Minor Surgeries Outcomes with Efanesoctocog Alfa: 4 Years' Experience in the XTEND Clinical Program

Pratima Chowdary,[1] Azusa Nagao,[2] Johannes Oldenburg,[3] Lynn Malec,[4] María Teresa Álvarez-Román,[5] Umer Khan,[6] Helena Palmborg,[7] Sriya Gunawardena,[8] Mahnouch Georget,[7] Jennifer Dumont,[6] Anthony KC Chan[9]

[1]Katharine Dormandy Haemophilia and Thrombosis Centre, Royal Free Hospital, London, UK; [2]Department of Hematology and Oncology, Kansai Medical University Hospital, Osaka, Japan; [3]University Hospital Bonn, Bonn, Germany; [4]Versiti Blood Research Institute, and the Division of Hematology and Oncology, Departments of Medicine and Pediatrics, Medical College of Wisconsin, Milwaukee, WI, USA; [5]Department of Hematology, Universitario Hospital La Paz, Universidad Autónoma de Madrid, Madrid, Spain; [6]Sanofi, Cambridge, MA, USA; [7]Sobi, Stockholm, Sweden; [8]Sanofi, Bridgewater, NJ, USA; [9]McMaster Children's Hospital, McMaster University, Hamilton, Ontario, Canada

PB0847

Introduction

- Minor surgical interventions in patients with hemophilia are associated with a higher risk of bleeding in the absence of replacement therapy, both in the intraoperative and perioperative period[1]
- Efanesoctocog alfa is a first-in-class high-sustained factor VIII replacement therapy designed to decouple recombinant factor VIII from endogenous von Willebrand factor, enabling surgery with fewer injections[2,3]
- Perioperative management with efanesoctocog alfa has previously been reported to be highly efficacious and well tolerated in the pivotal trials, XTEND-1 (NCT04161495)[4] and XTEND-Kids (NCT04759131)[5]
- Patients completing these studies could continue weekly efanesoctocog alfa prophylaxis in the long-term extension study, XTEND-ed (NCT04644575)

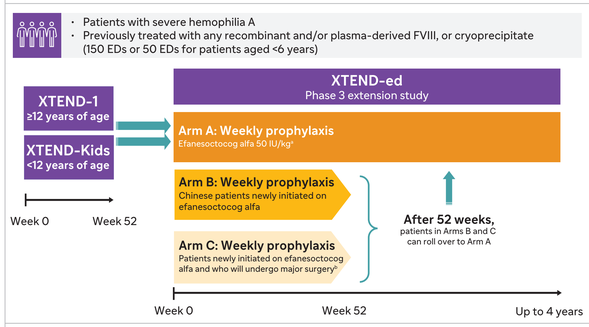
Objective

- We report 4 years of minor surgery data from parent studies' baseline through the second interim analysis of XTEND-ed

Methods

- Patients provided informed consent; the study was approved by applicable review boards
- Patients entering XTEND-ed Arm A from XTEND-1/XTEND-Kids, and those newly initiating prophylaxis (Arms B [China] and C [planned major surgery]), who could roll over into Arm A after 52 weeks of treatment) were included in this analysis (**Figure 1**)
- This interim analysis included vascular access, endoscopic, and ophthalmic procedures and other minor surgeries; dental surgeries were excluded, and have been previously reported[6]
- A loading dose of 50 IU/kg was recommended for minor surgeries
- Short-term perioperative thromboembolic prophylaxis was permitted
- The data cutoff date for this analysis was February 22, 2024

Figure 1. XTEND program study design



[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 ≥6 initial EDs and within 26 weeks from entry.
ED, exposure day; FVIII, factor VIII; IU, international unit.

Study endpoints

- The number and dose of injections to maintain hemostasis, total consumption, investigator assessment of hemostatic response, amount of blood loss/number of transfusions, and safety were assessed descriptively
  - Investigator assessment of response occurred at 24 hours post surgery using the International Society on Thrombosis and Haemostasis 4-point response for surgical procedures scale; scores ranged from excellent, good, and moderate to none
- Safety was assessed in the safety analysis population

Results

Patient population

- Twenty-nine males underwent 33 minor surgeries (**Table 1**); 9 had vascular access surgeries, 9 had endoscopic procedures, 2 had ophthalmic procedures, and 9 had other minor surgeries

Table 1. Patient demographics and baseline disease characteristics

	Vascular access surgeries	Endoscopic procedures	Ophthalmic procedures	Other minor surgeries[a]
Number of patients	9	9	2	9
Number of surgeries	9	10	4	10
Age at enrollment in XTEND-ed, years				
Mean (SD)	7.8 (4.2)	41.2 (22.9)	70.0 (5.7)	39.8 (22.7)
Age range, n (%)				
<12 years	7 (77.8)	2 (22.2)	0	2 (22.2)
12–17 years	2 (22.2)	0	0	1 (11.1)
18–64 years	0	6 (66.7)	0	6 (66.7)
≥65 years	0	1 (11.1)	2 (100)	0
Sex, n (%)				
Male	9 (100)	9 (100)	2 (100)	9 (100)
Race, n (%)				
White	7 (77.8)	5 (55.6)	1 (50)	7 (77.8)
Black	2 (22.2)	1 (11.1)	0	0
Asian	0	3 (33.3)	1 (50)	2 (22.2)
BMI, mean (SD), kg/m²	17.6 (1.5)	24.6 (6.0)	23.0 (3.3)	22.8 (5.5)

[a]Other minor surgery type included a combination of orthopedic, urology, and interventional radiology.
BMI, body mass index; NR, not reported; SD, standard deviation.

Management during minor surgery procedures (Days -1 to 0)

- As per protocol, hemostasis during surgery was maintained with a single preoperative injection in all cases (**Table 2**)
  - The median total dose to maintain hemostasis during surgery ranged from 50.0 to 52.1 IU/kg across different minor surgeries

Hemostatic response was rated excellent for all surgeries

- The median (range) number of injections during the perioperative period was 2 for vascular access, endoscopic, and other minor surgeries, and 1 for ophthalmic procedures (**Table 2**)
- Consumption during the entire perioperative period (Days -1 to 7) was low and comparable to routine prophylaxis for all surgeries (**Table 2**)
- The median number of days between surgery start date and return to routine prophylaxis ranged from 7.0 to 8.5 days across different minor surgeries (**Table 2**)
- Estimated blood loss was minimal
  - For vascular access surgeries, estimated median (range) blood loss was 7.5 (0–15) mL during surgery (n=4) and 0 (0–5) mL postoperatively (n=5)
  - For other minor surgeries, estimated median (range) blood loss was 0 (0–2) mL during surgery (n=6) with no blood loss postoperatively
  - No blood loss was reported for endoscopic or ophthalmic procedures
- Timelines for 4 selected surgeries are presented in **Figure 2**

Safety

- There were 22 treatment-emergent adverse events across all 33 surgeries (**Table 3**)
- No treatment-related adverse events were reported

Conclusions

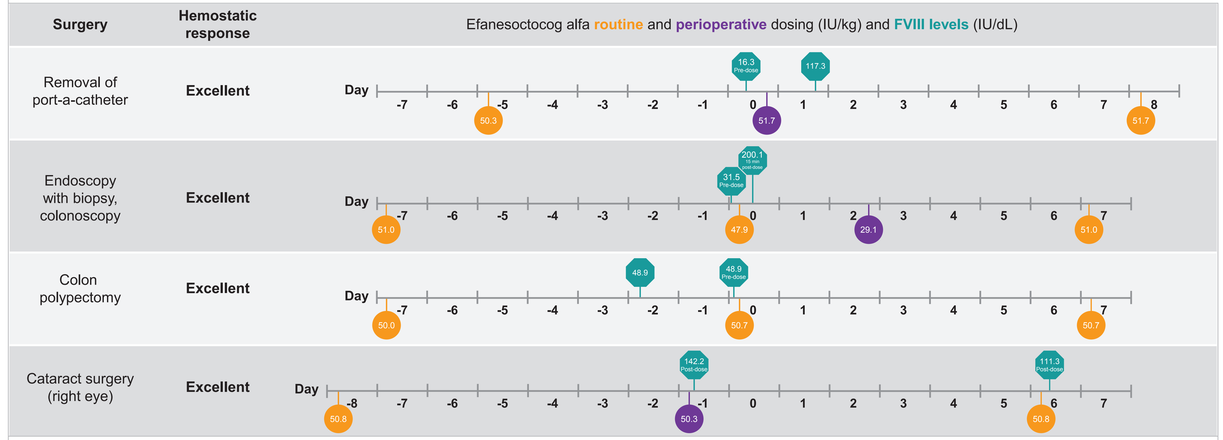
- **Data from 4 years of experience in the XTEND clinical program demonstrate that**
  - **A single preoperative injection with efanesoctocog alfa is highly effective and remains well tolerated for management of a wide variety of minor surgeries in patients with severe hemophilia A**
  - **Minor surgery for patients receiving efanesoctocog alfa is often performed under routine prophylaxis, minimizing the impact on the patient and the healthcare system**

Table 2. Perioperative management of minor surgeries (Days -1 to 7)

	Vascular access surgeries	Endoscopic procedures	Ophthalmic procedures	Other minor surgeries	Overall
Number of patients	9	9	2	9	29
Number of surgeries	9	10	4	10	33
Median (range) number of doses per surgery[a–c]					
Days -1 to 0	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)
Days -1 to 7	2 (1–6)[d]	2 (1–3)	1 (1–2)	2 (1–3)	2 (1–6)
Median (range) consumption, IU/kg[b,c,e]					
Days -1 to 0	52.1 (48.1–57.1)	50.0 (38.5–57.7)	51.6 (50.3–52.4)	50.1 (32.6–53.8)	50.7 (32.6–57.7)
Days -1 to 7	104.2 (48.1–199.2)	101.0 (50.0–135.7)	52.5 (50.3–101.6)	103.2 (51.2–150.0)	101.5 (48.1–199.2)
Median (Q1, Q3) days between start of surgery and return to routine prophylaxis	8.0 (7.0, 9.0)	8.0 (6.0, 8.0)	8.5 (7.0, 11.0)	7.0 (4.0, 7.0)	7.0 (6.0, 8.0)

[a]Median (range) number of injections are summarized for all efanesoctocog alfa injections (including preoperative injections and routine prophylaxis) administered during the referenced time interval in the surgical/rehabilitation period. [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]Number of surgeries having injections within the related interval. [d]The surgery with 6 injections was listed as a "Revision Port-A-Cath" with a median dose of 34 IU/kg per injection. [e]Total efanesoctocog alfa consumption is summarized over all injections during the referenced time interval in the surgical/rehabilitation period.
IU, international unit; Q, quartile.

Figure 2. Management of minor surgeries with efanesoctocog alfa in the XTEND program: Selected case studies



Day 0 was the day of surgery. FVIII levels were measured locally and then again at the central lab by aPTT-based one-stage clotting assay using Actin FSL (central lab values are noted). The number of injections to maintain hemostasis 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.
aPTT, activated partial thromboplastin time; FVIII, factor VIII; IU, international unit.

Table 3. Safety outcomes during the surgical/rehabilitation period (Days -1 to 7)

	Vascular access surgeries	Endoscopic procedures	Ophthalmic procedures	Other minor surgeries
Number of surgeries	9	10	4	10
Number of TEAEs	7	4	2	9
Surgeries with ≥1 TEAE, n (%)	4 (44.4)	4 (40.0)	1 (25.0)	4 (40.0)
Number of related TEAEs	0	0	0	0
Number of TESAEs	2	3	0	3
Surgeries with ≥1 TESAE, n (%)	2 (22.2)	3 (30.0)	0	2 (20.0)
Number of related TESAEs	0	0	0	0
TEAEs leading to death	0	0	0	0
TEAEs leading to treatment discontinuation	0	0	0	0

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

References

1. Lowell AE, et al. *Curr Anesthesiol Rep*. 2024;14:354–65. 2. Konkle BA, et al. *N Engl J Med*. 2020;383:1018–27. 3. Chhabra ES, et al. *Blood*. 2020;135:1484–96. 4. von Drygalski A, et al. *N Engl J Med*. 2023;388:310–18. 5. Malec L, et al. *N Engl J Med*. 2024;391:235–46. 6. Chowdary P, et al. Presented at: World Federation of Hemophilia 2025 Comprehensive Care Summit; April 23–25, 2025; Dubai, United Arab Emirates. *Haemophilia*. 2025;31(suppl 2):21-109. Abstract PP-022.

Disclosures

PC has received advisory role expenses from ApcinteX, Bayer, Boehringer Ingelheim, Chugai, CSL Behring, Freeline, Novo Nordisk, Pfizer, Roche, Sanofi, Sobi, Spark, and Takeda. **AN** has received investigator-initiated research/education grant funding from Bayer Yakuhin Ltd, Chugai Pharmaceutical Co, Ltd, and Pfizer Japan Inc. AN has served as a medical advisor for Chugai Pharmaceutical Co, Ltd and KM Biologics. **AN** has received honoraria from Bayer Yakuhin Ltd, Chugai Pharmaceutical Co, Ltd, CSL Behring, Fujimoto Pharmaceutical Corporation, KM Biologics, Novo Nordisk Pharma Ltd, Pfizer Japan Inc, Sanofi KK, and Takeda Pharmaceutical Co, Ltd. **JO** has received research funding from Bayer, Biotest, CSL Behring, Octapharma, Pfizer, Sobi, and Takeda. **JO** has received consultancy and speakers bureau honoraria and scientific advisory board and travel expenses from Bayer, Biogen Idec, BioMarin, Biotest, Chugai, CSL Behring, Freeline, Grifols, LFB, Novo Nordisk, Octapharma, Pfizer, Roche, Sanofi, Sobi, Spark Therapeutics, and Takeda. **LM** has received consultative/advisory board expenses from CSL Behring, Novo Nordisk, Sanofi, Sobi, Spark Therapeutics, and Takeda and has served on the speakers bureau for CSL Behring and Sanofi. **MTAR** has received speaker, advisory board, and sponsored symposia expenses from Amgen, CSL Behring, Novartis, Novo Nordisk, Octapharma, Pfizer, Roche, Sobi, and Takeda. **UK, SG, and JD** are employees of Sanofi and may hold shares and/or stock options in the company. **HP** and **MG** are employees of Sobi and may hold shares and/or stock options in the company. **AKCC** has received research support for clinical trials from Bayer, Novo Nordisk, Pfizer, Sanofi, and Takeda and advisory board expenses from Bayer, Novo Nordisk, Octapharma, Pfizer, Sanofi, and Takeda.

Funding

This study and medical writing support were funded by Sanofi and Sobi.

Acknowledgments

Medical writing support for the development of this poster was provided by Barrie Anthony, PhD, and Helen Jones, PhD, of Envision Pharma Group. The authors thank Emily Ly, PharmD (Sanofi) and Nick Fulcher, PhD, CMPP (Sobi) for publication coordination, and Erin Fang (Sanofi) for biostatistical support. Sanofi and Sobi personnel reviewed this poster. The authors had full editorial control of the poster and provided their final approval of all content.