Health-related quality of life (HRQoL), physical activity (PA) and joint health in people with severe haemophilia A (PwSHA) and a bleeding phenotype receiving emicizumab – results from the HemiNorth 2 study

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Summary

People with severe haemophilia A (PwSHA) have varying lifestyles and levels of physical activity (PA). Many PwSHA have impaired health-related quality of life (HRQoL) and may limit their PA due to perceived bleeding risk, even when on prophylaxis

HemiNorth 2 is an interventional study evaluating the impact of changing from factor (F)VIII prophylaxis to emicizumab on HRQoL, PA and joint health in PwSHA without FVIII inhibitors in the Nordic countries

PA and joint health outcomes were maintained whilst bleeding outcomes improved and the proportion of participants with zero bleeds increased. Almost all participants reported a preference for emicizumab over previous FVIII prophylaxis

In 28 enrolled participants, HRQoL outcomes remained stable across most domains, and treatment burden improved in adults and adolescents

Background

- Despite treatment with factor (F)VIII prophylaxis, a perceived increased risk of bleeding persists among some people with severe haemophilia A (PwSHA), which may limit physical activity (PA) and impact health-related quality of life (HRQoL).
- Emicizumab, a bispecific humanised monoclonal antibody that mimics activated FVIII, is given subcutaneously at 1.5mg/kg every week, 3mg/kg every 2 weeks, or 6mg/kg every 4 weeks,[1] which may reduce the treatment burden associated with FVIII prophylaxis. Improvements in HRQoL have also been reported in people treated with emicizumab.[2,3]
- Here, we present the primary and final analysis of HemiNorth 2 (MO42245; EudraCT# 2020-003256-32), an interventional study evaluating the impact of changing treatments from FVIII prophylaxis to emicizumab in PwSHA without FVIII inhibitors with a need for improved prophylaxis in the Nordic countries.

Methods

- Prior to enrolment in HemiNorth 2, participants had completed ≥24 weeks on FVIII prophylaxis in the HemiNorth (MO42590; EudraCT# 2020-003256-32) multicentre, non-interventional study (hereafter referred to as the NIS).[4]
  - Eligible participants for the NIS were aged ≥12–60 years, had experienced ≥1 treated joint or muscle bleed in the previous 52 weeks, and had a medical need for a treatment change as assessed by the investigator.
  - One participant enrolled in HemiNorth 2 who completed the NIS was not compliant regarding their FVIII prophylaxis regime. A sensitivity analysis run to exclude this patient was consistent.
- PwSHA enrolling in HemiNorth 2 received emicizumab per label for 48 weeks.
- The primary endpoint was the impact of emicizumab on HRQoL and change from baseline (NIS Week 24) to study Week 49 via the Comprehensive Assessment Tool for Challenges in Hemophilia (CATCH) for adolescents (12–<18 years) and adults (≥18 years).
- Secondary endpoints included PA (International Physical Activity Questionnaire-Short Form [IPAQ-SF] and an intra-participant comparison of FitBit [activity tracker] data between NIS Week 17–24 and treatment Week 41–48); treatment preference (via Emicizumab Preference [EmiPref] survey); Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US); Total Hemophilia Joint Health Score (HJHS); model-based annualised bleeding rates (ABRs); and adverse events (AEs).

Results

- Twenty-eight male participants (including 12 adolescents) enrolled in the HemiNorth 2 study. The mean (standard deviation [SD]) observation period was 51.1 (9.1) weeks.
- Median (range) age at baseline was 26.5 (12.0–52.0) years. Most participants reported high physical activity in the NIS. Four (14.3%) had target joints at study entry.

Most CATCH domain scores remained stable between baseline and Week 49

- CATCH domain scores for risk perception and impact of daily, social, and recreational activities, as well as work/school impact and preoccupation, were maintained through the study period (**Table 1**).
- Mean treatment burden improved from baseline to Week 49 for adults (-17.77; -55.7% change) and adolescents (+16.74; +33.4% change).

Table 1. Adult and adolescent CATCH questionnaire score changes from baseline to Week 49*

	Adults		Adolescents	
	n	Mean (SD) change from baseline to Week 49	n	Mean (SD) change from baseline to Week 49
Daily activity risk perception	15	-1.85 (11.90)	9	-1.59 (4.76)
Daily activity impact	15	-1.94 (12.99)	9	-3.67 (10.15)
Social activity risk perception	15	-1.47 (11.51)	9	-1.59 (9.96)
Social activity impact	15	3.44 (12.89)	9	-4.71 (10.80)
Recreational activity risk perception	11	2.16 (14.97)	9	-1.36 (21.34)
Recreational activity impact	10	-3.62 (15.57)	8	-1.15 (14.73)
Work/school impact	11	-0.35 (9.88)	9	-0.37 (4.50)
Preoccupation	15	-3.33 (14.44)	9	-3.67 (13.75)
Treatment burden	15	-17.77 (21.10)*	9	16.74 (15.53)*
Pain in last 7 days				
Worst pain	15	-0.27 (3.15)	9	-0.11 (2.32)
Least pain	15	-0.53 (1.92)	NR	NR
Average pain	15	-0.53 (2.13)	NR	NR

*For treatment burden only, decreased CATCH scores indicate improvement in adults, while increased scores indicate improvement in adolescents; for all other domains, decreased scores indicate improvements in both groups.
CATCH, Comprehensive Assessment Tool for Challenges in Hemophilia; NR, not reported; SD, standard deviation.

Joint health outcomes remained stable following initiation of emicizumab

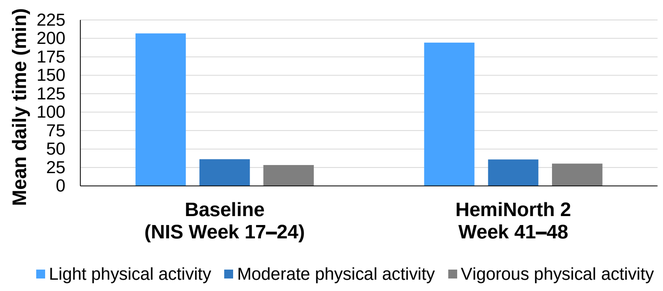
- No changes in synovitis status were observed for most joints between baseline and Week 49, as assessed by HEAD-US. No clinically relevant changes in osteochondral damage were observed.
- No meaningful changes were observed from baseline to Week 49 for median HJHS total score.

Physical activity levels remained stable after initiating emicizumab prophylaxis

- The IPAQ-SF questionnaire results remained consistent between baseline (NIS Week 1) and Week 49 for all participants.
- Mean daily step counts, time spent in PA, and sum of metabolic equivalents of tasks (METs) were maintained between the NIS and HemiNorth 2 (**Figure 1**).

Figure 1. Intra-participant analysis of physical activity in participants aged ≥13 years using a FitBit* (n=12)

Mean time spent in light, moderate, or vigorous physical activity



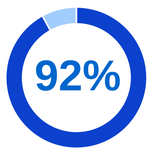
Summary of mean step counts and METs

Item, mean (SD)	Baseline (NIS Week 17–24) (n=12)	Study Week 41–48 (n=12)	Change from baseline (n=12)
Daily total steps, n	7982.2 (2834.49)	8618.78 (3787.11)	636.58 (2879.39)
Sum of METs	1701.94 (387.03)	1720.54 (438.67)	18.60 (271.99)

*For each visit, only participants with the device worn (while the participant was awake) for at least 7 hours per day and with at least 100 steps recorded, on at least 21 days, were included.
METs, metabolic equivalents of tasks; min, minutes; SD, standard deviation.

EmiPref results indicated preference for emicizumab over previous prophylactic treatment

Figure 2. EmiPref survey outcomes



23/25 (92%) participants preferred emicizumab treatment over their previous FVIII prophylaxis at Week 49

Top factors influencing treatment preference:

- Frequency of treatments is lower (n=16 [69.6%])
- Better QoL (n=10 [43.5%])
- Route of administration easier (n=8 [34.8%])
- Less worry about finding a vein (n=7 [30.4%])

EmiPref, Emicizumab Preference; F, factor.

Bleeding rates and participants with zero bleeds improved after switching from FVIII prophylaxis to emicizumab

- Rates of all bleeds, treated bleeds, and treated bleeds related to participation in PA improved (**Table 2**).

Table 2. Intra-participant ABRs and participants with zero bleeds

	FVIII prophylaxis (N=28)†	Emicizumab (N=28)
Median observation time, years	0.52	0.92
Treated bleeds		
Participants with zero bleeds, n (%)	8 (28.6)	16 (57.1)
Model-based ABR (95% CI)	5.9 (3.68, 9.40)	1.6 (0.81, 3.19)
ABR ratio (95% CI)	0.27 (0.13, 0.60)	
All bleeds		
Participants with zero bleeds, n (%)	3 (10.7)	12 (42.9)
Model-based ABR (95% CI)	9.2 (6.31, 13.43)	2.5 (1.44, 4.36)
ABR ratio (95% CI)	0.27 (0.16, 0.47)	
Treated bleeds related to participation in PA*		
Participants with zero bleeds, n (%)	11 (39.3)	21 (75.0)
Model-based ABR (95% CI)	2.8 (1.76, 4.49)	1.0 (0.36, 2.71)

*Within the previous 24 hours. †13 (46.4%) participants were treated with SHL prophylaxis and 15 (53.6%) with EHL prophylaxis. Eleven (40.7%) were treated with FVIII at an intermediate dose (15−25 IU FVIII/kg, 3 days per week); 16 (59.3%) were treated with high-dose FVIII (25−40 IU FVIII/kg every 2 days); one participant had missing information.
ABR, annualised bleed rate; CI, confidence interval; EHL, extended half-life; F, factor; PA, physical activity; SHL, standard half-life

Emicizumab was well tolerated, with no new safety signals

- Nine participants experienced ≥1 AE reported as related to emicizumab, including: injection-site reaction (n=5 [17.9%]), headache (n=2 [7.1%]), fatigue (n=1 [3.6%]), nausea (n=1 [3.6%]), anger (n=1 [3.6%]), and altered mood (n=1 [3.6%]). In total, 15 AEs were reported as related to emicizumab.
- One participant experienced three serious AEs; all were traumatic bleeds due to accidents.

Conclusions

- **These results indicate that emicizumab improved treatment burden and was preferred over FVIII prophylaxis by both adults and adolescents in this relatively young, physically active population.**
- **Bleeding rates improved with emicizumab, despite PA remaining high, which is consistent with previous findings.[5–7] There were no clinically significant changes in joint health and no new safety signals.**
- **Results should not be over-interpreted, given the small study population, which may not have been representative of the overall Nordic population with HA, as well as the descriptive nature of the study and the fact that changes in subjective joint outcomes are challenging to observe with a follow-up time of <1 year.[8,9]**

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References

1. European Medicines Agency. Hemlibra SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/hemlibra-epar-product-information_en.pdf. [Accessed January 2025].
2. Mahlangu J, et al. N Engl J Med 2018;379:811–22.
3. Skinner MW, et al. Haemophilia 2021;27:854–65.
4. Ranta S, et al. RPTH 2024;8(Supp 2):102504.
5. Nogami K, et al. Int J Hematol 2024;119:14–23.
6. Nogami K, et al. Blood 2024;144(1):1211.
7. Shima M, et al. Blood 2023;142:3991.
8. Kiialainen A, et al. Haemophilia 2022;28:1033–43.
9. Shima M, et al. Blood 2022;140:2742–4.

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Disclosures

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