Emicizumab prophylaxis improves acute and chronic pain-related outcomes in people with haemophilia A (PwHA): post hoc analysis of 470 patients from HAVEN 1, 3, 4 and STASEY

Authors: Cedric Hermans,[1]* Mark W. Skinner,[2,3] Brittany Gentile,[4] Elise Lim,[4] Miranda Minhas,[4] Katya Moreno,[5] Eunice Tzeng,[4] Tyler W. Buckner[6]

**presenting author*

Affiliations: [1]Cliniques Universitaires Saint-Luc, Brussels, Belgium; [2]McMaster University, Hamilton, Canada; [3]Institute for Policy Advancement Ltd, Washington, DC, USA; [4]Genentech, Inc., South San Francisco, CA, USA; [5]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [6]University of Colorado Anschutz Medical Campus, CO, USA

Summary

People with haemophilia A (PwHA) experience substantial **acute and chronic pain** due to their disease, which can impact quality of life (QoL)

This post hoc analysis assessed the effect of **emicizumab** on **pain-related QoL** measures in PwHA, using pooled data from the HAVEN 1, 3, 4 and STASEY clinical trials

Additional studies are warranted to **evaluate pain assessment** in PwHA, with a focus on pain medication use over time

Pain-related QoL measures **improved** from baseline upon treatment with emicizumab, and improvements were **maintained** until final assessment

Background

- People with haemophilia A (PwHA) experience substantial acute and chronic pain due to their disease, which can impact quality of life (QoL) and is associated with swelling, reduced function and disability.[1]
- The pain experienced by PwHA may be influenced by demographic factors, such as age,[1] and clinical characteristics, such as the development of target joints[1] or factor VIII (FVIII) inhibitors,[2] or the treatment that PwHA receive.[3]
- This post hoc analysis, the largest to date, assessed the effect of emicizumab on pain-related QoL in adults and adolescents with haemophilia A (HA), with or without FVIII inhibitors, using pooled data from the HAVEN 1, 3, 4 and STASEY clinical trials[4–7]
  - Pain-related QoL measures were assessed in the overall population and the population of participants with target joints at baseline
  - Subgroup analyses of pain-related QoL were stratified by age, inhibitor status, and prior treatments received.

Methods

- Adults and adolescents with HA received emicizumab during HAVEN 1, 3, 4, and STASEY as previously reported.[4–7]
- Pain was measured via patient-reported outcomes (PROs): pain-specific questions from the physical health domain of Haem-A-QoL (≥18 years; five questions) and Haemo-QoL-SF (12–17 years; three questions) and the EQ-5D-5L pain/discomfort dimension.
- The Haem-A-QoL/Haemo-QoL-SF questions ask participants to respond based on their experience in the past month, while the EQ-5D-5L questions ask participants to respond based on the day of assessment.
- Responses were recorded at baseline, and at regular prespecified points for up to 78 weeks following initiation of emicizumab prophylaxis
  - Response options for Haem-A-QoL/Haemo-QoL-SF were 'never', 'seldom/rarely', 'sometimes', 'often', and 'always/all the time'
  - Response options for the EQ-5D-5L pain/discomfort dimension were 'extreme', 'severe', 'moderate', 'slight' or 'no' pain/discomfort.
- In this post hoc analysis, responses were assessed in all participants (overall population) and in participants with target joints at baseline (target joint population)
  - Target joints were defined according to the ISTH definition[8]
  - The overall population was stratified and assessed by subgroups, including age, FVIII inhibitor status and prior treatment.

Results

- In total, 504 PwHA enrolled in the HAVEN 1, 3, 4 and STASEY clinical trials (**Table 1**).
- Median emicizumab exposure was 2.04 (range 0.02–4.25) years and total exposure in patient-years was 1,150.0 years.
- Of the 504 participants, 336 (66.7%) had target joints at baseline.

Table 1. Baseline characteristics in the overall population

	Overall population N=504
Mean (SD) age, years	34.6 (15.8)
Median (range) emicizumab exposure in efficacy period, years	2.04 (0.02–4.25)
Therapy prior to enrolment, n (%)	
Prophylactic only	173 (34.3)
Episodic only	281 (55.8)
Prophylactic and episodic	49 (9.7)
Data missing*	1 (0.2)
Bleeds in the 24 weeks prior to study entry, n (%)	
<9†	296 (58.7)
≥9‡	207 (41.1)
Data missing*	1 (0.2)
Target joints at study entry, n (%)	
0	167 (33.1)
1	102 (20.2)
≥2§	234 (46.4)
Data missing*	1 (0.2)
Inhibitors at study entry, n (%)	
Yes	283 (56.2)
No	221 (43.8)

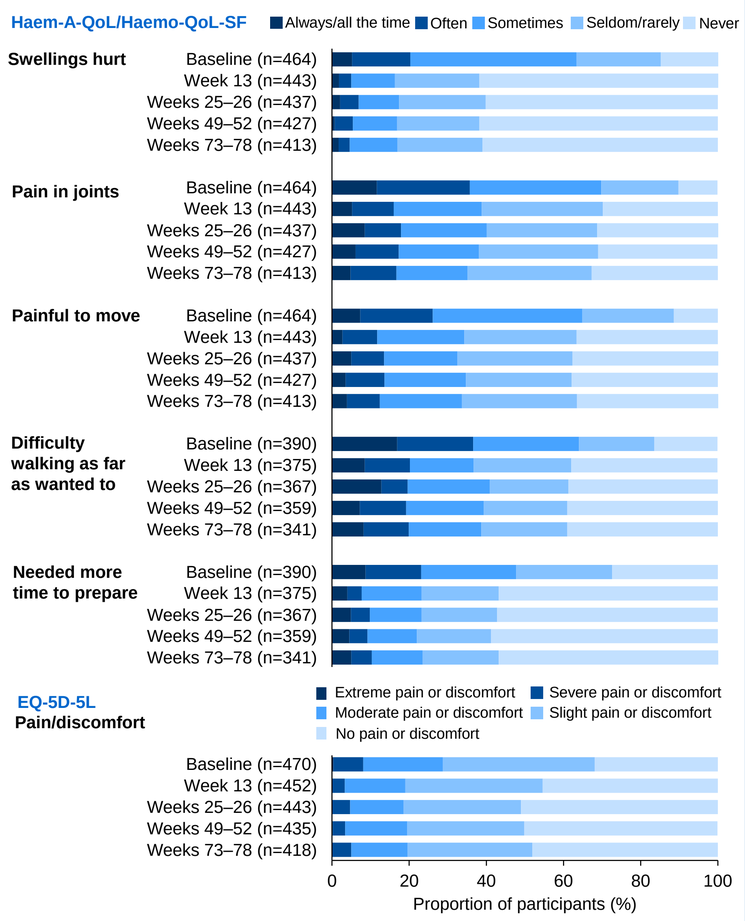
*Missing data at study entry. †Range of bleeds recorded: 0–8.
‡Range of bleeds recorded: 9–180. §Range of target joints recorded: 2–18.
SD, standard deviation.

Pain-related QoL measures in the overall population improved by Week 13, and were maintained through Weeks 73–78

Overall population

- Data were available for 464 and 470 PwHA in response to the Haem-A-QoL/Haemo-QoL-SF and EQ-5D-5L, respectively.
- Improvement in pain was consistently observed from baseline through to the final assessment (Weeks 73–78) across all PROs (**Figure 1**).
- Improvements were observed beginning at the first assessment time point common across studies (Week 13, although HAVEN 1 had additional assessments at Week 5 and 9, where similar improvements were observed) and were sustained until the final assessment (Weeks 73–78).
- The largest improvement was observed for 'my swellings hurt': the proportion of participants who responded 'never' increased from baseline (14.9%) to Week 13 and beyond (60.2–61.9%) for this question.

Figure 1. Pain-related QoL outcomes in the overall population



Target joint population

- In the subgroup of PwHA with target joints, 308 completed the questions related to pain in the physical health domain of the Haem-A-QoL/Haemo-QoL-SF, and 313 completed the EQ-5D-5L pain/discomfort dimension
  - Similar trends were seen compared with the overall population.

Patient-reported pain was assessed by age, inhibitor status, and prior treatment

Age

- Among the different age subgroups (12–17, 18–34, 35–49, and ≥50 years), the greatest improvement in the proportion of participants responding 'never' or 'seldom/rarely' was observed in the 12–17 year age group across all Haem-A-QoL and Haemo-QoL-SF questions (selected questions shown in **Figure 2**).
- Improvement was observed in participants aged ≥50 years, but to a lesser degree compared with other age groups.

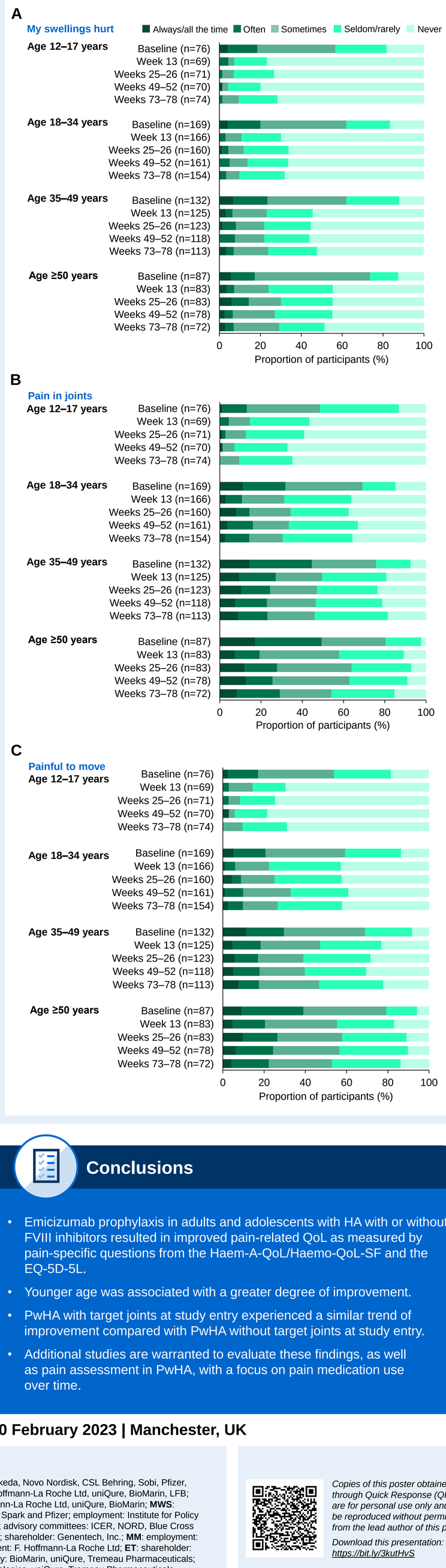
FVIII inhibitor status

- When analysed by inhibitor status, both groups (with and without FVIII inhibitors) demonstrated improvement similar to the overall population, with slightly higher proportions of participants receiving emicizumab responding 'never' or 'seldom/rarely' in the FVIII inhibitor group.

Prior treatment regimen

- When analysed by prior treatment regimen (prophylaxis, episodic treatment, or both), improvements in the proportion of participants responding 'never' or 'seldom/rarely' were comparable to those seen in the overall population.

Figure 2. Pain-related QoL outcome of (A) 'my swellings hurt', (B) 'pain in joints', and (C) 'painful to move' questions by age



Conclusions

- Emicizumab prophylaxis in adults and adolescents with HA with or without FVIII inhibitors resulted in improved pain-related QoL as measured by pain-specific questions from the Haem-A-QoL/Haemo-QoL-SF and the EQ-5D-5L.
- Younger age was associated with a greater degree of improvement.
- PwHA with target joints at study entry experienced a similar trend of improvement compared with PwHA without target joints at study entry.
- Additional studies are warranted to evaluate these findings, as well as pain assessment in PwHA, with a focus on pain medication use over time.

Presented at The European Association for Haemophilia and Allied Disorders (EAHAD) Annual Meeting | 7–10 February 2023 | Manchester, UK

References

1. Kennedy M, et al. Eur J Haematol 2022;108:518–27;
2. duTreil S. J Blood Med. 2014;5:115–22;
3. Pasi J, et al. Ther Adv Hematol 2022;13; doi:10.1177/20406207221079482;
4. Oldenburg J, et al. N Engl J Med. 2017;377(9):809–18;
5. Mahlangu J, et al. N Engl J Med 2018;379(9):811–22;
6. Pipe S, et al. Lancet Haematol 2019;6(6):E295–305;
7. Jiménez-Yuste V, et al. Res Pract Thromb Haemost 2022;6(8):e12837;
8. Blanchette VS, et al. J Thromb Haemost 2014;12(11):1935–39.

Acknowledgements

The HAVEN 1, 3, 4 and STASEY trials were led and funded by F. Hoffmann-La Roche Ltd. Third party medical writing assistance, under the direction of the authors, was provided by Anna Nagy, BSc, Jen Evans, BSc, and Phoebe Tate, MSc, of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

Disclosures

CH: grant/research support: Shire/Takeda, Pfizer, Novo Nordisk, CSL Behring, Sobi; consultancy: Bayer, Shire/Takeda, Novo Nordisk, CSL Behring, Sobi, Pfizer, CAF-DCF, LFB; speakers' bureau: Bayer, Shire/Takeda, Pfizer, Novo Nordisk, CSL Behring, Sobi, CAF-DCF, F. Hoffmann-La Roche Ltd, uniQure, BioMarin, LFB; honoraria: Bayer, Shire/Takeda, Pfizer, Novo Nordisk, CSL Behring, Octapharma, Sobi, CAF-DCF, LFB, F. Hoffmann-La Roche Ltd, uniQure, BioMarin; **MWS**: grant/research support: BioMarin, Freeline, uniQure; consultancy: NHF, Bayer, Genentech, Inc., BioMarin, Sanofi, Spark and Pfizer; employment: Institute for Policy Advancement Ltd; honoraria: Bayer, BioMarin, Novo Nordisk, F. Hoffmann-La Roche Ltd/Genentech, Inc., Takeda; advisory committees: ICER, NORD, Blue Cross Blue Shield MAP, NHF MASAC, WFH USA; **BG**: employment: Genentech, Inc.; **EL**: employment: Genentech, Inc.; shareholder: Genentech, Inc.; **MM**: employment: Genentech, Inc.; shareholder: F. Hoffmann-La Roche Ltd; **KM**: shareholder: F. Hoffmann-La Roche Ltd; employment: F. Hoffmann-La Roche Ltd; **ET**: shareholder: Genentech, Inc.; employment: Genentech, Inc.; **TWB**: grant/research support: Genentech, Inc., ATHN; consultancy: BioMarin, uniQure, Tremeau Pharmaceuticals; advisory board: CSL Behring, Novo Nordisk, Pfizer, Spark, BioMarin, Genentech, Inc., Takeda, Kedrion, HEMA Biologics, uniQure, Tremeau Pharmaceuticals.