Interim analysis of the A-MORE real-world study: 4-year treatment outcomes with a recombinant factor VIII Fc in the overall and non-severe populations

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CONCLUSIONS

- **The fifth interim analysis of the A-MORE study demonstrates that prophylaxis with recombinant factor VIII Fc fusion protein (rFVIIIFc) provides sustained protection against bleeding and supports maintenance of joint status across 4 years for persons with haemophilia A in the overall population and non-severe subgroup.**
- **In the overall population and non-severe subgroup, average bleed rates remained low, high proportions of patients had zero bleeding episodes, and injection frequency and dose remained stable across 4 years.**

INTRODUCTION

- Inadequate management of persons with haemophilia A (PwHA) can lead to haemophilic arthropathy, with pain, disability and reduced quality of life.[1,2]
- Joint health improved with prophylactic extended half-life (EHL) efmoroctocog alfa (rFVIIIFc; Elocta®) in Phase 3 and 4 studies;[3–5] however, longer-term evidence in larger datasets would be beneficial.
- A-MORE (NCT04293523) is an ongoing, 48-month, prospective, non-interventional study in PwHA of all ages/severities receiving rFVIIIFc prophylaxis in 14 European/Middle Eastern countries.[6]

AIM

- To report treatment outcomes across 4 years in the overall population and non-severe subgroup of PwHA in the fifth interim analysis of the ongoing A-MORE study (data cutoff: 29 August 2025).

METHODS

- A-MORE study design and endpoints are shown in **Figure 1**.
- Annualised bleeding rate (ABR) and annualised joint bleeding rate (AJBR) were investigated with an unadjusted negative binomial regression model, resulting in model-based means and 95% confidence intervals (CI).
- The following were descriptively calculated: target joint development, resolution and recurrence (defined under **Figure 1**); the proportions of patients with zero bleeds and zero joint bleeds; median (interquartile range; IQR) weekly prescribed dose and weekly injection frequency.
- Joint health data were assessed with Hemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) and Hemophilia Joint Health Score (HJHS), with least-squares means (95% CI) estimated using mixed model repeated measures.

RESULTS

Demographics and observation time

- Of 423 PwHA, 38 had non-severe haemophilia (**Table 1**).
- Median (IQR) observation time was 38.3 (30.0–44.1) months in the overall population and 39.2 (31.2–46.5) months in the non-severe subgroup.

Bleeding rates and rFVIIIFc prophylaxis usage

- ABR and AJBR remained low throughout the 4-year observation period (**Table 2 and Figure 2**) and were slightly lower in the non-severe subgroup versus the overall population despite comparable weekly doses and injection frequencies (**Table 2**).
- High proportions of PwHA experienced zero bleeds and zero joint bleeds through 4 years in the overall population and non-severe subgroup (**Table 2 and Figure 3**).
- Weekly doses and injection frequencies remained stable through 4 years in the overall population and non-severe subgroup.

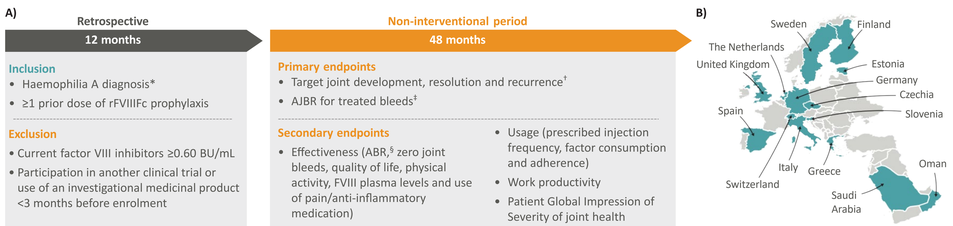
Target joints

- Of 26 target joints in 17 PwHA:
  - 21 target joints (14 PwHA) were observed at enrolment, including 4 joints (3 PwHA) in the non-severe subgroup.
  - 5 target joints (4 PwHA) developed during the study; none were observed in the non-severe subgroup.
  - 22 target joints (13 PwHA) resolved; all 4 target joints in the non-severe subgroup resolved.
  - none were recurring.

HEAD-US and HJHS

- For PwHA in the overall population with available data (HEADS-US, n=162; HJHS, n=191), average joint health scores remained stable throughout the 4-year observation period (**Table 3**).
- HEADS-US and HJHS were not calculated for the non-severe subgroup due to low sample size.

Figure 1: A-MORE study design (NCT04293523)



*Regardless of severity, sex or age; †Target joint: a single joint in which ≥3 spontaneous bleeds occur within a consecutive 6-month period. Target joint resolution: ≤2 bleeds into the joint within a consecutive 12-month period. Target joint recurrence: ≥3 spontaneous bleeds in a single joint within any consecutive 6-month period after target joint resolution; ‡AJBR for treated bleeds was defined as: (total number of treated bleeding episodes started during the observation period/length of observation period) × 365.25. Calculated only for patients with an observation period of ≥3 months. Surgery bleeds were excluded; §ABR for treated and total bleeds are evaluated. Panel B shows countries with participating study sites where patients have been enrolled.

Table 1: Baseline demographics*

	Overall population (N=423)	Non-severe subgroup (n=38)
Age (years), median (range)	22.0 (0–83)	33.2 (3–77)
Age category (years), n (%)		
<12	140 (33.1)	10 (26.3)
12–17	51 (12.1)	4 (10.5)
18–39	137 (32.4)	11 (28.9)
40–64	81 (19.1)	10 (26.3)
≥65	14 (3.3)	3 (7.9)
Sex, n (%)		
Male	422 (99.8)	38 (100)
Female	1 (0.2)	0
Weight (kg), median (range)	67.0 (5.9–134.0)	71.5 (14.8–128.5)
Haemophilia severity, n (%)		
Severe	385 (91.0)	0
Moderate	31 (7.3)	31 (81.6)
Mild	7 (1.7)	7 (18.4)
Impaired joints at enrolment†		
Patients with impaired joints, n (%)	134 (31.7)	16 (42.1)
No data reported, n (%)	4 (0.9)	2 (5.3)
Number of impaired joints	341	38
Target joints at enrolment‡		
Patients with target joints, n (%)	14 (3.3)	3 (7.9)
Number of target joints	21	4
FVIII treatment for ≥3 months in 12 months prior to enrolment, n (%)§		
EHL FVIII		
rFVIIIFc	389 (92.0)	34 (89.5)
Other EHL FVIII	1 (0.2)‖	0
SHL FVIII	54 (12.8)	8 (21.1)
History of inhibitors, n (%)	80 (18.9)	3 (7.9)

*For all patients enrolled in the study who met the inclusion criteria and none of the exclusion criteria; †Impaired joints were defined by the following question in the Case Report Form: 'Are there any additional joints, not currently reported in target joint or joint surgical history section, with clinically relevant structural or functional abnormalities present at study enrolment?'; ‡Target joints were considered independently of impaired joints and were reported separately by investigators. Target joints are defined in a Figure 1 footnote; §Multiple answers were possible for the treatments used within 12 months prior to enrolment; ‖One patient received another EHL product before switching to rFVIIIFc in the 12-month period prior to enrolment.

Table 2: Outcomes across the 4-year observation period

	Overall population (N=414*)	Non-severe subgroup (n=36*)
ABR (treated bleeds), mean†‡ (95% CI)	**0.59** (0.50–0.70)	**0.39** (0.23–0.67)
AJBR (treated bleeds), mean†‡ (95% CI)	**0.37** (0.30–0.45)	**0.29** (0.15–0.56)
Zero bleeds across 4 years, % of PwHA‡	**46.9** (n=194)	**52.8** (n=19)
Zero joint bleeds across 4 years, % of PwHA‡	**62.3** (n=258)	**66.7** (n=24)
Weekly prescribed dose (IU/kg), median (IQR)	**83** (63–104)	**82** (65–101)
Weekly injection frequency, median (IQR)	**2.0** (2.0–2.7)	**2.0** (1.9–2.3)

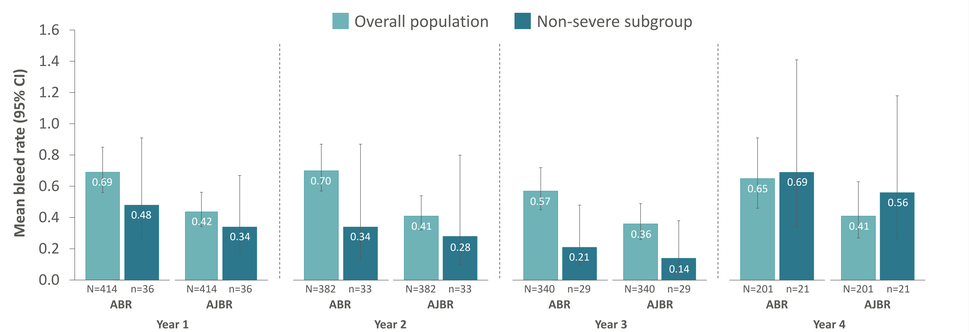
*PwHA with ≥3 months follow-up only. †Unadjusted negative binomial regression model. ‡Excluding bleeds due to surgery.

Table 3: Joint health scores in the overall population

	Baseline	Year 1	Year 2	Year 3	Year 4
HEAD-US (n=162)					
Total score, least-squares mean (95% CI)	**8.49** (6.66–10.32)	**8.15** (6.38–9.92)	**8.14** (6.35–9.93)	**8.24** (6.31–10.17)	**8.45** (6.44–10.46)
HJHS (n=191)					
Total score, least-squares mean (95% CI)	**10.16** (7.64–12.67)	**10.19** (7.70–12.67)	**10.23** (7.70–12.77)	**10.62** (8.01–13.23)	**10.31** (7.69–12.92)

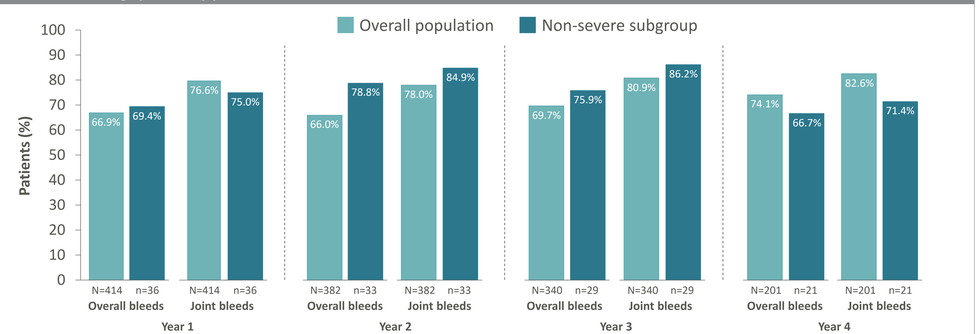
Mixed model repeated measures, based on patients with ≥1 assessment (n). HEADS-US and HJHS were not calculated for the non-severe subgroup due to low sample size. HEAD-US possible range: 0–48. HJHS possible range (including gait score): 0–124.

Figure 2: Bleeding rates (treated) by year



PwHA with ≥3 months follow-up only. Unadjusted negative binomial regression. Excluding bleeds due to surgery.

Figure 3: Zero bleeding episodes by year



PwHA with ≥3 months follow-up only. Excluding bleeds due to surgery.

Abbreviations

ABR, annualised bleeding rate; **AJBR,** annualised joint bleeding rate; **BU,** Bethesda unit; **CI,** confidence interval; **EHL,** extended half-life; **HEAD-US,** Hemophilia Early Arthropathy Detection with Ultrasound; **HJHS,** Hemophilia Joint Health Score; **IQR,** interquartile range; **IU,** international units; **kg,** kilograms; **PwHA,** persons with haemophilia A; **rFVIIIFc,** recombinant factor VIII Fc fusion protein; **SHL,** standard half-life.

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