WFH COMPREHENSIVE CARE SUMMIT

New Developments in Bleeding Disorders and MSK

PP-044

Long-Term Outcomes of Prophylaxis With Efanesoctocog Alfa in Adults and Adolescents Previously Treated on Demand: Second Interim Analysis of XTEND-ed

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PLAIN LANGUAGE SUMMARY

Why did we perform this research?

- The standard of care for people with haemophilia A involves regular injections of factor VIII replacement therapy to prevent bleeding episodes, which is a treatment known as prophylaxis.
- Efanesoctocog alfa is a once-weekly FVIII replacement therapy that can enable people with haemophilia A to achieve FVIII levels in the non-haemophilia range (>40%) for most of the week.
- This report describes the long-term efficacy and safety of efanesoctocog alfa in adults and adolescents who transitioned from on-demand treatment (used only when bleeding episodes occur) to regular preventive therapy (prophylaxis).

How did we perform this research?

- In the XTEND-1 clinical trial, one group of patients (Arm B) with severe haemophilia A was given efanesoctocog alfa as needed for 26 weeks, followed by weekly prophylaxis with efanesoctocog alfa for 26 weeks.
- These patients could choose to continue into the XTEND-ed long-term extension trial.
- The XTEND-ed trial aimed to assess whether the efficacy and safety profile of efanesoctocog alfa prophylaxis was sustained long term in this patient group.
- Here, we present results from the second interim analysis of XTEND-ed.

What were the findings of this research and the implications?

- No inhibitors developed in adults and adolescents in the XTEND-ed study.
- Low bleed rates and improvements in patient wellbeing seen in Arm B patients in the XTEND-1 study were maintained through the XTEND-ed study to the cut-off date for this analysis.
- Once-weekly efanesoctocog alfa prophylaxis continued to be effective and well tolerated in adults and adolescents with severe haemophilia A who transitioned from on-demand therapy to prophylaxis.

INTRODUCTION

- Prophylaxis to prevent bleeding episodes, preserve joint function and improve quality of life is the standard of care for severe haemophilia; on-demand treatment is no longer considered a long-term treatment option.[1]
- Efanesoctocog alfa is a first-in-class high-sustained (also called ultra-long half-life) factor VIII (FVIII) replacement therapy designed to decouple FVIII from endogenous von Willebrand factor.
- In the Phase 3 XTEND-1 study (NCT04161495), once-weekly efanesoctocog alfa demonstrated superior bleed protection over prior FVIII prophylaxis, was well tolerated and provided FVIII activity within the non-haemophilia range (>40%) for most of the week.[2]

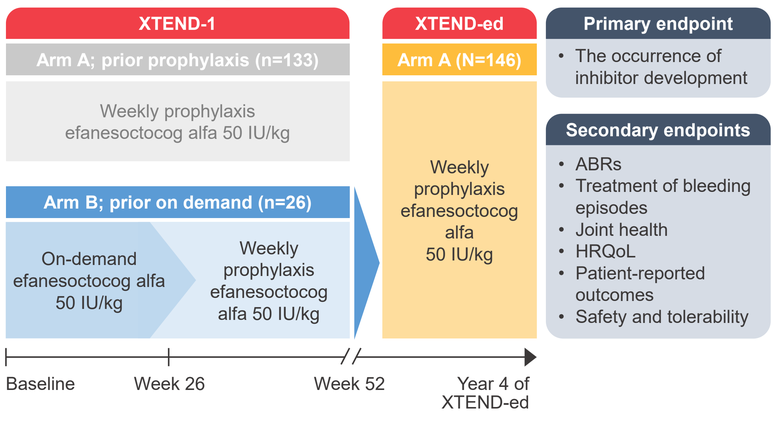
AIM

- We present long-term safety and efficacy data from adults with severe haemophilia A who switched from on-demand to weekly prophylactic efanesoctocog alfa therapy in the XTEND-1 study and continued prophylactic treatment in the ongoing XTEND-ed study (NCT04644575; second interim analysis).

METHODS

- Patients who received 26 weeks of on-demand treatment, followed by 26 weeks of weekly prophylaxis in XTEND-1 (Arm B), could continue efanesoctocog alfa (50 IU/kg, once-weekly) prophylaxis in the multicentre, open-label, long-term XTEND-ed study (**Figure 1**, Arm A).
- The primary endpoint of XTEND-ed was incidence of FVIII inhibitor development. Secondary endpoints included ABRs, HJHS, HRQoL (Haem-A-QoL), PROMIS SF physical function, and safety.
- The data cut for this second interim analysis was 22 February 2024.

Figure 1: Study design



ABR, annualised bleed rate; HRQoL, health-related quality of life.

CONCLUSIONS

- No inhibitors were detected in XTEND-1 and XTEND-ed. Patients switching from on-demand therapy to prophylaxis with once-weekly efanesoctocog alfa in XTEND-1 experienced improvements in annualised bleed rate (ABR), haemophilia joint health score (HJHS), health-related quality of life (HRQoL), and physical functioning.[2]
- Continued improvements in ABR and HJHS were observed in the long-term XTEND-ed study, alongside stable maintenance of HRQoL (Haem-A-QoL) and physical functioning (Patient-Reported Outcomes Measurement Information System Short Form [PROMIS SF]).
- Efanesoctocog alfa was well tolerated throughout both studies.
- These findings highlight the sustained benefits of efanesoctocog alfa prophylaxis for adults previously treated on demand, offering high efficacy and good tolerability over an extended period.

RESULTS

Patient characteristics

- Overall, 25/26 males treated with prior on-demand efanesoctocog alfa in XTEND-1 enrolled into XTEND-ed (**Table 1**; one patient did not continue into XTEND-ed).
- In XTEND-1, the mean (standard deviation [SD]) duration of the efficacy period was 25.1 (1.1) and 22.9 (6.0) weeks in the on-demand and prophylaxis periods, respectively, in these patients.
- The mean (SD) duration of the efficacy period in XTEND-ed up to the second data cut-off was 108.6 (25.6) weeks in patients from Arm B of XTEND-1.
- During XTEND-ed, mean (SD) weekly prophylactic dose was 51.12 (1.76) IU/kg.

Primary endpoint

- No FVIII inhibitors were detected during XTEND-ed; incidence of inhibitor formation was 0 (95% confidence interval, 0, 13.7).

Secondary endpoints

- The mean ABR for patients from Arm B of XTEND-1 remained low during the first 2 years of XTEND-ed (0.46 [SD 0.86]; **Figure 2**).
- Overall, 15 (60.0%) patients had zero bleeds over the entire XTEND-ed efficacy period. This compares with 0 (0%) and 20 (76.9%) patients during the on-demand period and prophylaxis periods of XTEND-1, respectively (**Figure 3**).
- Improvements were observed in XTEND-1 and were maintained during XTEND-ed for total HJHS, total Haem-A-QoL and PROMIS SF physical function mean T-score (**Figure 4**).

Safety

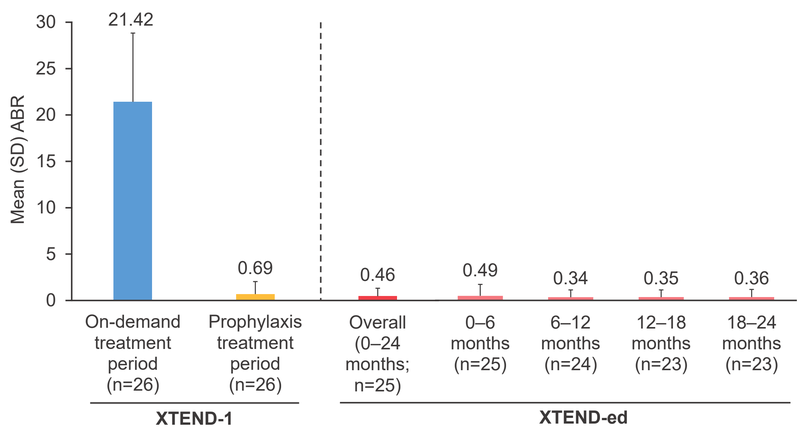
- During XTEND-ed, 13 (52.0%) patients experienced one or more treatment-emergent adverse events (TEAEs). Most common were:
  - Viral infections ie COVID-19, influenza, gastroenteritis (16.0%)
  - Falls (16.0%).
- Three patients (12.0%) experienced one or more serious TEAEs, including one patient with a femur fracture who discontinued because of prohibited concomitant medication use.

Table 1: Baseline characteristics of patients enrolled in Arm B of XTEND-1

	Patients enrolled in Arm B of XTEND-1 (n=26)
Sex, n (%) Male Female	 26 (100) 0
Age, mean (SD) 12–17 years, n (%) 18–64 years, n (%) ≥65 years, n (%)	42.8 (11.7) 0 25 (96.2) 1 (3.8)
BMI,* mean (SD)	26.9 (5.6)
White, n (%)	26 (100)
Family history of inhibitor, n (%) Yes No Unknown	 0 25 (96.2) 1 (3.8)

*BMI is only available in n=25.
BMI, body mass index; SD, standard deviation.

Figure 2: Mean ABR during the XTEND-1 and XTEND-ed trials in patients who were in Arm B of the XTEND-1 trial*



*Mean ABR data from XTEND-1 were previously published in Von Drygalski A *et al.*[2]
ABR, annualised bleed rate; SD, standard deviation.

Figure 3: Proportion of participants from XTEND-1 Arm B who had zero bleeds during the XTEND-1 and XTEND-ed trials

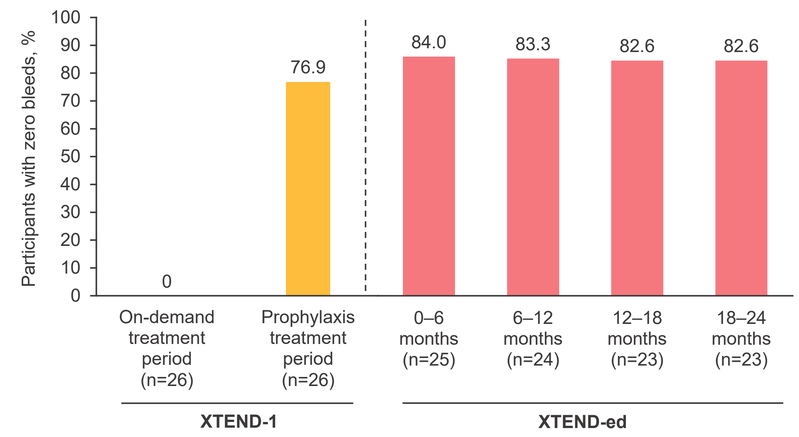
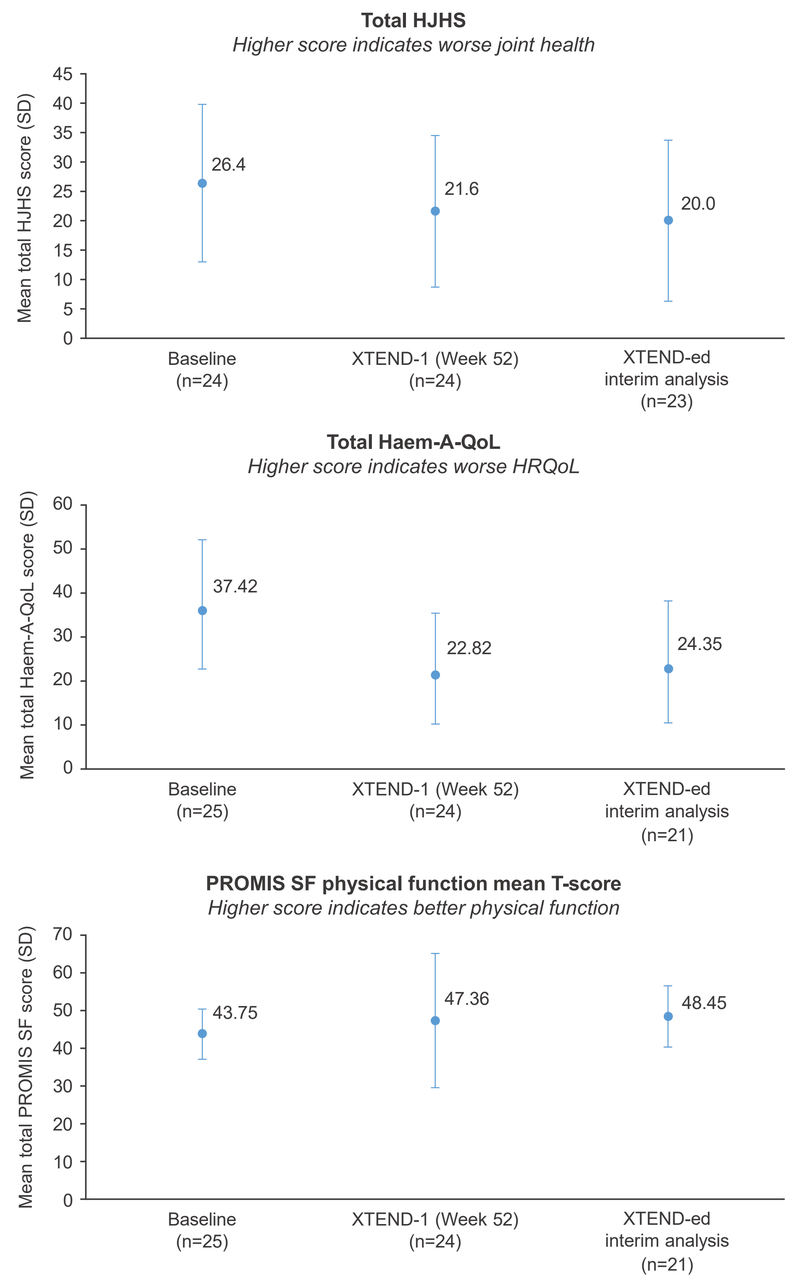


Figure 4: Joint health, HRQoL and physical function



HJHS, haemophilia joint health score; HRQoL, health-related quality of life; PROMIS SF, Patient-Reported Outcomes Measurement Information System Short Form; SD, standard deviation.

REFERENCES: 1. Srivastava A *et al. Haemophilia* 2020;26(Suppl 6):1–158; 2. Von Drygalski A *et al. N Engl J Med* 2023;388:310–8.

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