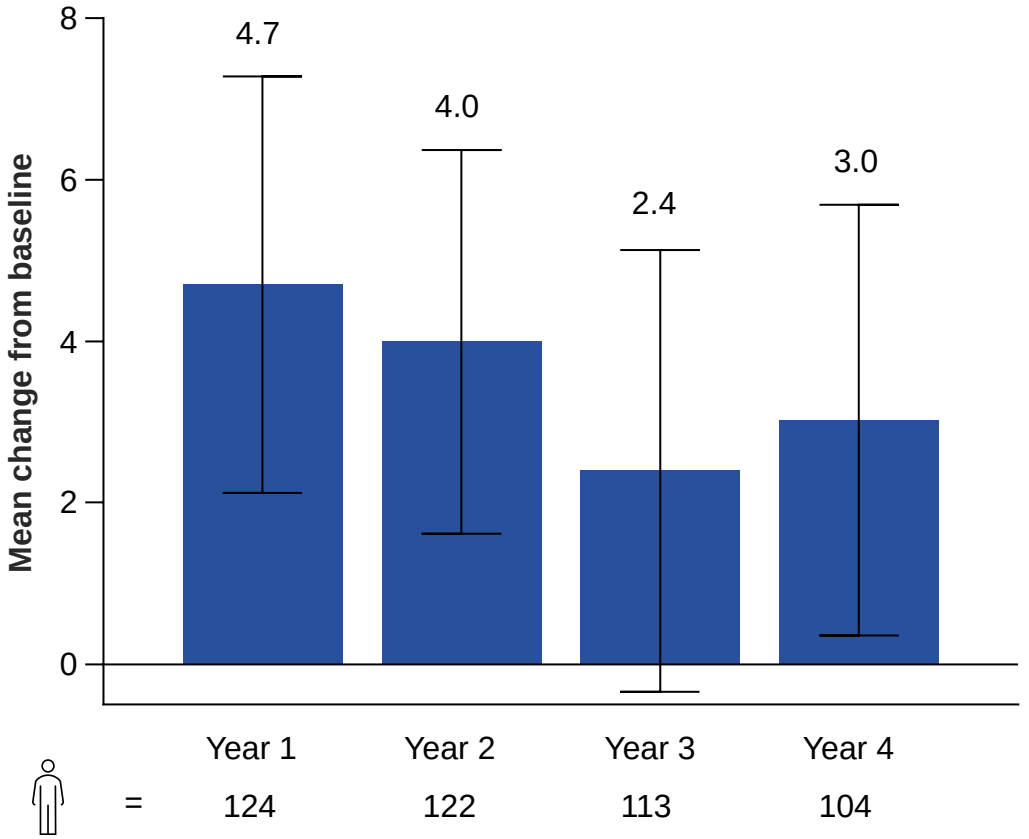
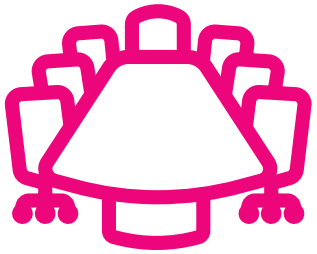
HAL Summary Score improved over 4 years

mITT population



Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.
HAL, Haemophilia Activities List; mITT, modified intention-to-treat.

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



"In general, how many hours per week do you usually work/attend classes?"

"During the past seven days, how many hours did you miss from work/class or school because of problems associated with your hemophilia?"

"During the past seven days, how much did hemophilia affect your productivity while you were working/while at school or attending classes in an academic setting?"

"During the past seven days, how much did your hemophilia affect your ability to perform your normal daily activities, other than your job or attending classes?"

0 Hemophilia had no effect on my work/classwork

10 Hemophilia completely prevented me from working/doing my classwork

WPAI+CIQ:HS, Work Productivity and Impairment plus Classroom Impairment Questions: Hemophilia Specific.

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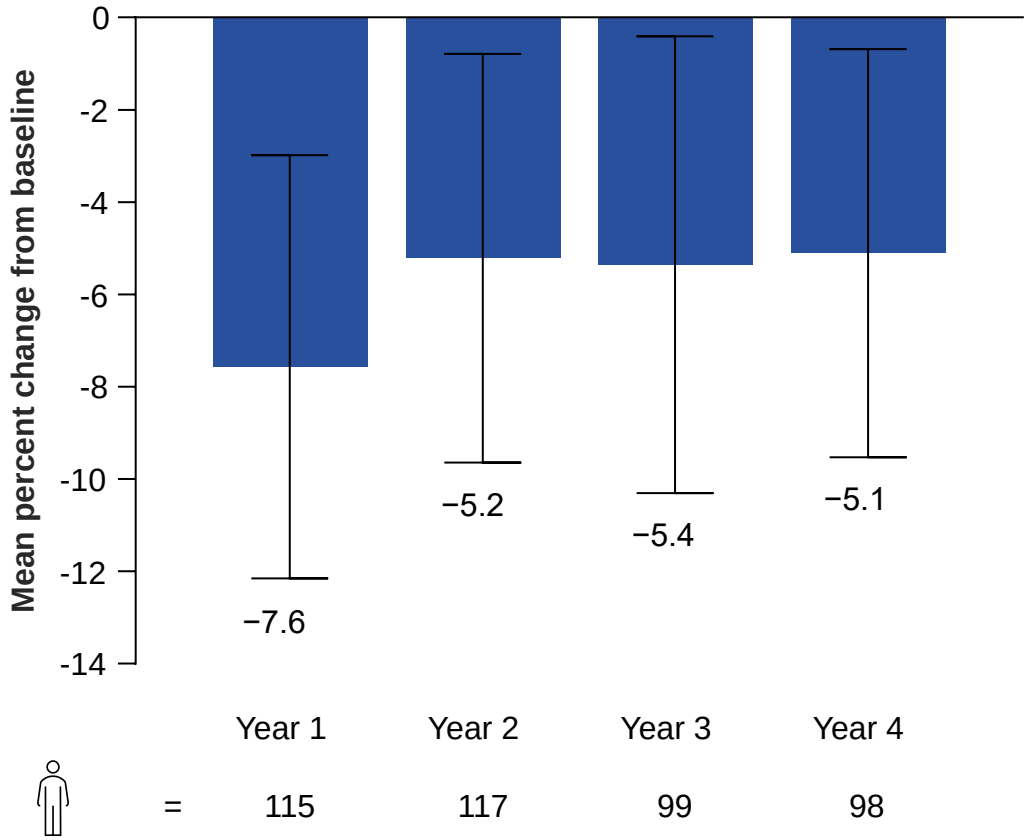
WPAI+CIQ:HS activity impairment was reduced over 4 years

mITT population



Results are based on available data at each time point. Error bars represent 95% confidence intervals. Data after participants resumed prophylaxis were not included.
mITT, modified intention-to-treat; WPAI+CIQ:HS, Work Productivity and Impairment plus Classroom Impairment Questions: Hemophilia Specific.

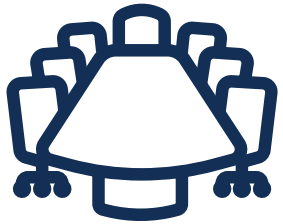
Conclusions

Haemo-QOL-A

- Valoctocogene roxaparvovec provides **clinically meaningful HRQOL improvements** over 4 years
- The meaningful improvements also apply to **participants with FVIII activity below 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

Haemo-QOL-A, Haemophilia-Specific Quality of Life Questionnaire for Adults; FVIII, factor VIII; HAL, Haemophilia Activities List; HRQOL, health-related quality of life; WPAI+CIQ:HS, Work Productivity and Impairment plus Classroom Impairment Questions: Hemophilia Specific.

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