Efanesoctocog Alfa for the Perioperative Management of Patients with Severe Hemophilia A: 4 Years of Experience in the XTEND Clinical Program in North America

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Introduction

- Surgical interventions can pose a significant bleeding risk for patients with hemophilia A[1]
- Efanesoctocog alfa (formerly BIVV001) is a first-in-class high-sustained factor VIII (FVIII) replacement therapy designed to maintain higher FVIII activity levels for longer by overcoming the half-life ceiling imposed by von Willebrand factor[2,3]
- In the XTEND-1 (NCT04161495) and XTEND-Kids (NCT04759131) studies, once weekly prophylaxis with efanesoctocog alfa 50 IU/kg provided highly effective bleed protection, maintaining HSF levels in the normal to near-normal range (>40%) for approximately 4 days in adults and adolescents, and for about 3 days in children[4,5]
- Efanesoctocog alfa proved effective for perioperative management across all age groups[6,7]

Objective

- To evaluate efanesoctocog alfa for perioperative management of surgeries in participants from North America in the Phase 3 XTEND clinical program (XTEND-1 [NCT04161495], XTEND-Kids [NCT04759131] and XTEND-ed [NCT04644575])

Methods

Study design and population

- XTEND-1 and XTEND-Kids studies assessed safety and efficacy of efanesoctocog alfa in previously treated patients ≥12 and <12 years old, respectively, with severe hemophilia A (<1 IU/dL endogenous FVIII)
  - Participants from each study could continue treatment in the XTEND-ed study
- Participants from North America completing XTEND-1/XTEND-Kids and continuing efanesoctocog alfa prophylaxis (50 IU/kg/week) in XTEND-ed Arm A and those newly initiated on prophylaxis in Arm C of XTEND-ed (planned surgery), were included
- Participants undergoing surgery were to receive a preoperative loading dose of efanesoctocog alfa 50 IU/kg
  - For major surgeries, postoperative doses of 30 or 50 IU/kg every 2–3 days were allowed
- The dose and number of injections to maintain intraoperative hemostasis, total consumption, blood loss/transfusion, and investigator assessment of response are described
- Data cut-off for XTEND-ed study was February 22, 2024

Surgeries

- Surgeries were considered major if they were an invasive procedure that required opening a major body cavity, operating on a joint, removing an organ, dental extraction of any molar teeth or ≥3 non-molar teeth, alteration of normal anatomy, or crossing mesenchymal barriers
- Surgeries were considered minor if they were any invasive operative procedure in which only skin, mucous membranes, or superficial connective tissue were manipulated and did not meet the criteria for major surgery

Dosing and consumption

- Analyses are based on surgeries during the treatment period, excluding any surgery conducted after the last dose of efanesoctocog alfa
- Efanesoctocog alfa injections and consumption were summarized over all injections during the referenced time interval in the surgical/rehabilitation period

Hemostatic response

- The surgeon's/investigator's assessment of hemostatic response (performed 24 hours after surgery) was based on the International Society on Thrombosis and Haemostasis 4-point response for surgical procedures scale (excellent, good, fair, or poor)[8]

Results

Demographics

- Overall, 20 participants from North America, all male, underwent surgeries (**Table 1**)
- A total of 8 participants underwent 8 major surgeries (of which two were orthopedic surgeries, a left hip revision and left olecranon arthroplasty)
- A total of 12 participants underwent 15 minor surgeries

Table 1. Key patient demographics and characteristics of participants from North America

	Major surgeries	Minor surgeries
Number of participants	8	12
Sex, n (%)		
Male	8 (100)	12 (100)
Age, years		
Mean (SD)	28.1 (25.4)	21.0 (23.2)
Median (range)	17.5 (5–74)	10.5 (2–74)
Age groups, years, n (%)		
<12 years	2 (25.0)	6 (50.0)
12–17 years	2 (25.0)	2 (16.7)
18–64 years	3 (37.5)	3 (25.0)
≥65 years	1 (12.5)	1 (8.3)
Race, n (%)		
White	7 (87.5)	10 (83.3)
Black or African American	1 (12.5)	2 (16.7)
Weight, kg		
Mean (SD)	55.03 (27.95)	44.86 (31.97)
Median (range)	64.20 (16.1–81.0)	37.00 (11.4–101.0)

Data cut: February 22, 2024
SD, standard deviation.

Types of surgeries performed in North American participants

- The types of major and minor surgeries performed are listed in **Table 2** and **Table 3**, respectively:

Table 2. Types of major surgeries performed in North American participants

	Major surgeries (N=8)
Orthopedic surgeries (n=2)	
Hip revision	1
Olecranon arthroplasty	1
Major dental surgeries (n=3)	
Dental restoration and tooth extraction	1
Removal of molars	1
Extraction of wisdom teeth	1
Port related (n=2)	
Mediport removal and exchange	1
Portacath removal	1
General surgery (n=1)	
Laparoscopic abdomen hernia repair	1

Data cut: February 22, 2024
N, total number of major surgeries; n, total number of individual surgeries in each subcategory

Table 3. Types of minor surgeries performed in North American participants

	Minor surgeries (N=15)
Port related minor surgeries (n=4)	
Portacath removal	1
Porthcath removal and insertion	1
Port replacement	2
Minor dental surgeries (n=4)	
Full dental rehabilitation with extraction	2
Baby tooth extraction	1
Extraction and bone graft	1
Ophthalmologic minor surgeries (n=2)	
Age-related cataracts	2
GI procedures (n=5)	
Cecostomy tube change	2
Upper endoscopy with tissue biopsy	1
Colonoscopy with biopsy	1
EGC with biopsies showing no signs of aspiration	1

Data cut: February 22, 2024
EGD, Esophagogastroduodenoscopy; GI, gastrointestinal; N, total number of major surgeries; n, total number of individual surgeries in each subcategory

Perioperative management and hemostatic response during major surgery:

- For all major surgeries, hemostasis was maintained with one injection of efanesoctocog alfa (**Table 4**)
- Hemostatic response was rated excellent for all major surgeries
- For five surgeries with available data, the median (range) of estimated intraoperative blood loss was 4.0 (0.0–50.0) mL
- For all major surgeries, during the post-operative period (the day following end of surgery to the date of hospital discharge), the median (range) of estimated blood loss was 0.5 (0.0–200.0) mL
  - The left hip revision surgery reported 200.0 mL of post-operative blood loss
  - None of the major surgeries required blood transfusion

Table 4. Major surgery: Dosing frequency and consumption during the XTEND clinical program in North American participants

	Overall pooled major surgeries (N=8)[a,b]
Number of doses to maintain hemostasis during major surgery, median (range)	1.0 (1.0–1.0)
Number of doses per major surgery, median (range)[c,d,e]	
Day -1 to 0 (n=8)	1.0 (1.0–1.0)
Day 1 to 3 (n=6)	1.0 (1.0–2.0)
Day 4 to 14 (n=8)	2.0 (1.0–4.0)
Day -1 to 14 (n=8)	4.0 (2.0–7.0)
Consumption (IU/kg), median (range)[d,e,f]	
Day -1 to 0 (n=8)	51.57 (49.8–61.9)
Day 1 to 3 (n=6)	45.11 (32.4–103.0)
Day 4 to 14 (n=8)	106.29 (53.2–206.1)
Day -1 to 14 (n=8)	200.28 (106.4–360.6)
Number of injections required to maintain hemostasis, n (%)	
0	0 (0.0)
1	8 (100.0)
Hemostatic response, n (%)	
Excellent	8 (100.0)
Estimated blood loss during surgery (mL)	
n	5
Median (range)	4.0 (0.0–50.0)
Estimated blood loss post-operatively (mL)[g]	
n	8
Median (range)	0.50 (0.0–200.0)
Number of transfusions per surgery, n (%)	
0	8 (100.0)

[a]Data cutoff was February 22, 2024. [b]Analyses are based on major surgeries during the treatment period, excluding any surgery conducted after the last dose of efanesoctocog alfa. [c]Efanesoctocog alfa injections are summarized over all injections during the referenced time interval in the surgical/rehabilitation period. [d]Day 0 is defined as the surgery day; the loading dose for the surgery is the pre-operative injection, administered either on the day of surgery or one day prior to the surgery (Day -1). [e]n is the number of surgeries having surgical injections within the related interval. [f]Total efanesoctocog alfa consumption is summarized over all injections during the referenced time interval in the surgical/rehabilitation period; [g]Post-operative period refers to the day following the end of surgery to the date of hospital discharge.

Perioperative management and hemostatic response during minor surgery:

- Of 15 minor surgeries among 12 participants, hemostasis was maintained with one injection of efanesoctocog alfa in 14 (93.3%) cases
  - One minor surgery did not require any injection
- Hemostatic response was rated excellent for all minor surgeries with an assessment (**Table 5**)
- For 10 minor surgeries, median (range) estimated blood loss during surgery was 0.0 (0.0–5.0) mL
- For nine minor surgeries, during the post-operative period (the day following end of surgery to the date of hospital discharge), the median (range) of estimated blood loss was 0.0 (0.0–5.0) mL
  - None of the minor surgeries required blood transfusion

Conclusions

- A total of 8 major and 15 minor surgeries were safely performed with efanesoctocog alfa in the XTEND clinical development program across North American participants of all ages
- A single preoperative dose (50 IU/kg) maintained hemostasis during all major surgeries and most (93.3%) minor surgeries
- Hemostatic response to efanesoctocog alfa was rated as excellent for all major and minor surgeries with an evaluation
- Postoperative factor consumption was low during both major and minor surgeries
- The study demonstrated that efanesoctocog alfa continues to remain highly effective for perioperative management of major and minor surgeries in North American participants with severe hemophilia A

Table 5. Minor surgeries: Dosing frequency and consumption during the XTEND clinical program in North American participants

	Overall pooled minor surgeries (N=15)[a,b]
Number of doses to maintain hemostasis during minor surgery, median (range)	1.0 (1.0–1.0)
Number of doses per minor surgery, median (range)[c,d,e]	
Day -1 to 0 (n=14)	1.0 (1.0–1.0)
Day 1 to 3 (n=6)	1.0 (1.0–1.0)
Day 4 to 14 (n=6)	1.0 (1.0–1.0)
Day -1 to 14 (n=15)	2.0 (1.0–2.0)
Consumption (IU/kg), median (range)[d,e,f]	
Day -1 to 0 (n=14)	52.00 (48.10–59.50)
Day 1 to 3 (n=6)	54.49 (50.00–59.50)
Day 4 to 14 (n=6)	53.68 (51.50–57.80)
Day -1 to 14 (n=15)	103.09 (48.10–119.00)
Number of injections required to maintain hemostasis, n (%)	
0	0 (0.0)
1	14 (93.3)[g]
Hemostatic response, n (%)[h]	
Excellent	11 (100.0)
Good	0 (0)
Fair	0 (0)
Poor	0 (0)
Estimated blood loss during surgery (mL)	
n	10
Median (range)	0.0 (0.0–50.0)
Estimated blood loss post-operatively (mL)[i]	
n	9
Median (range)	0.0 (0.0–5.0)
Number of transfusions per surgery, n (%)	
0	15 (100.0)

[a]Data cutoff was February 22, 2024. [b]Analyses are based on minor surgeries during the treatment period, excluding any surgery that was conducted after the last dose of efanesoctocog alfa. [c]Efanesoctocog alfa injections are summarized over all injections during the referenced time interval in the surgical/rehabilitation period. [d]Day 0 is defined as the surgery day; the loading dose for the surgery is the pre-operative injection, administered either on the day of surgery or one day prior to the surgery (Day -1). [e]n is the number of surgeries having surgical injections within the related interval. [f]Total efanesoctocog alfa consumption is summarized over all injections during the referenced time interval in the surgical/rehabilitation period. [g]One minor surgery did not require any injection. [h]Percentage based on number of surgeries with an assessment; assessment not available for 4 minor surgeries. [i]Post-operative period refers to the day following end of surgery to the date of hospital discharge.

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