PO079

Real-World Effectiveness and Usage of a Recombinant Factor VIII Fc: Interim Analysis in Children and Adolescents 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 effective bleed protection over a prolonged period (36 months) in paediatric and adolescent patients (<18 years) with haemophilia A.**
- **Bleed outcomes were similar across paediatric age groups and a high proportion of patients had zero bleeding episodes. Additionally, joint health scores remained stable across the study, demonstrating effective joint protection with rFVIIIFc prophylaxis.**

INTRODUCTION

- Management of persons with haemophilia A (PwHA) can be insufficient and lead to haemophilic arthropathy, resulting in pain, disability and reduced health-related quality of life.[1,2]
- Prophylaxis with extended half-life (EHL) efmoroctocog alfa (Elocta®; herein rFVIIIFc) has been associated with long-term improvements in joint health in phase 3 and 4 studies.[3–5]
- However, continued real-world evidence is needed to confirm these findings.
- A-MORE (NCT04293523) is an ongoing 48-month prospective, non-interventional study in PwHA of all ages/severities receiving rFVIIIFc prophylaxis across 14 countries in Europe and the Middle East.[6]

AIM

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

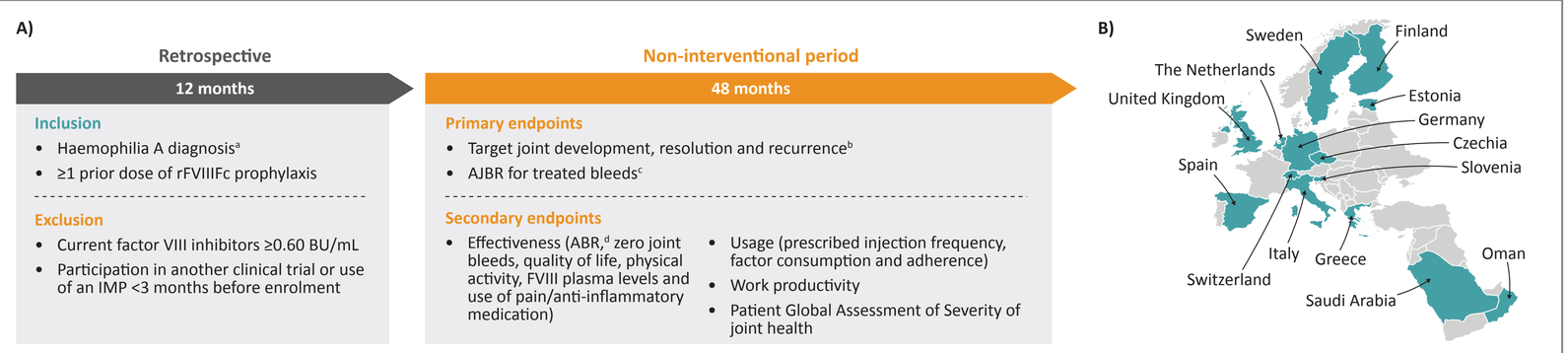
METHODS

- This descriptive analysis presents data from the fourth interim analysis (data cut off: 08 July 2024) of the A-MORE study, focusing on paediatric and adolescent PwHA (<18 years at enrolment) receiving rFVIIIFc prophylaxis with 12-month retrospective period data and a recorded follow-up.
- The A-MORE study design is shown in **Figure 1**.
- 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).
- Joint health data were assessed with least square means, estimated through a mixed model repeated measures approach, for patients with ≥1 assessment.
- Bleeds data are grouped by those aged <12 years (paediatric) and 12 to <18 years (adolescents).

RESULTS

- Of 426 PwHA enrolled in A-MORE, 187 paediatric PwHA (all males) had recorded follow-up.
  - Median (range) age was 8.3 (0–17) years (**Table 1**). Median (interquartile range [IQR]) observational period from enrolment to data cut-off was 26.9 (21.1–34.0) months.
- Within 12 months pre-study, 169 (90.4%) and 20 (10.7%) PwHA received ≥3 months rFVIIIFc and standard half-life (SHL) FVIII products, respectively.
- At enrolment, paediatric patients had rFVIIIFc treatment for a median (IQR) of 375 (149–778) days.
- Over 36 months, ABRs and AJBRs were low across age groups with a slightly higher tendency in patients aged 12 to <18 years (n=48; **Figure 2A**).
- Mean ABRs and AJBRs were low at baseline (n=187) and remained low at the 12-, 24- and 36-month visits (n=182, n=168 and n=90, respectively; subset with available data post-baseline; **Figure 2B**).
- The proportion of patients with zero overall and joint bleeds remained stable from baseline to 36 months (**Figure 3**).
- Average weekly injection frequency (**Figure 4A**) and prescribed dose (**Figure 4B**) remained consistent over 36 months; however, direct comparisons over time should be made with caution due to the differing population size.
  - Mean prescribed dose (SD) during the observational period for paediatric patients was 97 (50) International Units (IU)/kg/week, with a median (IQR) weekly injection frequency of 2.0 (2.0–2.5).
- 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**).
- 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=187)
Age (years), median (range)	8.3 (0–17)
Age category (years), n (%)	
<12	139 (74.3)
12–<18	48 (25.7)
BMI (kg/m²),[a] mean (SD)	18.3 (4.0)
Haemophilia severity, n (%)	
Severe	174 (93.1)
Moderate	10 (5.4)
Mild	3 (1.6)
Prior prophylaxis type, n (%)	
Primary	111 (59.4)
Secondary	69 (36.9)
Tertiary	4 (2.1)
Unknown	3 (1.6)
Surgical history (ankle, elbow, knee), n (%)	0 (0.0)
History of inhibitors,[b] n (%)	33 (17.7)
Pain/anti-inflammatory medication use in 30 days prior to enrolment, n (%)	4 (2.1)
History of treated bleeds 12 months prior to enrolment,[c] n (%)	
No bleeds	116 (62.0)
No joint bleeds	155 (82.9)
Target joints, n (%) [number of target joints]	6 (3.2) [6]
Impaired joints, n (%) [number of impaired joints]	17 (9.1) [25]

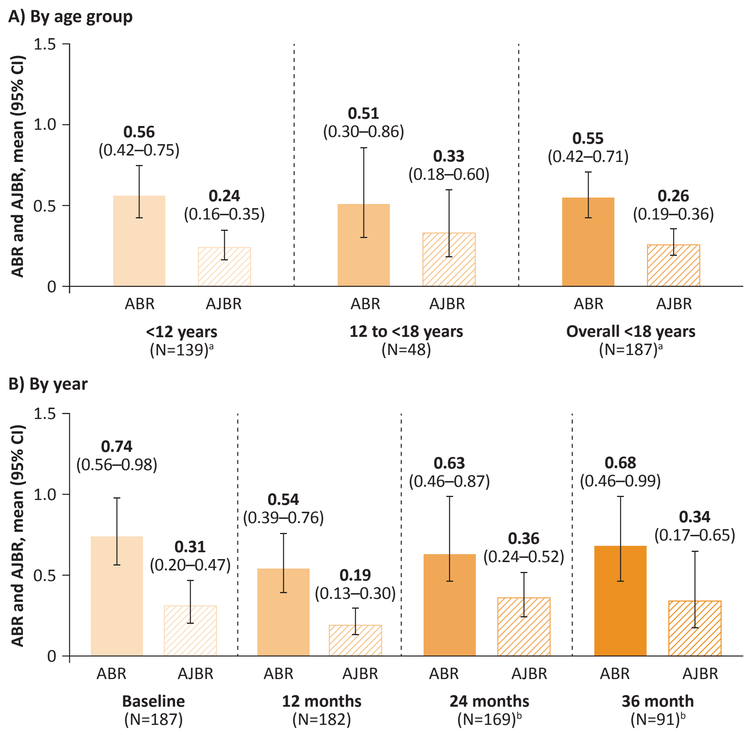
[a]Data missing for n=9 patients. [b]Inhibitor titres ≥0.60 BU/mL. [c]Data missing for n=1 patient.

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]	1.2 (0.6–1.9), [n=41]	1.0 (0.5–1.5), [n=52]	1.0 (0.4–1.7), [n=41]	1.5 (0.6–2.4), [n=20]
HJHS[b]				
Total score, mean (95% CI), [n]	1.2 (0.6–1.8), [n=63]	1.2 (0.5–1.8), [n=63]	1.3 (0.6–1.9), [n=50]	1.6 (0.9–2.4), [n=30]

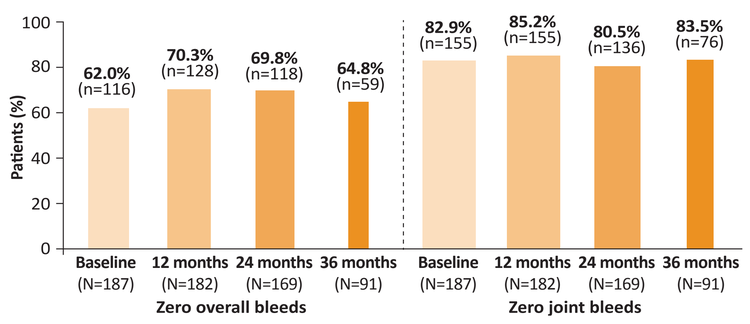
Least-square estimated mean (95% CI) at Baseline to 36 months was estimated through a mixed model repeated measures approach, based on patients with at ≥1 assessment; 59 and 90 patients for [a]HEAD-US and [b]HJHS, respectively. Patients may not be the same at each timepoint. n is the number of patients with observed score at each timepoint. HEAD-US score maximum possible range: 0–48. HJHS maximum possible range: 0–120. By year data are not cumulative.

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



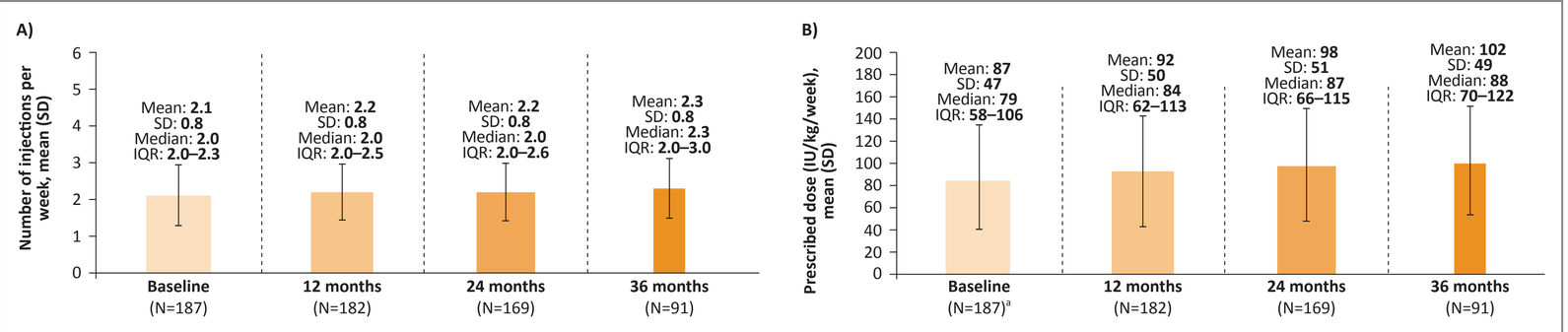
Data presented in the graphs are model-based mean (95% CI) ABR, derived from an unadjusted negative binomial regression model, using baseline values only for patients who recorded values at each visit and ≥3 months follow-up data. Median ABR and AJBR were 0.0 for all age groups and timepoints. Bleeding episodes due to surgery are not included. By year data are not cumulative. [a]n=5 missing. [b]n=1 missing.

Figure 3: Proportion of patients with zero bleeding episodes from baseline to 36 months



Baseline data include patients who received SHL and/or EHL treatment. 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 includes patients 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. [a]n=3 missing.

References

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Abbreviations

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

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