Perioperative Management with Efanesoctocog Alfa in Patients with Haemophilia A in the XTEND Clinical Trial Programme: A European Subanalysis

Flora Peyvandi,[1] Pratima Chowdary,[2] Umer Khan,[3] Elena Santagostino,[4] Linda Bystrická,[4] Sophie Susen[5]

[1]Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Katharine Dormandy Haemophilia and Thrombosis Centre, Royal Free Hospital, London, UK; [3]Sanofi, Cambridge, Massachusetts, USA; [4]Sobi, Basel, Switzerland; [5]Institut d'Hématologie-Transfusion, Centre Hospitalier Universitaire de Lille, Université de Lille, Lille, France

PO-19

Background

- Efanesoctocog alfa is a first-in-class, high sustained factor VIII (FVIII) replacement therapy (also known as ultra-long half-life FVIII) that has been designed to overcome the von Willebrand factor-imposed half-life ceiling.[1,2]
- XTEND-1 (NCT04161495) and XTEND-Kids (NCT04759131) showed once-weekly efanesoctocog alfa (50 IU/kg) was highly efficacious and well-tolerated during surgery in patients with severe haemophilia A.[3–5]
- Patients completing XTEND-1 and XTEND-Kids could continue once-weekly efanesoctocog alfa prophylaxis in Arm A of the extension study, XTEND-ed (NCT04644575).[6]

Aim

- To report up to 4 years of perioperative management of a subset of patients from Europe (including Türkiye) with severe haemophilia A, treated with efanesoctocog alfa from XTEND-1/XTEND-Kids through the second interim analysis of XTEND-ed.

Methods

Study design

- The study design for the XTEND clinical trial programme is shown in **Figure 1**.
- Patients undergoing surgery received a preoperative loading dose of 50 IU/kg efanesoctocog alfa. For major surgeries, postoperative doses of 30 or 50 IU/kg could be given every 2–3 days as needed. Short-term perioperative thromboembolic prophylaxis was permitted as needed.

Endpoints

- Surgery endpoints include:
  - Number of injections to maintain haemostasis during surgery (Day before surgery [Day –1] to day of surgery [Day 0]) for surgeries requiring ≥1 injection to maintain haemostasis;
  - Number of injections during the perioperative period (Day –1 to Day 14 for major surgeries and Day –1 to Day 7 for minor surgeries) for those requiring ≥1 injection to maintain haemostasis;
  - Efanesoctocog alfa consumption during the perioperative period;
  - Assessment of haemostatic response;
  - Blood loss and number of blood transfusions during surgery.

Results

Study population

- Overall, at the data cut-off for the second interim analysis of XTEND-ed (22nd February 2024; up to 4 years' follow-up), 45 patients had 61 major surgeries and 47 patients had 56 minor surgeries.
- In this subanalysis of European patients, 17 patients had 27 major surgeries (of which 18 were orthopaedic surgeries) and 23 patients had 27 minor surgeries.
- Baseline characteristics are shown in **Table 1**.

Major surgeries

- During major surgeries, haemostasis was maintained with ≤1 injection in 26/27 (96.3%) cases; 2 surgeries were reported as having no preoperative injection (**Figure 2A**).
- Median (range) total dose to maintain haemostasis during surgery was 50.0 (12.7–84.7) IU/kg.
- Total median (range) perioperative consumption was 173.0 (98.4–293.1) IU/kg with a median (range) of 4 (2–9) injections (**Figure 3**).
- Haemostatic response was rated excellent or good by the investigator/surgeon for all 27 major surgeries.

Minor surgeries

- During minor surgeries, haemostasis was maintained with ≤1 injection in all 27 cases; 7 surgeries did not require a preoperative injection (**Figure 2B**).
- Median (range) total dose to maintain haemostasis during surgery was 51.2 (30.1–58.8) IU/kg.
- Total median (range) perioperative consumption was 99.6 (47.6–199.2) IU/kg with a median (range) of 2 (1–6) injections (**Figure 4**).
- Haemostasis efficacy was rated excellent by the investigator/surgeon for all 18 minor surgeries with available data.

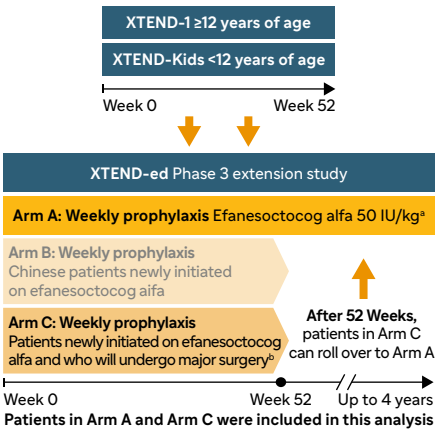
Blood loss and transfusions

- Mean (SD) estimated intraoperative blood loss was 228.7 (282.4) mL for major surgeries; for major orthopaedic (n=10) and non-orthopaedic (n=4) surgeries, estimated blood loss during surgery was 305.0 (303.0) mL and 38.0 (47.4) mL, respectively.
- For minor surgeries, estimated intraoperative blood loss was 3.1 (5.9) mL.
- No blood transfusions were required during major and minor surgeries.
- No inhibitor development was reported.

Conclusions

- **Surgical data from the second interim analysis of European patients in the XTEND programme indicate that efanesoctocog alfa is highly effective for the perioperative management of patients with severe haemophilia A, consistent with surgeries in the overall XTEND population.**
- **Efanesoctocog alfa consumption was low and similar to regular prophylaxis for both major and minor surgeries.**

Figure 1 Patients included from the XTEND clinical trial programme



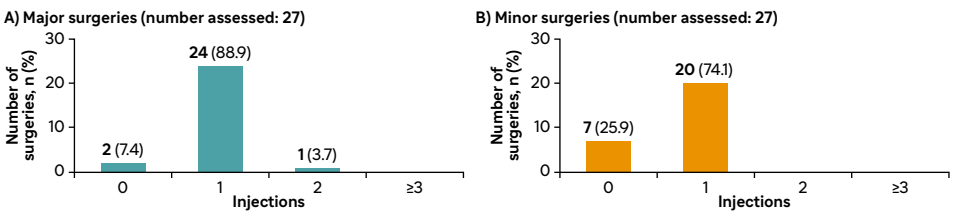
[a] Patients in Arm A will continue receiving efanesoctocog alfa prophylaxis for a cumulative total of ≥100 exposure days from XTEND-1/XTEND-Kids and XTEND-ed. These patients could continue in XTEND-ed for up to 4 years, unless efanesoctocog alfa is commercially available in their participating country; **[b]** Major surgery planned after ≥6 initial exposure days and within 26 weeks from Day 1.

Table 1 Baseline characteristics

	Pooled major surgeries (N=27)[a]	Pooled minor surgeries (N=27)
Number of patients, n	17	23
Sex, n (%)		
Male	17 (100)	23 (100)
Age at XTEND-ed enrolment, years		
Mean (SD)	38.1 (16.8)	31.4 (24.2)
Age category, n (%)		
<12 years	1 (5.9)	8 (34.8)
12 to 17 years	2 (11.8)	3 (13.0)
18 to 64 years	14 (82.4)	11 (47.8)
≥65 years	0	1 (4.3)
Race, n (%)		
Asian	1 (5.9)	3 (13.0)
Black or African American	0	1 (4.3)
White	12 (70.6)	15 (65.2)
Not reported	4 (23.5)	4 (17.4)
Weight, kg		
Mean (SD)	71.7 (24.1)	56.2 (29.6)

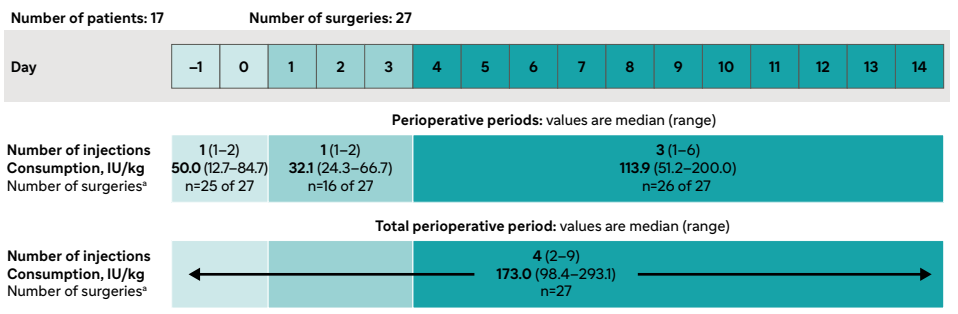
[a] Including 18 orthopaedic surgeries.

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



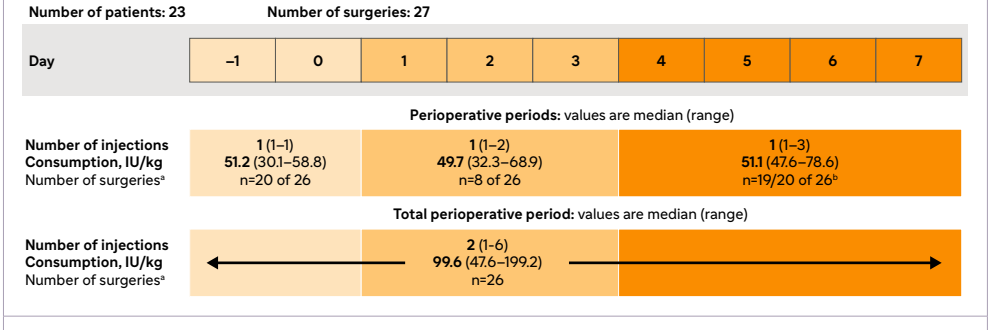
Analyses are based on major and minor surgeries during the treatment period, excluding any surgery conducted after the last efanesoctocog alfa injection. Two major and 7 minor surgeries were reported as having no preoperative injection; however, factor coverage was provided by doses recorded as other injection types either on the day of, or the day before surgery. The loading dose for a surgery was the preoperative injection, administered either on Day –1 or Day 0. The number of injections to maintain haemostasis during surgery includes all injections from the loading dose to the end of surgery.

Figure 3 Perioperative management of haemostasis in major surgeries



Analyses are based on major surgeries during the treatment period which required ≥1 injection to maintain haemostasis, excluding any surgery conducted after the last efanesoctocog alfa injection. **[a]** Number of surgeries having surgical injections within the related interval (including planned prophylaxis injections).

Figure 4 Perioperative management of haemostasis in minor surgeries



Analyses are based on minor surgeries during the treatment period which required ≥1 injection to maintain haemostasis, excluding any surgery conducted after the last efanesoctocog alfa injection. One patient who underwent minor dental surgery received an injection on Day –1; however, this data point was not included since, per protocol, this injection occurred within the surgical rehabilitation period of a previous major surgery that ended on the day of minor surgery (Day 0). **[a]** Number of surgeries having surgical injections within the related interval (including planned prophylaxis injections); **[b]** For Days 4 to 7, number of injections and consumption are based on 20 and 19 minor surgeries, respectively.

References: **1.** Chhabra ES, et al. *Blood* 2020;135:1484–96; **2.** Konkle BA, et al. *N Engl J Med* 2020;383:1018–27; **3.** Von Drygalski A, et al. *N Engl J Med* 2023;388:310–8; **4.** Malec L, et al. *N Engl J Med* 2024;391:235–46; **5.** Klamroth R, et al. *Haemophilia* 2025;31:391–400; **6.** ClinicalTrials.gov (NCT04644575).

Disclosures: **FP:** Participation at educational meetings and advisory boards of BioMarin, Grifols, Roche, Sanofi, Sobi and Takeda; **PC:** Served on advisory boards for Apcintex, Bayer, Baxalta/Shire, Biogen Idec, Boehringer Ingelheim, CSL Behring, Chugai, Freeline, Novo Nordisk, Pfizer, Roche, Sanofi and Sobi; received research funding from Bayer, CSL Behring, Novo Nordisk, Pfizer and Sobi; **UK:** Employee of Sanofi and may hold shares and/or stock options in the company; **ES, LB:** Employees of Sobi and may hold shares and/or stock options in the company; **SS:** Research support from Biomarin, Bioverativ, CorWave, CSL Behring, Roche-Chugai, Sanofi, Shire/Takeda, Siemens Healthineers, Sobi and Stago LFB; scientific advisory boards for Biomarin, CSL Behring, LFB, Novo Nordisk, Roche, Sanofi, Sobi and Takeda.

Abbreviations: **FVIII:** factor VIII; **IU:** international unit; **kg:** kilogram; **SD:** standard deviation.

Acknowledgements: We thank the patients and investigators who participated in the study. The authors acknowledge Nick Fulcher, PhD, CMPP from Sobi and Monique Bidell, PharmD, CMPP from Sanofi for publication coordination, Ria Gill, Costello Medical, UK for medical writing and editorial assistance, and Peter Lang, Costello Medical, UK for design assistance, funded by Sobi. Sobi and Sanofi reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content. This research is funded by Sobi and Sanofi.

Access poster via the Sobi Science Library

Access poster via the Sanofi Library of Congresses

Copies of this poster obtained through QR Code are for personal use only