Long-term observational joint health study in patients initiating efanesoctocog alfa: baseline data

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INTRODUCTION

- Efanesoctocog alfa is a first-in-class, high-sustained FVIII therapy designed to overcome the half-life limitations imposed by interaction with endogenous von Willebrand factor (VWF).[1]
- The efficacy and safety of efanesoctocog alfa for bleed prevention and treatment have been demonstrated in pivotal Phase 3 clinical trials, XTEND-1 and XTEND-Kids.[2, 3]
  - Prophylactic treatment for 52 weeks with once-weekly efanesoctocog alfa (50 IU/kg) led to improvement in joint health from baseline in the XTEND-1 study.
- While the efficacy and safety of efanesoctocog alfa have been demonstrated in these pivotal trials, real-world evidence is limited.

OBJECTIVE

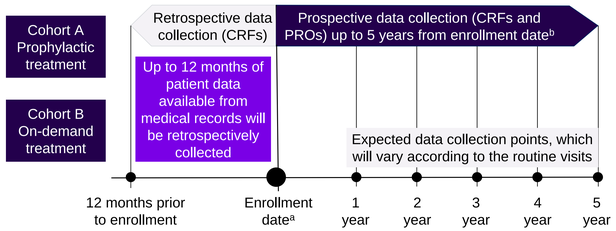
- To evaluate the real-world effectiveness of efanesoctocog alfa prophylaxis on clinical joint status and prevention and treatment of bleeding episodes in patients with hemophilia A in the United States (US).
- To report retrospective data for the 12-month period before initiating efanesoctocog alfa (data cut off: July 25, 2024).

METHOD

Study design:

- This prospective, observational study (NCT05911763) aims to enroll 120 participants newly receiving either prophylactic (Cohort A) or on-demand (Cohort B) efanesoctocog alfa **(Figure 1)** across 31 sites in the US.
- Up to 12 months of retrospective data prior to treatment initiation were collected from participants' medical records, including demographics, hemophilia treatment history, clinical outcomes, and prior use of healthcare resources.
- The enrollment period is expected to last for approximately 24 months. Prospectively, data on effectiveness, safety, and usage of efanesoctocog alfa are collected during routine visits (annual or semi-annual) for up to 5 years following enrollment/treatment initiation.
- The study was approved by local ethics committees; participants or, in the case of a minor, a parent or legal guardian provided informed consent.

Figure 1: Schematic of study design



CRF, case report form; PRO, patient reported outcome.
[a]The enrollment date is the date when the participant signs the informed consent form. [b]Patients will be followed up until the end of the prospective data collection period, efanesoctocog alfa discontinuation, lost to follow-up, study withdrawal, enrollment in a clinical trial, or death, whichever occurs first.

Participant selection criteria:

Inclusion	Exclusion
• Diagnosis of hemophilia A	• Diagnosed with another known bleeding disorder
• Initiated efanesoctocog alfa no more than one month before enrollment for on-demand, prophylactic treatment, or surgery	• Participation in an investigational medicinal product trial at enrollment or use of an investigational medicinal product within 3 months before inclusion
• Physician's decision to prescribe efanesoctocog alfa made independently of study participation	• Current diagnosis of FVIII inhibitor (titer ≥0.60 BU/mL)

Primary objective and associated endpoints

The primary objective is to describe the effectiveness of efanesoctocog alfa prophylaxis on clinical joint status over 5-years (prophylactic cohort). This will be assessed by the following endpoints:
Change from baseline in annualized joint bleeding rate (AjBR) for treated and all (treated and untreated) bleeds (at 1, 2, 3, 4, 5 years).
Change from baseline in the number and percentage of target joint development, resolution and/or recurrence (at 1, 2, 3, 4 and 5 years).

Secondary objectives and associated endpoints

To assess efanesoctocog alfa effectiveness over 5 years by measuring change from baseline in Hemophilia Joint Health Score (HJHS) (v2.1) total and domain scores at annual intervals.
To assess efanesoctocog alfa effectiveness and usage as a prophylaxis treatment for the prevention of bleeding episodes or as on-demand treatment of bleeding episodes over 5 years.
To assess safety and tolerability.

RESULTS

- Cohort A (prophylactic treatment) enrolled 47 patients, including 1 female (mean [standard deviation] age 24 [17] years); the majority (81%) had severe hemophilia A.
- Among participants in Cohort A, 47% had no comorbidities at enrollment, while the remaining 53% had other health conditions **(Table 1).**

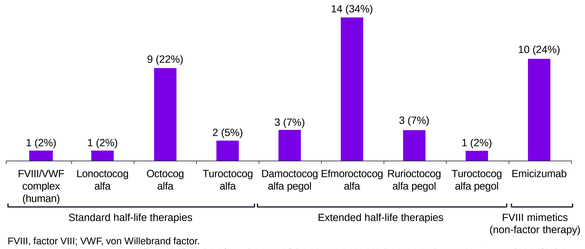
Table 1: Demographics and baseline characteristics of participants in Cohort A

Categories	Value
Number of participants, N	47
Age at baseline in years,	
Mean (SD)	24.3 (16.8)
Median (IQR)	21 (12, 32)
Gender (M/F)	46/1
Age at hemophilia A diagnosis in years,	
Mean (SD)	4.5 (13.7)
Median (IQR)	0 (0, 0)
Severity of hemophilia A at baseline, n (%)	
Severe hemophilia: patients with <1% baseline factor FVIII	38 (81)
Moderate hemophilia: patients with 1-5% baseline factor FVIII	4 (9)
Mild hemophilia: patients with >5% to <40% baseline factor FVIII	5 (11)
Current comorbidities (present at enrollment date) n (%)[a]	
Depression	2 (4)
Cancer	3 (6)
Non-hemophilic acute or chronic medical conditions causing mobility/joint problems	1 (2)
Other[b]	25 (53)
None	22 (47)
Presence of target joints[c] at enrollment date, n (%)	
Yes	12 (26)
No	35 (75)

FVIII, factor VIII; F, female; IQR, interquartile range; M, male; SD, standard deviation.
[a]None of the enrolled participants in Cohort A has human immunodeficiency virus or hepatitis C virus. [b]The most common comorbidities include joint disease (arthralgia, hemarthrosis or hemophilic arthropathy) in 6 (12.8%) participants, developmental disorders (attention deficit hyperactivity disorder, autism spectrum disorder or speech disorder) in 6 (12.8%) participants and factor VIII deficiency in 6 (12.8%) participants. [c]Major joint (e.g., hip, elbow, wrist, shoulder, knee or ankle) into which ≥3 spontaneous bleeding episodes occurred in a consecutive 6-month period
Note: Percentages are calculated excluding "unknowns" in the denominator, unless otherwise stated. Values are rounded off to reflect the true precision of each measure or determinant. In some cases, the percentages may not total exactly 100, owing to rounding.

- In the 12 months prior to initiating efanesoctocog alfa, the most frequently used prophylactic treatments in Cohort A were efmoroctocog alfa (34%), emicizumab (24%), and octocog alfa (22%) **(Figure 2).**

Figure 2: Prophylactic treatment(s) received during 12 months before efanesoctocog alfa initiation by participants (n=41) in Cohort A, n (%)



FVIII, factor VIII; VWF, von Willebrand factor.
Note: Categories are not mutually exclusive; therefore, the sum of the percentages can be greater than 100%. Denominator is the number of participants who received prophylaxis treatment regimen before efanesoctocog alfa initiation.

- Key reasons for initiating efanesoctocog alfa were 'to reduce injection frequency while maintaining bleed protection' (56%), and 'improving bleed protection' (30%) in Cohort A **(Table 2).**
- The main reason for switching from emicizumab to efanesoctocog alfa (n=8) was 'to improve bleed protection' (38%) in Cohort A **(Table 2).**

Table 2: Reasons for initiating or switching to efanesoctocog alfa prophylaxis by participants in Cohort A

Reason for initiating efanesoctocog alfa prophylaxis, n (%)[a]	
n	43
Reduce injection frequency while maintaining protection from bleeds	24 (56)
Improve protection from bleeds	13 (30)
Other	4 (9)
Unknown	4
Improve protection to increase physical activity level	2 (5)
Reason for initiating efanesoctocog alfa prophylaxis among participants who switched from emicizumab to efanesoctocog alfa prophylaxis, n (%)[b]	
n	8[c]
Improve protection from bleeds	3 (38)
Reduce injection frequency while maintaining protection from bleeds	2 (25)
Other	2 (25)
Unknown	2
Improve protection to increase physical activity level	1 (13)

[a]Denominator is the total number of participants exposed to prophylactic treatment regimen at enrollment. [b]Denominator is the total number of participants exposed to prophylaxis treatment regimen at enrollment and who switched from emicizumab. [c]While 10 patients switched from emicizumab only 8 gave responses to this question.
Note: Percentages are calculated excluding "unknowns" in the denominator, unless otherwise stated. Values are rounded off to reflect the true precision of each measure or determinant. In some cases, the percentages may not total to exactly 100, owing to rounding.

- The median (interquartile range) dose of efanesoctocog alfa was 50 (50.0, 50.0) IU/kg; 45 of 47 patients dosed once weekly **(Table 3)**.

Table 3: Treatment regimen prescribed at efanesoctocog alfa initiation for prophylaxis

Dose, IU/Kg[a]	
n	46
Mean (SD)	56 (52)
Median (IQR)	50 (50, 50)
Unknown	1
Frequency, n (%)[a]	
n	46
Once weekly	45 (98)
Every 2 weeks	1 (2)
Unknown	1

IQR, interquartile range; SD, standard deviation.
[a]Denominator is the total number of participants exposed to prophylaxis treatment regimen at enrollment.

CONCLUSIONS

- Baseline data from patients in the US on prior prophylaxis (Cohort A) showed initiation of efanesoctocog alfa 50 IU/kg, once weekly with most transitioning from extended half-life FVIII prophylaxis.
- Primary reasons for switching were to reduce injection frequency and to enhance bleed protection.

- Among participants with ≥6 months of prior prophylaxis, the overall pre-switch ABR was >3.
- Median baseline ABRs for traumatic, spontaneous and joint bleeds were 0.00.
- The mean baseline AjBR was 1.46 for treated bleeds and 1.53 for treated and untreated bleeds **(Table 4).**

Table 4: Baseline annualized bleed rates among study participants with at least 6 months of prophylaxis prior to starting efanesoctocog alfa

Categories	Treated bleeds	Treated and untreated bleeds
Number of participants	32	32
Number of bleeds	88	90[a]
ABRs		
All bleeds		
Mean (SD)	3.12 (5.16)	3.26 (5.34)
Median (IQR)	1.02 (0.00, 3.74)	1.07 (0.00, 4.27)
Traumatic bleeds		
Mean (SD)	1.74 (2.98)	1.77 (3.00)
Median (IQR)	0.00 (0.00, 2.49)	0.00 (0.00, 2.49)
Spontaneous bleeds		
Mean (SD)	1.18 (3.01)	1.22 (3.16)
Median (IQR)	0.00 (0.00, 1.03)	0.00 (0.00, 1.03)
Joint bleeds (AjBR)		
Mean (95% CI)	1.46 (0.49, 2.43)	1.53 (0.51, 2.56)
Median (IQR)	0.00 (0.00, 2.21)	0.00 (0.00, 2.21)

ABR, annualized bleed rate; AjBR, annualized joint bleed rate; CI confidence interval; IQR interquartile range; SD, standard deviation.
[a]Among the two patients with untreated bleeds, one was receiving antihemophilic factor (recombinant) and one was receiving emicizumab

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DISCLOSURES:

JR has disclosed potential conflicts of interest arising from academic consulting, participation in grant application review groups, and receipt of honoraria sponsored by F. Hoffmann-La Roche AG, Genentech, Sobi, Novo Nordisk, Pfizer, Sanofi, and Takeda. Additionally, **JR** also participates in speakers' bureaus for Novo Nordisk, Takeda and Sanofi. **LB** has served on scientific advisory boards for Sanofi and Bayer Health. **EG** has served on scientific advisory boards for Sanofi and CSL Behring. **AS** has served on scientific advisory boards for BioMarin and CSL Behring. **JD**, **CS** and **NT** are current employee of Sanofi and may hold shares/stock options

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