PO120

Real-World Effectiveness and Usage of a Recombinant Factor VIII Fc: Interim Analysis in Adults from the 48-Month Prospective, Observational A-MORE Study

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CONCLUSIONS

- **Real-world data from the fourth interim analysis of the ongoing A-MORE study indicate that prophylaxis with recombinant factor VIII Fc fusion protein (rFVIIIFc) can provide and maintain long-term effective bleed protection in adults (≥18 years) with haemophilia A, aligning with previous analyses.**
- **Bleed outcomes were consistent across adult age groups. A high proportion of patients experienced zero bleeding episodes and stable average joint health scores, demonstrating effective joint protection with rFVIIIFc prophylaxis.**

INTRODUCTION

- The treatment management of persons with haemophilia A (PwHA) can be insufficient and lead to pain, disability and overall reduced health-related quality of life.[1,2]
- Improvements in joint health have been observed in PwHA undergoing extended half-life (EHL) efmoroctocog alfa (Elocta®; herein referred to as rFVIIIFc) prophylaxis (PPX) in phase 3 and 4 studies.[3–5]
- However, long-term real-world data are needed to further corroborate this finding.
- A-MORE (NCT04293523) is an ongoing 48-month prospective, non-interventional study in PwHA of all ages/severities receiving rFVIIIFc PPX across 14 countries in Europe and the Middle East.[6]

AIM

- To report results from the fourth interim analysis in the adult population enrolled in the ongoing A-MORE study.

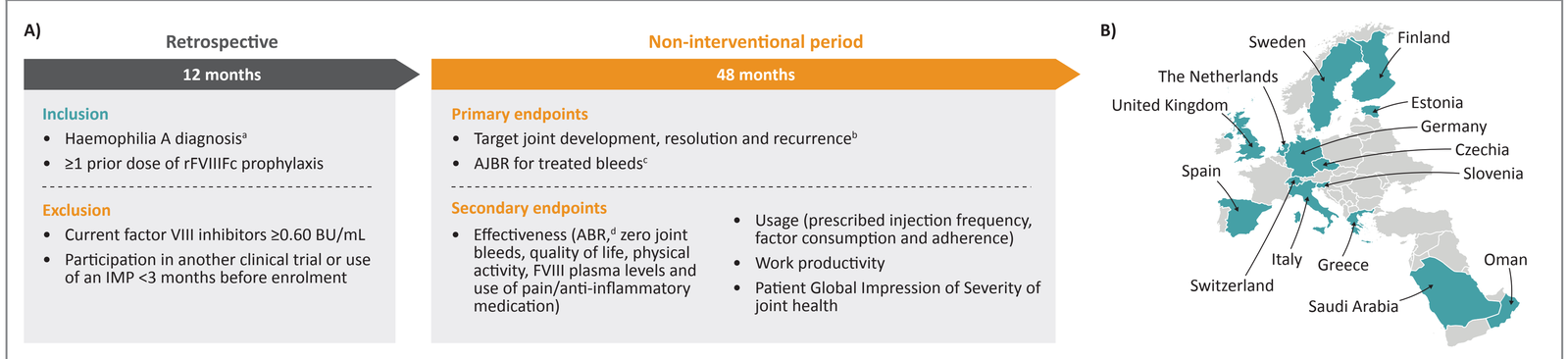
METHODS

- The A-MORE study evaluates bleeding and joint health outcomes in PwHA receiving ≥1 dose of rFVIIIFc PPX.
- This analysis presents data from the fourth interim analysis (data cut off: 08 July 2024), focusing on the adult population (≥18 years old at enrolment) with 12-month retrospective period data and a recorded follow-up.
- The A-MORE study design is shown in **Figure 1**.
- Here, modelled mean data are presented for overall and joint annualised bleeding rate (ABR and AJBR) which represent the estimated mean from an unadjusted negative binomial regression model with the corresponding 95% confidence interval (CI).
  - ABR and AJBR data are grouped by those aged 18 to <40 years, 40 to <65 years and ≥65 years.
- Joint health data were assessed with least square means (with the corresponding 95% CI), estimated using a mixed model repeated measures approach, for patients with ≥1 assessment.
- Zero bleeds, weekly injection frequency and weekly factor consumption data are reported for adult patients over time.
- Health-related quality of life was assessed using the EQ-5D-5L Visual Analogue Scale (VAS).

RESULTS

- Of the 426 PwHA enrolled in A-MORE, 232 (1 female PwHA) had recorded follow-up with ≥12 months retrospective period.
  - Median (range) age was 35.0 (18–83) years (**Table 1**). Median (interquartile range [IQR]) observational period from enrolment to data cut-off was 29.8 (23.4–35.3) months.
- Within 12 months pre-study, 218 (94.0%) and 32 (13.8%) PwHA received ≥3 months EHL and standard half-life (SHL) FVIII products, respectively.
- At enrolment, 231 adult patients (n=1 missing) had been on rFVIIIFc prophylaxis for a median (IQR) of 757.0 (327.0–1,057.0) days, corresponding to 2.14 (0.9–2.9) years.
- Over 36 months, ABRs and AJBRs across the age groups were low and tended to be highest in the 40 to <65 age group (**Figure 2A**).
- Mean ABRs and AJBRs were low at baseline and remained low at the 12-, 24- and 36-month visits (n=224, n=205 and n=137, respectively; subset with available data post-baseline; **Figure 2B**).
- The proportion of adult patients with zero overall and joint bleeds increased from baseline to 36 months (**Figure 3**).
- Average weekly injection frequency (**Figure 4A**) and prescribed weekly dose (**Figure 4B**) remained consistent over 36 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 36 months (**Table 2**).
- Mean (standard deviation [SD]) EQ-5D-5L VAS remained stable from a baseline value of 74.7 (18.9) to 76.6 (19.2) and 78.1 (15.3) at 12 and 24 months, respectively. Data at 36 months are not reported due to a limited number of patients.
- rFVIIIFc treatment was well tolerated with safety data in this interim analysis consistent with the previously reported safety profile.

Figure 1: A-MORE study design (NCT04293523)



[a]Regardless of severity, of any sex and age. [b]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. [c]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. [d]ABR for treated and total bleeds are evaluated. Panel B shows countries with participating study sites where patients have been enrolled into the study at the interim data cut (08 July 2024; N=426).

Table 1: Patient demographics and baseline characteristics

	Total analysis population (N=232)
Age (years), median (range)	35.0 (18–83)
Age category (years), n (%)	
18–<40	138 (59.5)
40–<65	80 (34.5)
≥65	14 (6.0)
BMI (kg/m²),[a] mean (SD)	25.9 (4.8)
Haemophilia severity, n (%)	
Severe	208 (89.7)
Moderate	20 (8.6)
Mild	4 (1.7)
Prior prophylaxis type, n (%)	
Primary	46 (19.8)
Secondary	89 (38.4)
Tertiary	60 (25.9)
Unknown	37 (16.0)
Surgical history (ankle, elbow, knee), n (%)	71 (30.6)
History of inhibitors,[b] n (%)	46 (19.8)
Pain/anti-inflammatory medication use in 30 days prior to enrolment, n (%)	79 (34.1)
History of treated bleeds 12 months prior to enrolment, n (%)	
No bleeds	148 (63.8)
No joint bleeds	176 (75.9)
Target joints, n (%) [number of target joints]	9 (3.9) [15]
Impaired joints,[c] n (%) [number of impaired joints]	115 (49.6) [313]

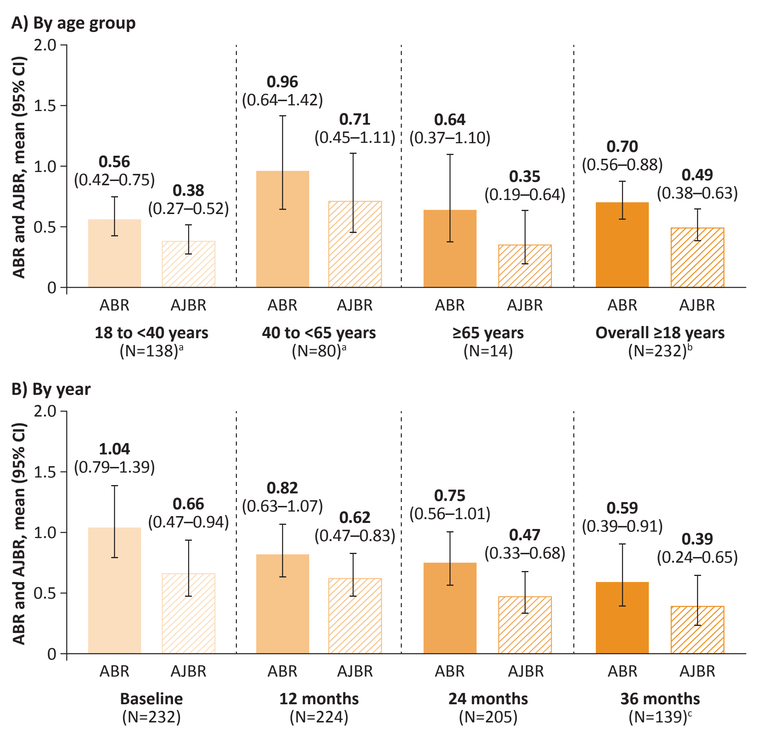
[a]Data missing for n=5 patients. [b]Inhibitor titres ≥0.60 BU/mL. [c]Data missing for n=7 patients.

Table 2: Total joint health scores over 36 months

	Baseline	12 months	24 months	36 months
HEAD-US[a]				
Total score, mean (95% CI), [n]	12.53 (10.01–15.05), [n=47]	12.29 (9.81–14.78), [n=50]	11.60 (9.07–14.12), [n=48]	11.13 (8.79–13.47), [n=23]
HJHS[b]				
Total score, mean (95% CI), [n]	19.94 (15.16–24.71), [n=46]	19.98 (15.36–24.56), [n=52]	19.90 (15.11–24.69), [n=56]	20.42 (15.41–25.41), [n=32]

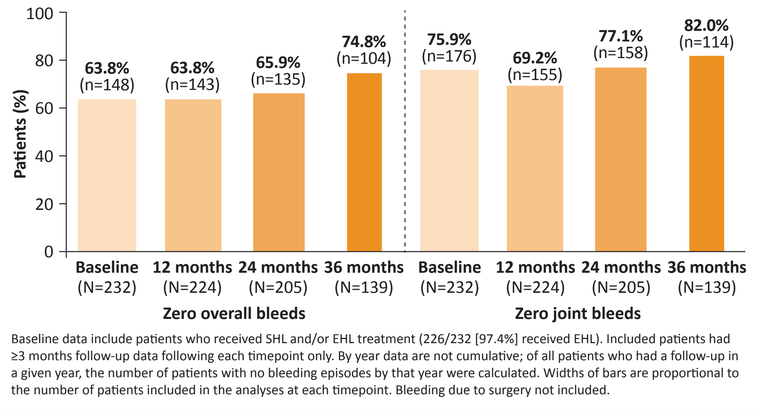
Least-square estimated mean (95% CI) at Baseline to 36 months was estimated through a mixed model repeated measures approach, based on patients with at ≥1 assessment; 83 and 87 patients for [a]HEAD-US and [b]HJHS, respectively. Patients may not be the same at each timepoint. HEAD-US score maximum possible range: 0–48. HJHS maximum possible range: 0–120. n is the number of patients with observed score at each timepoint. By year data are not cumulative.

Figure 2: Mean ABR and AJBR (treated bleeds) in patients receiving rFVIIIFc PPX by age (A) and year (B)



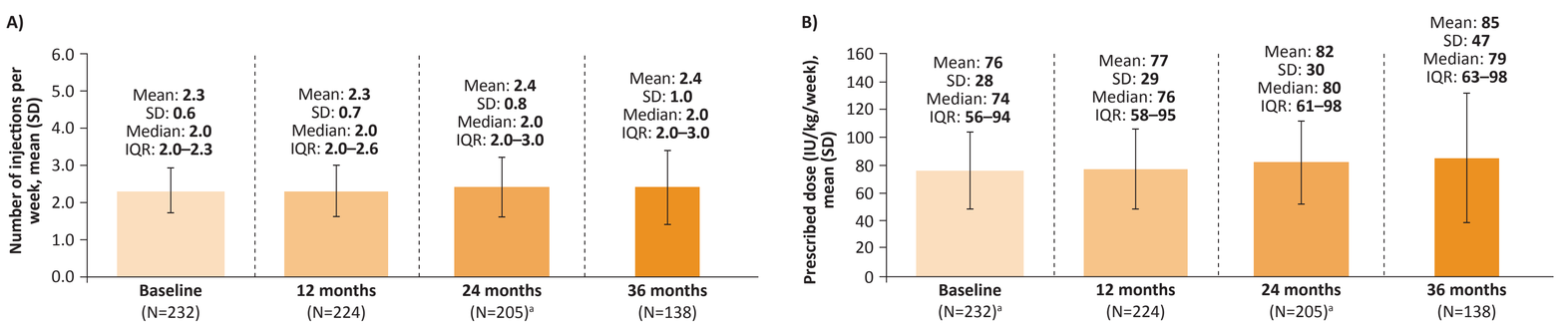
Data presented in the graphs are model-based mean (95% CI) ABR, derived from an unadjusted negative binomial regression model, using baseline values only for patients who recorded values at each visit and ≥3 months follow-up data. Baseline AJBR data are based on patients with ≥12 months retrospective follow-up. Bleeding episodes due to surgery are not included. By year data are not cumulative. [a]n=4 missing. [b]n=8 missing. [c]n=2 missing.

Figure 3: Proportion of patients with zero bleeding episodes (treated bleeds) from baseline to 36 months



Baseline data include patients who received SHL and/or EHL treatment (226/232 [97.4%] received EHL). Included patients had ≥3 months follow-up data following each timepoint only. By year data are not cumulative; of all patients who had a follow-up in a given year, the number of patients with no bleeding episodes by that year were calculated. Widths of bars are proportional to the number of patients included in the analyses at each timepoint. Bleeding due to surgery not included.

Figure 4: Average weekly injection frequency (A) and prescribed dose (B) over 36 months



Baseline data include patients who received SHL and/or EHL treatment (226/232 [97.4%] received EHL). 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. [a]n=1 missing.

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.** Oldenburg J, et al. *Eur J Haematol.* 2024;0:1–10; **5.** Bidlingmaier C, et al. *Res Pract Thromb Haemost.* 2024;8:e102482; **6.** ClinicalTrials.gov (NCT04293523).

Disclosures

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Abbreviations

ABR: annualised bleeding rate; **AJBR:** annualised joint bleeding rate; **BU:** Bethesda unit; **BMI:** body mass index; **CI:** confidence interval; **EHL:** extended half-life; **FVIII:** factor VIII; **HEAD-US:** Hemophilia Early Arthropathy Detection with Ultrasound; **HJHS:** Hemophilia Joint Health Score; **IMP:** investigational medicinal product; **IQR**: interquartile range; **IU:** international units; **kg:** kilograms; **PPX:** prophylaxis; **PwHA:** persons with haemophilia A; **rFVIIIFc:** recombinant factor VIII Fc fusion protein; **SD:** standard deviation; **SHL:** standard half-life; **VAS:** visual analogue scale.

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