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Efanesoctocog Alfa for the Perioperative Management of Patients with Severe Haemophilia A: 4 years of Experience in the XTEND Clinical Programme

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Disclosure for Anthony KC Chan

In compliance with conflicts of interest policy, EAHAD requires the following disclosures to the session audience:

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Efanesoctocog Alfa: A First-in-Class High-Sustained Factor VIII Replacement Therapy

Undertaking surgical procedures in people with haemophilia places them at increased risk of bleeding, both intraoperatively and postoperatively;[1] such procedures are therefore reliant on the use of **factor replacement therapy**

Efanesoctocog alfa is a first-in-class high-sustained factor VIII replacement therapy that overcomes the von Willebrand factor-imposed half-life ceiling[2,3]

XTEND-1 (NCT04161495)[4] and **XTEND-Kids** (NCT04759131)[5] showed once-weekly efanesoctocog alfa (50 IU/kg) was highly efficacious and well tolerated during surgery in patients with severe haemophilia A

Patients completing these studies could continue efanesoctocog alfa prophylaxis in Arm A of the extension study, **XTEND-ed** (NCT04644575) for up to 4 years

IU, international units.

1. Olivieri M, et al. Lowell AE, *et al. Curr Anesthesiol Rep* 2024;14:354–65. 2. Chhabra ES, et al. *Blood* 2020;135:1484–96. 3. Konkle BA, et al. *N Engl J Med* 2020;383:1018–27;
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.

Objective

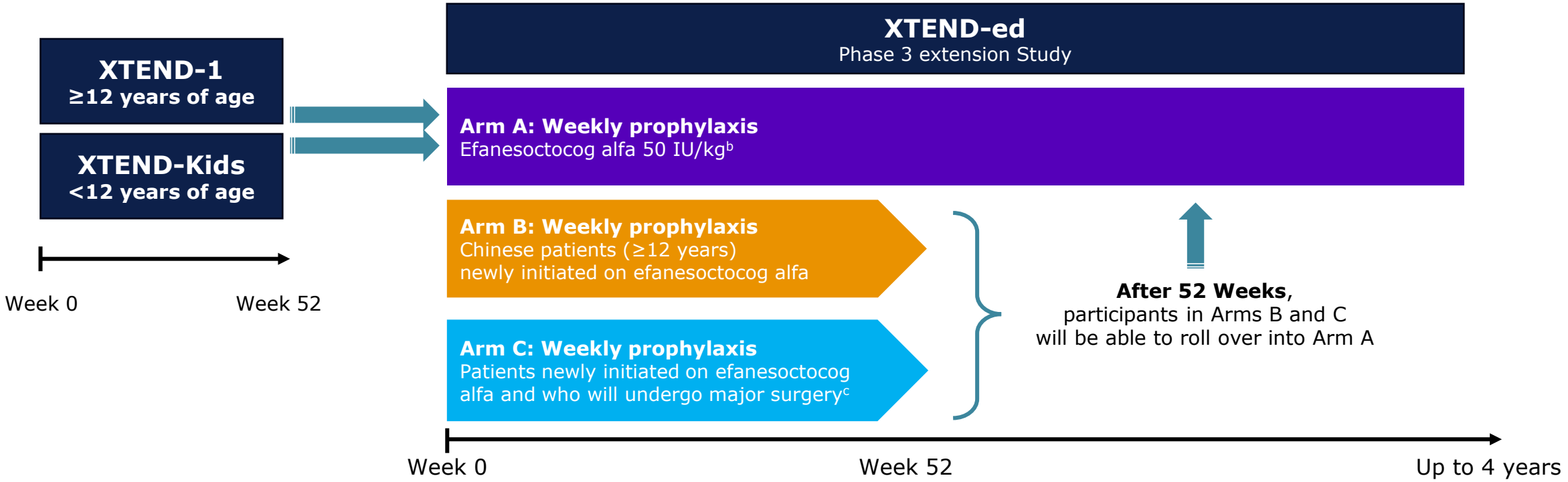
To report **4 years** of perioperative management in the XTEND clinical programme

Data cut: 22 February 2024[a]

[a]The XTEND-ed study commenced in February 2021.

The XTEND Clinical Trial Programme

- XTEND-1 and XTEND-Kids Phase 3 study patients could continue efanesoctocog alfa prophylaxis in the long-term extension study, XTEND-ed
- Severe haemophilia A (<1 IU/dL endogenous FVIII activity)[a]
- Previous treatment with any recombinant and/or plasma-derived FVIII, or cryoprecipitate



ED, exposure days; FVIII, factor VIII; IU, international units.
[a]Or a documented genotype known to produce severe haemophilia A. [b]Patients in Arm A will continue receiving efanesoctocog alfa prophylaxis for a cumulative total of ≥100 EDs from XTEND-1/XTEND-Kids and XTEND-ed. They can continue in XTEND-ed for up to 4 years, unless efanesoctocog alfa is commercially available in their participating country.
[c]Major surgery planned after ≥6 initial EDs and within 26 weeks from Day 1.
Clinical trials.gov. NCT04644575. Long-term safety and efficacy of efanesoctocog alfa (BIVV001) in previously treated patients with hemophilia A (XTEND-ed). https://clinicaltrials.gov/ct2/show/NCT04644575.

Perioperative Management in the XTEND Clinical Trial Programme

Methods

- 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

End Points

- Number and dose of injections to maintain haemostasis
- Assessment of haemostatic response[a]
- Efanesoctocog alfa consumption
- Blood loss
- Number and type of blood transfusions

Data cut: 22 February 2024

[a]Investigator assessment of response was assessed by the International Society on Thrombosis and Haemostasis (ISTH) 4-point response for surgical procedures scale; scores ranged from excellent, good, moderate, to none.

Patient Baseline Characteristics

	Patients with major surgeries (N=45)	Patients with minor surgeries (N=47)
Age, years		
Mean (SD)	35.6 (17.9)	33.1 (23.8)
Range	5–74	2–74
Age category, n (%)		
<12 years	3 (6.7)	14 (29.8)
12 to 17 years	7 (15.6)	6 (12.8)
18 to 64 years	33 (73.3)	23 (48.9)
≥65 years	2 (4.4)	4 (8.5)
Sex, n (%)		
Male	45 (100)	47 (100)
Race, n (%)		
White	26 (57.8)	31 (66.0)
Black or African American	1 (2.2)	3 (6.4)
Asian	13 (28.9)	9 (19.1)
Other	1 (2.2)	0
Not reported	4 (8.9)	4 (8.5)
BMI, kg/m^2		
Mean (SD)	23.9 (4.51)	23.0 (5.99)

BMI, body mass index; SD, standard deviation.

Management During Major Surgeries

	Orthopaedic surgeries[a]	Non-orthopaedic surgeries[b]	Overall
Number of major surgeries	30	31	61
Number of injections to maintain haemostasis during surgery[c]			
Mean (SD)	1.0 (0.2)	1.0 (0.2)	1.0 (0.2)
Median (min, max)	1.0 (1, 2)	1.0 (1, 2)	1.0 (1, 2)
Dose per injection to maintain haemostasis, IU/kg[c]			
Mean (SD)	46.1 (10.7)	51.3 (3.4)	48.8 (8.2)
Median (min, max)	50.0 (12.7, 53.8)	50.8 (45.4, 61.9)	50.0 (12.7, 61.9)

[a]22 patients had 30 orthopaedic surgeries. [b]30 patients had 31 non-orthopaedic surgeries. [c]Surgeries requiring at least 1 injection to maintain haemostasis on Days -1 to 0, with surgery occurring on Day 0.

Perioperative Management of Major Surgeries

	Orthopaedic surgeries[a]	Non-orthopaedic surgeries[b]	Overall
Number of major surgeries	30	31	61
Median (min, max) injections during perioperative period			
Day -1 to 0	1 (1, 2) n=28	1 (1, 2) n=30	1 (1, 2) n=58
Day 1 to 3	1 (1, 2) n=24	1 (1, 2) n=12	1 (1, 2) n=36
Day 4 to 14	3 (2, 6) n=29	2 (1, 4) n=30	2 (1, 6) n=59
Day -1 to 14	5 (2, 9) n=30	3 (1, 7) n=31	4 (1, 9) n=61
Median (min, max) total consumption during perioperative period, IU/kg			
Day -1 to 0	50.0 (12.7, 84.7)	51.1 (45.4, 100.0)	50.0 (12.7, 100.0)
Day 1 to 3	32.1 (29.7, 103.0)	33.1 (24.3, 99.8)	32.7 (24.3, 103.0)
Day 4 to 14	115.4 (82.5, 206.1)	101.0 (48.0, 167.5)	103.3 (48.0, 206.1)
Day -1 to 14	185.3 (98.4, 360.6)	154.5 (45.4, 317.2)	167.3 (45.4, 360.6)
Time from surgery to return to routine prophylaxis, days			
Median (Q1, Q3)	15.0 (10.0, 29.0) n=29	7.5 (6.0, 9.0) n=30	9.0 (7.0, 16.0) n=59

[a]22 patients had 30 orthopaedic surgeries. [b]30 patients had 31 non-orthopaedic surgeries. n=number of surgeries having surgical injections within the related interval.
IU, international units; Q, quartile; SD, standard deviation.

Estimated Blood Loss and Blood Transfusions for Major Surgeries

	Orthopaedic surgeries	Non-orthopaedic surgeries	Overall
Number of major surgeries	30	31	61
Median (min, max) estimated blood loss during surgery, mL	140 (0–1000)	1 (0–100)	50 (0–1000)
Median (min, max) estimated postoperative blood loss, mL	80 (0–1210)	0 (0–20)	0 (0–1210)

- 96.7% (59/61) surgeries did not require blood transfusion
- 2 orthopaedic surgeries[a] required red blood cell transfusions

[a]Open reduction and internal fixation of left femoral fracture and unilateral hip and knee replacement.

Management During Minor Surgeries

	Minor surgeries
Number of minor surgeries	56
Minor surgeries not requiring injections (Day -1 to 0), n (%)	9 (16.1)
Number of injections to maintain haemostasis during surgery (Day -1 to 0)[a]	
Mean (SD)	1.0 (0.0)
Median (min, max)	1.0 (1,1)
Dose per injection to maintain haemostasis (Day -1 to 0), IU/kg[a]	
Mean (SD)	50.5 (5.2)
Median (min, max)	51.1 (30.1, 59.5)
Total dose to maintain haemostasis (Day -1 to 0), IU/kg[a]	
Mean (SD)	50.5 (5.2)
Median (min, max)	51.1 (30.1, 59.5)

[a]Surgeries requiring at least 1 injection to maintain haemostasis.
IU, international units; SD, standard deviation.

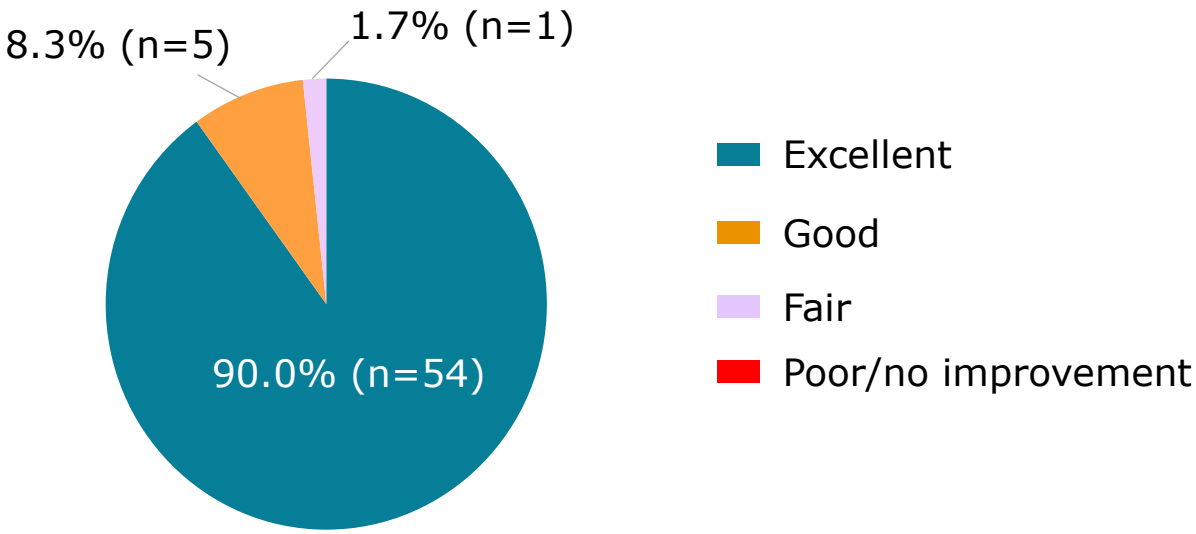
Perioperative Management of Minor Surgeries

	Minor surgeries
Number of minor surgeries	56
Median (min, max) number of injections during perioperative period	
Day -1 to 0	1 (1, 1) n=47
Day 1 to 3	1 (1, 2) n=19
Day 4 to 7	1 (1, 3) n=37
Day -1 to 7	2 (1, 6) n=55
Median (min, max) total consumption during perioperative period, IU/kg	
Day -1 to 0	51.1 (30.1, 59.5)
Day 1 to 3	50.0 (29.1, 68.9)
Day 4 to 7	51.2 (47.6, 78.6)
Day -1 to 7	101.5 (47.6, 199.2)
Time from surgery to return to routine prophylaxis, days	
Median (Q1, Q3)	7.0 (5.0, 8.0) n=56

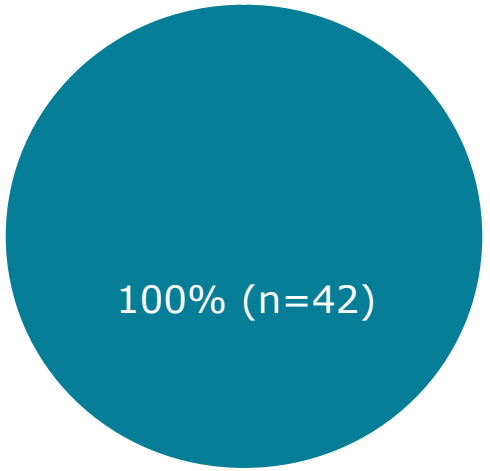
n=number of surgeries having surgical injections within the related interval.
IU, international units; Q, quartile; SD, standard deviation.

Investigator/Surgeons' Assessment of Patients' Haemostatic Response

Major surgeries (number assessed: 60)



Minor surgeries (number assessed: 42)



Safety Outcomes During the Surgical/Rehabilitation Period

	Major surgeries	Minor surgeries
Number of surgeries	61	56
Number of TEAEs Surgeries with ≥1 TEAE, n (%)	36 20 (32.8)	27 18 (32.1)
Number of related TEAEs Surgeries with ≥1 related TEAE, n (%)	2 2 (3.3)	0 0
Number of TESAEs Surgeries with ≥1 TESAE, n (%)	10 8 (13.1)	8 7 (12.5)
Number of related TESAEs	0	0
TEAEs leading to death	0	0
TEAEs leading to treatment discontinuation	0	0

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

Conclusions

- A single preoperative dose (50 IU/kg) of efanesoctocog alfa was sufficient to maintain haemostasis for major and minor surgeries
- Total perioperative efanesoctocog alfa consumption was low
- Haemostatic response to efanesoctocog alfa was rated as excellent for 90% of major surgeries and 100% of minor surgeries

These long-term data from the XTEND clinical trial programme show that efanesoctocog alfa:

- Is highly effective for perioperative management of patients with severe haemophilia A across a variety of major and minor surgeries with a limited number of injections, and
- Remains well tolerated

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