Treatment of Bleeding Episodes with Efanesoctocog Alfa in Adults and Adolescents with Severe Haemophilia A: Second Interim Analysis of the XTEND-ed Long-term Extension Study

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Conclusions

- **Long-term (>2-year) data from the second interim analysis of XTEND-ed show that efanesoctocog alfa is well tolerated and continues to provide highly effective prophylaxis and treatment for BEs in adults and adolescents with severe haemophilia A**
- **A single 50 IU/kg dose of efanesoctocog alfa resolved 94.6% of BEs, regardless of the bleed type or location**

Introduction

- Despite advances in treatment, people with severe haemophilia may still experience bleeding episodes (BEs), which affect health and quality of life[1,2]
- Efanesoctocog alfa is a first-in-class high sustained factor VIII (FVIII) replacement therapy that overcomes the von Willebrand factor–imposed half-life ceiling[3,4]
- The Phase 3, 12-month XTEND-1 trial (NCT04161495) showed that once-weekly efanesoctocog alfa prophylaxis was well tolerated and provided superior bleed prevention to prior FVIII prophylaxis in adults and adolescents with severe haemophilia A[5]
- Participants in XTEND-1 were eligible to continue once-weekly efanesoctocog alfa prophylaxis (50 IU/kg) in Arm A of the XTEND-ed extension study (NCT04644575)

Aim

- To report long-term (>2-year) efficacy and safety of efanesoctocog alfa for the treatment of BEs in adults and adolescents aged ≥12 years with severe haemophilia A completing the second interim analysis of XTEND-ed

Methods

- BEs were treated with a single injection of efanesoctocog alfa (50 IU/kg) with additional doses (30 or 50 IU/kg) administered as needed every 2–3 days
- The data cutoff date for this analysis was 22 February 2024
- Annualised bleed rates (ABRs), model-based ABRs (derived from a negative binomial model of treated BEs), numbers and locations of treated BEs, and the dose and number of efanesoctocog alfa administrations required to resolve BEs are presented descriptively
  - Data are based on treated BEs in the full analysis data set during the efficacy period (first efanesoctocog alfa injection in XTEND-ed Arm A to the day of the last dose), excluding periods of surgery/rehabilitation and long (>28 days) injection intervals
- Participants evaluated response to treatment at 72 hours after the initial treatment using the 4-point International Society on Thrombosis and Haemostasis (ISTH) scale[6]
- Safety was assessed in the safety analysis population, which was identical to the full analysis set

Results

Patient population

- In total, 146 adults/adolescents from Europe (52.1%), Asia (21.9%), North America (13.7%), and South America (12.3%) were enrolled (**Table 1**)
- At data cutoff, 125 participants were continuing the study, 10 participants had discontinued, and 11 had completed the study

Table 1. Patient demographics and baseline disease characteristics

	Participants aged ≥12 years (N=146)
Age, years[a]	
Mean (SD)	37.0 (15.1)
12–17 years, n (%)	21 (14.4)
18–64 years, n (%)	120 (82.2)
≥65 years, n (%)	5 (3.4)
Sex, n (%)	
Male	145 (99.3)
Female	1 (0.7)
Race, n (%)	
White	100 (68.5)
Black/African American	4 (2.7)
Asian	27 (18.5)
Other	2 (1.4)
NR	13 (8.9)
BMI, kg/m²	
Mean (SD)	25.6 (5.2)
Median (min–max)	25.7 (15.0–40.8)

Percentages are based on the number of participants with non-missing data in the full analysis set.
[a]Reported at XTEND-1 baseline. BMI, body mass index; NR, not reported; SD, standard deviation.

Bleeding episodes

- Mean (SD) treatment duration in XTEND-ed was 116.1 (21.9) weeks (range: 14.1–140.6) and mean (SD) treatment exposure was 116.5 (23.0) days (range: 14.0–147.0)
- Over >2 years of follow-up, there were 205 treated BEs (**Table 2**)
- At 1–12 and 12–24 months, 96/146 (65.8%) and 92/137 (67.2%) participants, respectively, had zero bleeds
- At 0–12 months, there were 25 (17.1%), 29 (19.9%), and 9 (6.2%) participants with spontaneous, traumatic, and unknown bleeds, respectively; the majority of these were in joints
- At 12–24 months, there were 22 (16.1%), 28 (20.4%), and 7 (5.1%) participants with spontaneous, traumatic, and unknown bleeds, respectively; these mostly occurred in joints and muscle

Table 2. Summary of annualised BEs over >2 years of follow-up in XTEND-ed

	0–12 months	12–24 months
Number of participants	146	137
Total number of BEs per participant		
Mean (SD)	0.68 (1.29)	0.62 (1.25)
Median (Q1–Q3)	0 (0–1)	0 (0–1)
Treated BEs per participant, n (%)		
0	96 (65.8)	92 (67.2)
1	23 (15.8)	27 (19.7)
2	18 (12.3)	9 (6.6)
3	3 (2.1)	4 (2.9)
4	3 (2.1)	1 (0.7)
5	1 (0.7)	2 (1.5)
>5	2 (1.4)	2 (1.5)
BEs per participant by type, mean (SD)[a]		
Spontaneous	0.24 (0.59)	0.23 (0.62)
Traumatic	0.34 (0.77)	0.30 (0.72)
Unknown	0.10 (0.46)	0.09 (0.49)
Total treated BEs by location, n (%)		
Joint	38 (26.0)	34 (24.8)
Muscle	13 (8.9)	15 (10.9)
Internal	5 (3.4)	7 (5.1)
Skin/mucosa	6 (4.1)	3 (2.2)
Unknown	3 (2.1)	2 (1.5)

[a]Median (Q1–Q3) values were all 0.
BE, bleeding episode; Q, quartile; SD, standard deviation.

Annualised bleeding rates

- During >2 years of XTEND-ed follow-up, the mean (95% CI) model-based ABR for all treated BEs was 0.64 (0.50–0.82)
  - Values for spontaneous, traumatic, and unknown types were 0.23 (0.16–0.32), 0.32 (0.23–0.43), and 0.08 (0.05–0.15)
- ABRs by location are reported in **Table 3**

Table 3. Summary of ABRs by location over >2 years of follow-up in XTEND-ed

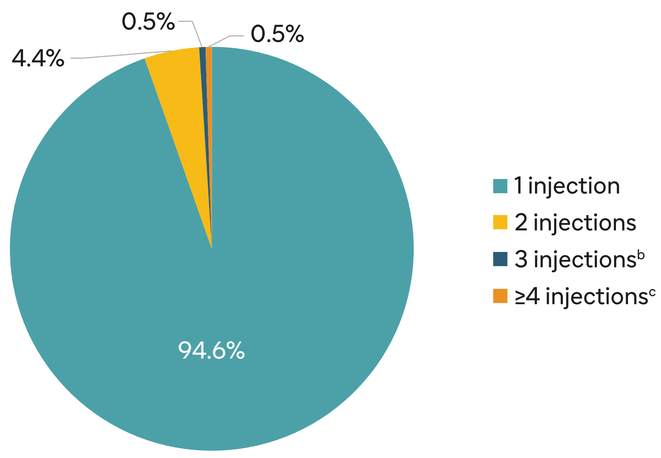
Location	ABR
Joint	
Model-based mean (95% CI)[a]	0.45 (0.33–0.62)
Median (range)	0 (0–4.8)
Muscle	
Model-based mean (95% CI)[a]	0.15 (0.09–0.23)
Median (range)	0 (0–2.2)
Internal	
Model-based mean (95% CI)[a]	0.05 (0.03–0.09)
Median (range)	0 (0–1.2)
Skin/mucosa	
Model-based mean (95% CI)[a]	0.04 (0.02–0.08)
Median (range)	0 (0–1.4)

[a]Model-based mean was estimated using a negative binomial model with the total number of treated BEs during the efficacy period as the response variable and log-transformed efficacy period duration (in years) as an offset variable.
ABR, annualised bleed rate; BE, bleeding episode; CI, confidence interval.

Treatment of bleeding episodes

- A single efanesoctocog alfa injection resolved 94.6% of BEs; 11 BEs required ≥2 injections (**Figure 1**)
- Median (Q1–Q3) average dose per injection and total dose required for BE resolution was 50.2 (32.3–51.4) and 50.3 (32.3–51.7) IU/kg, respectively
- Haemostatic response was rated excellent/good and moderate for 86.9% and 12.5% of BEs, respectively; no improvement was reported for 0.6% of BEs

Figure 1. Summary of BE treatment[a]



[a]All injections (including routine prophylaxis) given from the initial sign of a bleed until the last date/time within the bleed window are counted. [b]Three injections were recorded to treat a left ankle spontaneous bleed in a participant with a medical history of obesity and haemophilic arthropathy of both ankles and the right knee. This bleed was initially treated with 30 IU/kg followed by two doses of 50 IU/kg every other day. Response to the first injection was rated good. Routine prophylaxis resumed 7 days after the first injection. [c]Seven injections were recorded to treat an exercise-induced traumatic haematoma within the right iliopsoas muscle of a participant with poor compliance regarding treatment and completion of the ePD. Doses of 50 IU/kg were administered every other day, and the participant resumed routine prophylaxis 18 days after the first injection.
BE, bleeding episode; ePD, electronic patient diary; IU, international units.

Safety

- No participants developed inhibitors
- Treatment-related adverse events occurred in 2 participants (1.4%) over >2 years of follow-up; one had facial paralysis and another had decreased FVIII levels. Neither adverse event led to treatment discontinuation (**Table 4**)
- No treatment-related serious adverse events were detected

Table 4. Summary of safety over >2 years of follow-up in XTEND-ed

	Participants (N=146)
Participants with ≥1 TEAE, n (%)	117 (80.1)
Participants with ≥1 related TEAE, n (%)	2 (1.4)[a]
Participants with ≥1 TESAE, n (%)	22 (15.1)
Participants with ≥1 related TESAE, n (%)	0
TEAEs leading to death, n (%)	0
TEAEs leading to discontinuation, n (%)	2 (1.4)[b]

The table includes adverse events that occurred on the day the surgical/rehabilitation period started but not those that occurred during a major surgical/rehabilitation period. [a]Includes 1 case of facial paralysis and 1 case of decreased factor VIII level. [b]Fracture of left distal femur (n=1) and left lower extremity deep vein thrombosis (n=1); neither was related to study drug.
TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

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