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Long-Term Joint Health Outcomes With a Recombinant Factor VIII Fc From the 48-Month Prospective, Observational A-MORE Study: Third Interim Analysis of Up to 24 Months

Jan Astermark,[1] Johannes Oldenburg,[2] Rubén Berrueco,[3] Annarita Tagliaferri,[4] Mikaela Alenäs,[5] Markus Fusser,[5] Stefan Lethagen[5]

[1]Skåne University Hospital and Lund University, Department of Haematology, Oncology and Radiation Physics, Malmö, Sweden; [2]University Clinic Bonn, Institute of Experimental Haematology and Transfusion Medicine, Bonn, Germany; [3]Hospital Sant Joan de Déu, Pediatric Hematology Department, Barcelona, Spain; [4]University Hospital of Parma, Regional Reference Center for Inherited Bleeding Disorders, Parma, Italy; [5]Sobi, Stockholm, Sweden

CONCLUSION

- **Third interim real-world A-MORE data align with previous analyses, demonstrating that prophylaxis with a recombinant fusion VIII Fc fusion protein (herein referred to as rFVIIIFc) offers long-term effective bleed and joint protection in persons with hemophilia A.**
- **A high proportion of patients treated with rFVIIIFc prophylaxis had zero bleeding episodes, low average joint health scores, and stable injection frequency and dose over 24 months.**
- **Future analyses should stratify patients by prior extended half-life/standard half-life treatment, to understand the effect prior treatment may have on outcomes; such analyses over a longer period will further clarify the effectiveness of rFVIIIFc prophylaxis on joint health in a real-world setting.**

INTRODUCTION

- The management of persons with hemophilia A (PwHA) can sometimes be inadequate and lead to hemophilic arthropathy, causing pain, disability and reduced health-related quality of life.[1,2]
- Prophylaxis (PPX) with extended half-life (EHL) efmoroctocog alfa (Elocta®; herein referred to as rFVIIIFc), has demonstrated improved joint health in patients with severe hemophilia A in phase 3 studies;[3] however, more real-world data are needed.
- A-MORE (NCT04293523) is an ongoing 48-month prospective, non-interventional study, with the primary aim of evaluating the long-term effectiveness of rFVIIIFc on joint health in a real-world setting; results from the third interim analysis are reported here.[4]

METHODS

- The A-MORE study enrolled PwHA of all ages/severities receiving rFVIIIFc PPX across 14 countries in Europe/the Middle East. Eligible patients received ≥1 prior dose of rFVIIIFc prophylaxis.
- This descriptive analysis presents baseline characteristics and third interim data (data cut off: 7 July 2023) from the full baseline population, including 12-month retrospective and up to 24-month prospective data.
- The key objectives and endpoints for this study are shown in **Figure 1**.

RESULTS

- Overall, 419 PwHA were analyzed (418 males); median (range) age was 22 (0–83) years (**Table 1**). Median (range) on-study follow-up duration was 14.9 (0.0–35.0) months.
  - Within 12 months pre-study, 387 (92.4%) and 51 (12.2%) PwHA received ≥3 months EHL and standard half-life (SHL) FVIII PPX, respectively.
- Mean overall and joint annualized bleeding rates (ABRs) were low at baseline and remained low at the 12- and 24-month visits (n=356 and n=207, respectively, subset with available data post-baseline; **Figure 2**).
  - The proportion of patients with zero bleeds remained stable across these timepoints (**Figure 3**).
- Average weekly injection frequency (**Figure 4A**) and prescribed weekly dose (**Figure 4B**) remained consistent from baseline to 24 months; however, direct comparisons over time should be made with caution due to the differing population size.
- Average Total Hemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) score and Hemophilia Joint Health Score (HJHS) remained stable from baseline to 24 months in patients with data available at each timepoint (**Table 2**).

Figure 1: A-MORE study objectives and key endpoints

1 Primary objective: Evaluate long-term effectiveness of rFVIIIFc on joint health

Primary endpoints – joint health parameters:
- Target joint development, resolution, and recurrence[a]
- Annualised joint bleeding rate for treated bleeds[b]

Secondary endpoints to support primary objective:
- Ultrasound (HEAD-US, range 0–48)
- HJHS (range 0–124)
- World Federation of Hemophilia (WFH) Physical Examination Score (Gilbert Score)

2 Secondary objective: Further evaluate effectiveness and usage of rFVIIIFc

Secondary endpoints:
- Effectiveness: ABR,[c] occurrence of zero joint bleeds, quality of life, physical activity, FVIII plasma levels and use of pain/anti inflammatory medication
- Usage: Prescribed injection frequency and factor consumption, and adherence
- Work productivity
- Patient Global Impression of Severity (PGI-S) of joint health

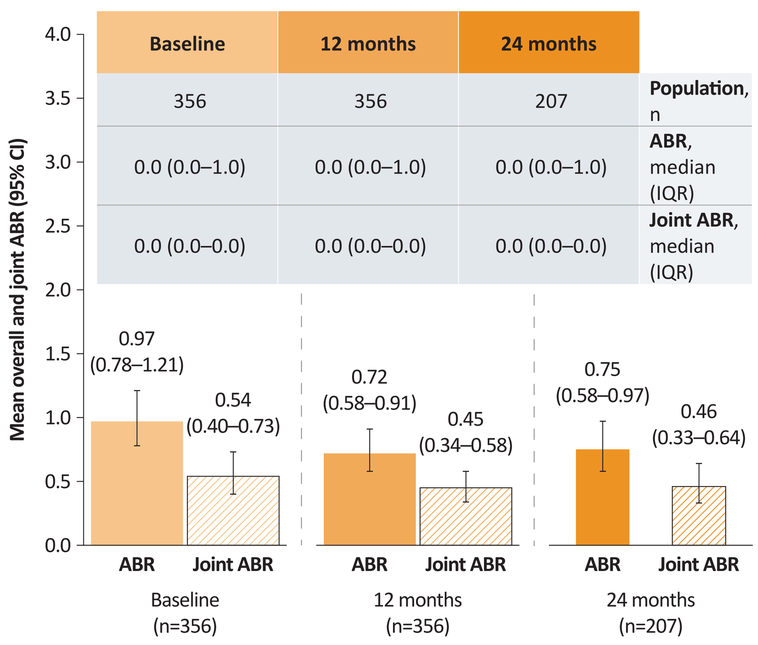
[a]Target joint: a single joint in which ≥3 spontaneous bleeds occur within a consecutive 6-month period. Target joint resolution: ≤2 bleeds into the joint within a consecutive 12-month period. Target joint recurrence: ≥3 spontaneous bleeds in a single joint within any consecutive 6-month period after target joint resolution. [b]Joint ABR 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. [c]ABR for treated and total bleeds are evaluated.

Table 1: Baseline demographics and characteristics

Characteristic (n [%] unless otherwise specified)	Overall population (N=419)
On-study follow-up duration (months),[a] mean (SD); (median [range])	15.0 (8.8); (14.9 [0.0–35.0])
Sex	
Male	418 (99.8)
Female	1 (0.2)
Age (years), mean (SD); (median [range])	25.1 (18.8); (22.0 [0.0–83.0])
Age groups (years)	
0–11	140 (33.4)
12–17	49 (11.7)
18–39	137 (32.7)
40–64	79 (18.9)
≥65	14 (3.3)
Weight (kg),[b] mean (SD); (median [range])	60.3 (29.8); (67.0 [5.9–134.0])
BMI (kg/m²),[c] mean (SD); (median [range])	
≥18 years (n=225)	25.9 (4.8); (25.4 [17.3–46.4])
<18 years (n=180)	18.4 (4.0); (17.2 [11.6–33.3])
Hemophilia severity	
Severe	381 (90.9)
Moderate	31 (7.4)
Mild	7 (1.7)
Previously untreated/minimally treated patients[d]	13 (3.1)
Prior prophylaxis type[e]	
Primary	158 (37.7)
Secondary	158 (37.7)
Tertiary	63 (15.0)
Unknown	40 (9.6)[f]
Surgical history (ankle, elbow, knee)	71 (17.0)[f]
History of inhibitors[g]	78 (18.6)
≥3 months FVIII treatment in 12 months prior to enrollment	407 (97.1)
EHL FVIII	387 (92.4)
rFVIIIFc	386 (92.1)
SHL FVIII	51 (12.2)
Pain/anti-inflammatory medication use in 30 days prior to enrollment	81 (19.3)
History of treated bleeds 12 months prior to enrollment[h]	
No bleeds	265 (63.2)[f]
No joint bleeds	331 (79.0)
Target joints,[i] patients [number of joints]	15 (3.6) [20]
Impaired joints,[j] patients [number of joints]	122 (29.1) [307]

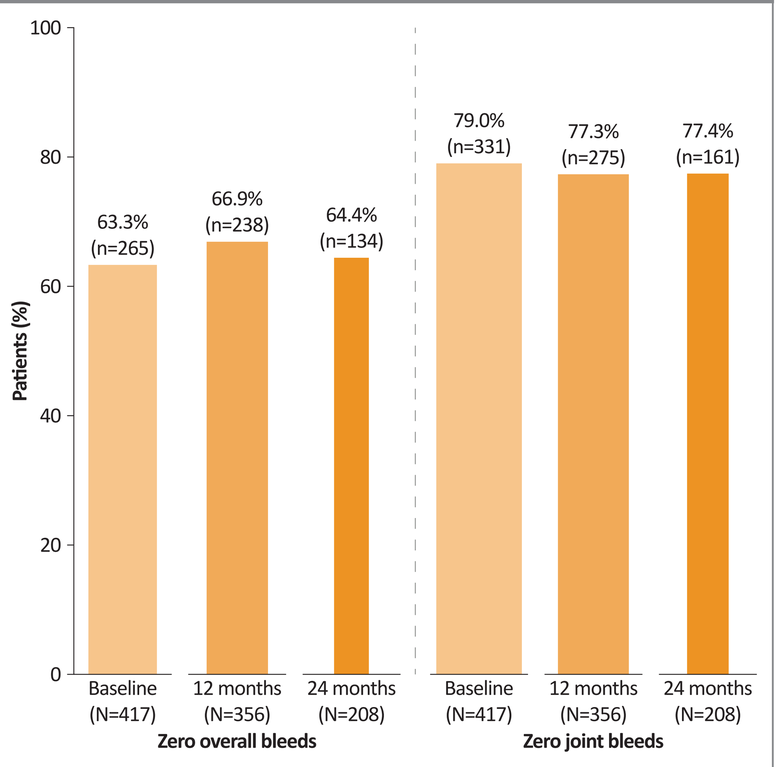
[a]Represents the timespan from enrollment to end of study. [b]n=415. [c]n=405. [d]Previously untreated/minimally treated patients had no previous prophylactic FVIII treatment (other than rFVIIIFc) prior to enrollment, were exposed to rFVIIIFc treatment prior to enrollment for a maximum of 50 days, and were ≤6 years old at enrollment; on-demand treatment with any other FVIII prior to rFVIIIFc was allowed. [e]5/419 patients also received on-demand treatment during the 12 months prior to enrollment. [f]Value differs slightly from abstract due to rounding. [g]Inhibitor titers ≥0.60 BU/mL. [h]n=417. [i]n=418. [j]n=401.

Figure 2: Average overall and joint ABR (treated bleeds) in patients receiving rFVIIIFc PPX at baseline, 12 months, and 24 months, with a post-baseline assessment



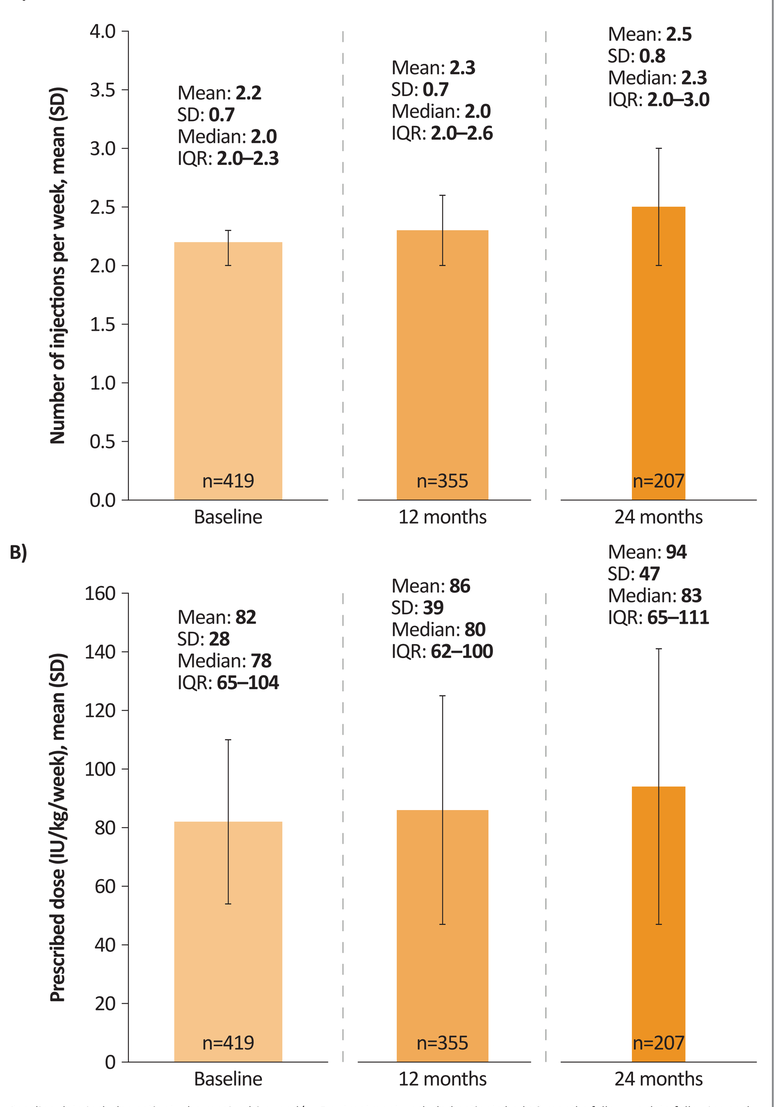
Baseline data include patients who received SHL and/or EHL treatment. Data presented in the graph are model-based mean (95% CI) ABR, derived from an unadjusted negative binomial regression model, using baseline values only for all patients that had recorded values at a 12-month visit and follow-up data of ≥3 months. Data presented in the table are median (IQR) for patients with values after baseline recorded at each timepoint. Bleeding episodes due to surgery are not included. Widths of bars are proportional to the number of patients included in the analyses at each timepoint.

Figure 3: Proportion of patients with zero bleeding episodes at baseline, 12 months, and 24 months



Baseline data include patients who received SHL and/or EHL treatment. Included patients had ≥3 months follow-up data following each timepoint only. Widths of bars are proportional to the number of patients included in the analyses at each timepoint.

Figure 4: Average weekly injection frequency and prescribed weekly dose at baseline, 12 months, and 24 months



Baseline data includes patient who received SHL and/or EHL treatment. Included patients had ≥3 months follow-up data following each timepoint only. Only prophylactic injections are included. Widths of bars are proportional to the number of patients included in the analyses at each timepoint.

Table 2: Total and change from baseline in joint health scores at 12 months and 24 months

	Baseline (N=419)	12 months (N=342)	24 months (N=163)
HEAD-US			
Total Score, median (IQR) [n]	3.0 (0.0–13.0) [88]	2.5 (0.0–10.0) [96]	1.0 (0.0–11.0) [47]
Change from baseline, mean (SD) [n]	N/A	–0.3 (2.0) [68]	–0.9 (1.9) [36]
HJHS Total			
Total Score, median (IQR) [n]	1.0 (0.0–15.0) [103]	2.0 (0.0–20.0) [85]	3.0 (0.0–25.0) [57]
Change from baseline, mean (SD) [n]	N/A	–0.3 (2.7) [47]	–0.2 (3.4) [29]

Included patients had ≥3 months follow-up data following each timepoint only and multiple assessments available. HEAD-US score maximum possible range: 0–48; HJHS maximum possible range: 0–124. HEAD-US baseline mean (SD) score: 7.4 (9.8), n=88; HJHS baseline mean (SD): 9.2 (15.4), n=103.

References

1. O'Hara J, et al. *Health Qual Life Outcomes* 2018;16:84; **2.** Fischer K, et al. *Haemophilia* 2016;22:833–40; **3.** Oldenburg J, et al. *Haemophilia* 2018;24:77–84; **4.** ClinicalTrials.gov (NCT04293523).

Disclosures

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Abbreviations

ABR: annualized bleeding rate; **BMI:** body mass index; **BU:** Bethesda Unit; **EHL:** extended half-life; **FVIII:** factor VIII; **HEAD-US:** Hemophilia Early Arthropathy Detection with Ultrasound; **HJHS:** Hemophilia Joint Health Score; **IU:** International Unit; **IQR:** interquartile range; **PwHA:** persons with hemophilia A; **PGI-S:** Patient Global Impression of Severity; **PPX:** prophylaxis; **rFVIIIFc:** recombinant factor VIII Fc fusion protein; **SD:** standard deviation; **SHL:** standard half-life; **WFH:** World Federation of Hemophilia.

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Ethics Statement

The A-MORE study protocol received approval from institutional review boards and/or ethics committees at participating institutions. Patients provided signed and dated informed consent before participating in the study.