Joint Replacement/Revision Surgery Outcomes with Efanesoctocog Alfa: 4 Years' Experience in the XTEND Clinical Program

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PO-12

Conclusions

- **The results of this post hoc analysis of the XTEND clinical trial programme show that efanesoctocog alfa provided highly effective bleed protection during joint replacement/revision surgeries in patients with severe haemophilia A**
  - **Ninety-five percent of surgeries were managed with ≤1 preoperative dose**
  - **Postoperative consumption was low**
- **Efanesoctocog alfa was well tolerated; there was no inhibitor development or thrombotic complications**

Introduction

- In people with haemophilia A, bleeding in joints that leads to haemophilic arthropathy and chronic joint pain may occur despite standard-of-care prophylaxis[1,2]; therefore, joint replacement/revision surgery is a key component of haemophilia management
- Efanesoctocog alfa is a first-in-class high-sustained factor VIII (FVIII) replacement therapy designed to decouple recombinant FVIII from endogenous von Willebrand factor to further extend its half-life[3-5]
- The phase 3 XTEND-1 (NCT04161495)[6] and XTEND-Kids (NCT04759131)[7] studies showed that once-weekly efanesoctocog alfa (50 IU/kg) prophylaxis
  - Achieved high-sustained FVIII levels in the normal to near-normal range (>40%) for most of the week in adults and adolescents (aged ≥12 years) and for 3 days in children aged <12 years
  - Provided highly effective bleed protection
  - Was well tolerated with no development of inhibitors
- Patients completing XTEND-1 and XTEND-Kids could continue weekly efanesoctocog alfa prophylaxis in the long-term extension study, XTEND-ed (NCT04644575)[8]
  - In addition, patients newly initiating efanesoctocog alfa from China (Arm B) and patients newly initiating efanesoctocog alfa with planned major surgery (Arm C) were able to enrol in XTEND-ed

Objective

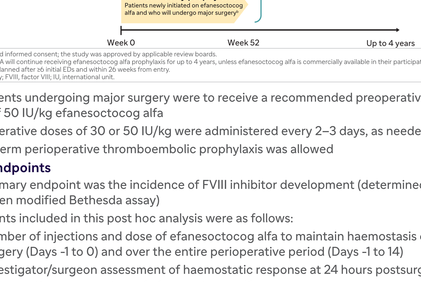
- To report perioperative management of joint replacement/revision surgeries through 4 years in the XTEND clinical trial programme

Methods

Study design and population

- The XTEND clinical trial programme is outlined in **Figure 1**
- This was a post hoc analysis of joint replacement/revision surgery outcomes from the XTEND programme through XTEND-ed interim analysis 2 (data cut: 22 February 2024)

Figure 1. XTEND clinical trial programme



Patients provided informed consent; the study was approved by applicable review boards.
[a]Patients in Arm A will continue receiving efanesoctocog alfa prophylaxis for up to 4 years, unless efanesoctocog alfa is commercially available in their participating country.
[b]Major surgery planned after 36 initial EDs and within 26 weeks from entry.
ED, exposure day; FVIII, factor VIII; IU, international unit.

- All patients undergoing major surgery were to receive a recommended preoperative loading dose of 50 IU/kg efanesoctocog alfa
- Postoperative doses of 30 or 50 IU/kg were administered every 2–3 days, as needed
- Short-term perioperative thromboembolic prophylaxis was allowed

Study endpoints

- The primary endpoint was the incidence of FVIII inhibitor development (determined by the Nijmegen modified Bethesda assay)
- Endpoints included in this post hoc analysis were as follows:
  - Number of injections and dose of efanesoctocog alfa to maintain haemostasis during surgery (Days -1 to 0) and over the entire perioperative period (Days -1 to 14)
  - Investigator/surgeon assessment of haemostatic response at 24 hours postsurgery
  - Perioperative consumption of efanesoctocog alfa
  - Time from surgery to return to routine prophylaxis
  - Blood loss; number and type of blood transfusions
  - Safety

Results

- Twenty-two joint replacement/revision surgeries (19 replacements and 3 revisions) were performed in 17 males
  - The mean (standard deviation [SD]) age at XTEND-ed enrolment was 48.9 (11.2) years (**Table 1**)
  - The number of surgeries per patient ranged from 1 to 3

Table 1. Patient demographics and baseline disease characteristics

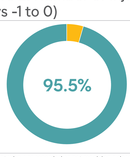
	N=17
Age at enrolment in XTEND-ed, years	
Mean (SD)	48.9 (11.2)
Median (range)	48.0 (27.0–74.0)
Age range at enrolment in XTEND-ed, n (%)	
<12 years	0
12–17 years	0
18–64 years	16 (94.1)
≥65 years	1 (5.9)
Sex, n (%)	
Male	17 (100)
Race, n (%)	
White	10 (58.8)
Black or African American	0
Asian	4 (23.5)
Not reported	2 (11.8)
Other	1 (5.9)
BMI, kg/m²	
Mean (SD)	25.8 (3.8)

BMI, body mass index; SD, standard deviation.

Haemostatic control during surgery procedures (Days –1 to 0)

- Most surgeries (21/22; 95.5%) were managed with ≤1 dose of efanesoctocog alfa (**Figure 2**)
  - Twenty patients were recorded as receiving 1 dose of efanesoctocog alfa on the day of surgery
  - One patient had a left knee joint replacement and received a preoperative dose of efanesoctocog alfa on the day of surgery that was erroneously recorded as being administered 4 days before
  - One patient (undergoing a knee arthroplasty revision) had 2 doses on the day of surgery, 1 preoperative and 1 postoperative
- The median (range) number of days from previous routine prophylaxis and the start of surgery was 7 (2–16) days

Figure 2. Number of injections to maintain haemostasis during surgery (Days -1 to 0)



95.5% (21/22) of surgeries were managed with ≤1 dose of efanesoctocog alfa to maintain haemostasis during surgery[a]

Median (range)	Surgeries requiring ≥1 injection to maintain haemostasis (n=21)
Number of injections[b]	1 (1–2[c])
Dose per injection, IU/kg	50.0 (13.0–53.8)
Total dose, IU/kg[c]	50.0 (13.0–84.7)

[a]The patient who was recorded as not receiving a dose of efanesoctocog alfa presurgery received a preoperative dose on the day of surgery that was erroneously recorded as being administered 4 days before. [b]The number of injections to maintain haemostasis during surgery includes all injections from loading dose (ie, the preoperative injection, administered either on the day of surgery or 1 day prior to the surgery) to the end of surgery. [c]One patient who underwent knee arthroplasty revision had 2 doses on the day of surgery, 1 preoperative and 1 postoperative. [d]Total dose is the sum across all injections either preoperatively or postoperatively on the day of or the day before surgery.
IU, international unit.

- Haemostatic response (recorded at 24 hours after surgery) was rated excellent/good in 95.5% of cases (**Figure 3**)

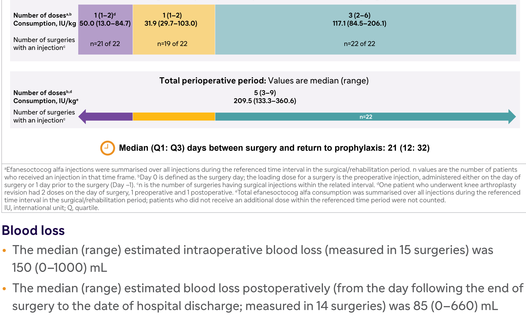
Figure 3. Investigator/surgeon-assessed haemostatic response at 24 hours post surgery

[a]Unilateral replacement of left hip joint and left knee joint in a 50-year-old Asian patient; a 50 IU/kg dose of efanesoctocog alfa was administered at Days -1 to 0; 31.3 IU/kg at Days 1 to 3; 125.0 IU/kg at Days 4 to 14 (total: 206.3 IU/kg from Days -1 to 14).
IU, international unit.

Management of surgeries during the perioperative period (Days -1 to 14)

- During the perioperative period (Days -1 to 14), the median (range)
  - Number of injections was 5 (3–9)
  - Total consumption was 209.5 (133.3–360.6) IU/kg (**Figure 4**)
- The median (Q1: Q3) time between surgery and return to routine prophylaxis was 21 (12: 32) days

Figure 4. Management of surgeries (Days -1 to 14)



[a]Efanesoctocog alfa injections were summarised over all injections during the referenced time interval in the surgical/rehabilitation period. n values are the number of patients who received an injection in that time frame. [b]Day 0 is defined as the surgery day; the loading dose for a surgery is the preoperative injection, administered either on the day of surgery or 1 day prior to the surgery (Day -1). [c]n is the number of surgeries having surgical injections within the related interval. [d]One patient who underwent knee arthroplasty revision had 2 doses on the day of surgery, 1 preoperative and 1 postoperative. [e]Total efanesoctocog alfa consumption was summarised over all injections during the referenced time interval in the surgical/rehabilitation period; patients who did not receive an additional dose within the referenced time period were not counted.
IU, international unit; Q, quartile.

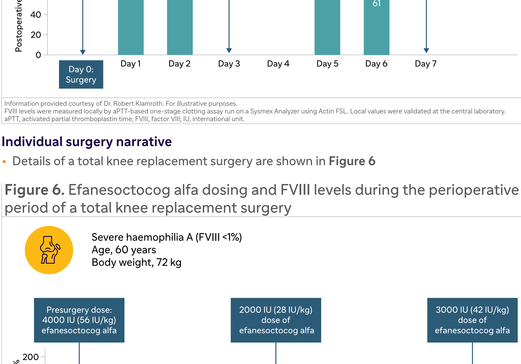
Blood loss

- The median (range) estimated intraoperative blood loss (measured in 15 surgeries) was 150 (0–1000) mL
- The median (range) estimated blood loss postoperatively (from the day following the end of surgery to the date of hospital discharge; measured in 14 surgeries) was 85 (0–660) mL
- Two surgeries (unilateral hip and knee replacement; right knee replacement) required red blood cell transfusion

Individual surgery narrative

- Details of an ankle replacement surgery are shown in **Figure 5**

Figure 5. Efanesoctocog alfa dosing and FVIII levels during the perioperative period of an ankle replacement surgery

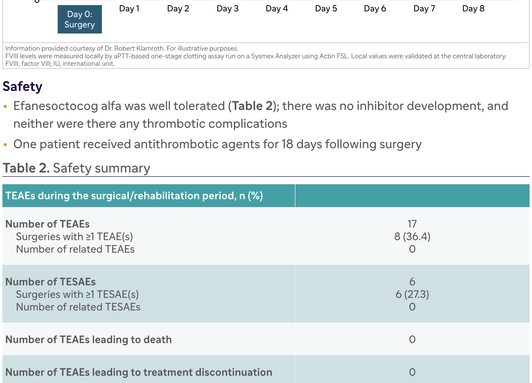


Information provided courtesy of Dr. Robert Klamroth. For illustrative purposes.
FVIII levels were measured locally by aPTT-based one-stage clotting assay run on a Sysmex Analyzer using Actin FSL. Local values were validated at the central laboratory.
aPTT, activated partial thromboplastin time; FVIII, factor VIII; IU, international unit.

Individual surgery narrative

- Details of a total knee replacement surgery are shown in **Figure 6**

Figure 6. Efanesoctocog alfa dosing and FVIII levels during the perioperative period of a total knee replacement surgery



Information provided courtesy of Dr. Robert Klamroth. For illustrative purposes.
FVIII levels were measured locally by aPTT-based one-stage clotting assay run on a Sysmex Analyzer using Actin FSL. Local values were validated at the central laboratory.
FVIII, factor VIII; IU, international unit.

Safety

- Efanesoctocog alfa was well tolerated (**Table 2**); there was no inhibitor development, and neither were there any thrombotic complications
- One patient received antithrombotic agents for 18 days following surgery

Table 2. Safety summary

TEAEs during the surgical/rehabilitation period, n (%)	
Number of TEAEs	17
Surgeries with ≥1 TEAE(s)	8 (36.4)
Number of related TEAEs	0
Number of TESAEs	6
Surgeries with ≥1 TESAE(s)	6 (27.3)
Number of related TESAEs	0
Number of TEAEs leading to death	0
Number of TEAEs leading to treatment discontinuation	0

TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

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