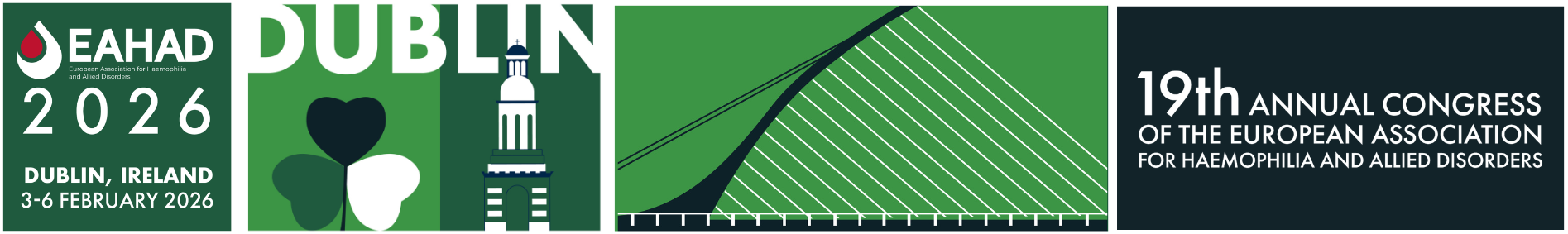

Efanesoctocog Alfa Prophylaxis for People with Severe Haemophilia A: Third Interim Results from the XTEND-ed Long-Term Extension Study

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Disclosures for Dr Pratima Chowdary

In compliance with COI policy, EAHAD requires the following disclosures to the session audience:

Shareholder	No relevant conflicts of interest to declare.
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Consultant	Served on advisory boards for Apcintex, Bayer, Baxalta/Shire, Biogen Idec, Boehringer Ingelheim, Chugai, CSL Behring, Freeline, Novo Nordisk, Pfizer, Roche, Sanofi and Sobi.
Employee	No relevant conflicts of interest to declare.
Paid Instructor	No relevant conflicts of interest to declare.
Speaker Bureau	No relevant conflicts of interest to declare.
Other	No relevant conflicts of interest to declare.

Efanesoctocog Alfa is a First-in-Class Ultra-Long Half-Life FVIII Replacement Therapy

FVIII replacement therapies

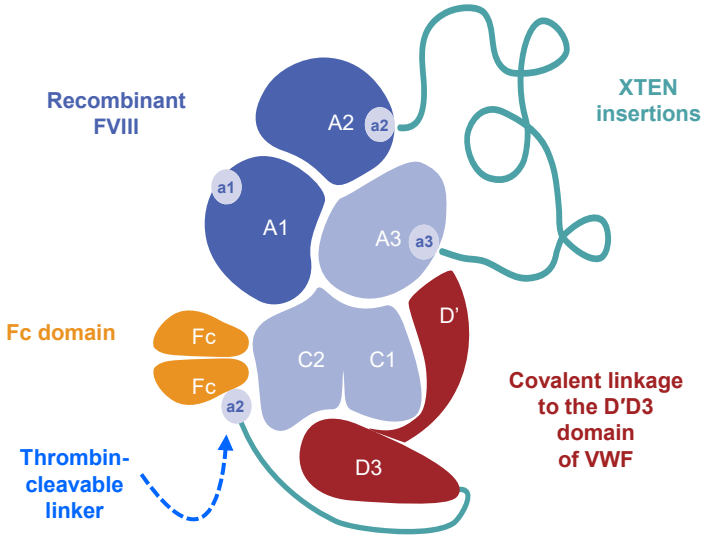
Standard half-life factor

Extended half-life factor

Ultra-long half-life factor*

Efanesoctocog alfa is a novel fusion protein that **overcomes the VWF-imposed half-life ceiling**[4,5]

Geometric mean **half-life** (95% CI)
Participants ≥12 years: **47.0 hours** (42.3 to 52.2)[1]
Participants <12 years: **40.0 hours** (38.5 to 41.5)[2]



Over **52 weeks** in the **Phase 3** studies **XTEND-1** (adults and adolescents) and **XTEND-Kids** (children), **once-weekly efanesoctocog alfa 50 IU/kg prophylaxis** was shown to provide:[1,2]

- **Sustained FVIII levels** in the **non-haemophilia range** (>40%)[3] at steady state for 4 and 3 days, respectively
- **Highly effective bleed protection** and was **well tolerated**

*Also known as High-Sustained Factor (HSF). CI, confidence interval; FVIII, factor VIII; VWF, von Willebrand factor
1. von Drygalski A *et al. N Engl J Med* 2023;388:310–8; 2. Malec L *et al. N Engl J Med* 2024;391:235–46; 3. Srivastava A *et al. Haemophilia* 2020;26:1–158; 4. Chhabra ES *et al. Blood* 2020;135:1484–96; 5. Konkle BA *et al. N Engl J Med* 2020;383:1018–27

XTEND-ed: an Ongoing, Multicentre, Open-label Study of the Long-term Safety and Efficacy of Efanesoctocog Alfa

Aim

Evaluate the **safety** and **efficacy** of **efanesoctocog alfa** in the **Phase 3 XTEND-ed long-term extension study** (third interim analysis; data cut off: **21 February 2025**)

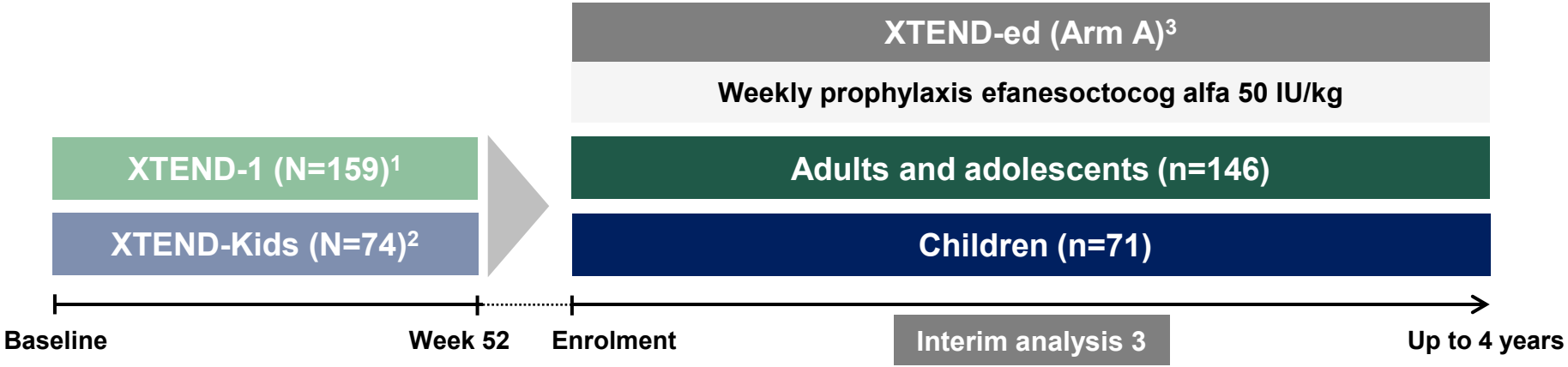
Participants

- **Previously treated patients** with **severe haemophilia A** (<1 IU/dL endogenous FVIII activity)
- **Completed XTEND-1**[1] (≥12 years) or **XTEND-Kids**[2] (<12 years) and rolled over to XTEND-ed Arm A[3]

FVIII, factor VIII

1. ClinicalTrials.gov. XTEND-1. Available at: https://clinicaltrials.gov/study/NCT04161495 (accessed January 2026); 2. ClinicalTrials.gov. XTEND-Kids. Available at: https://clinicaltrials.gov/study/NCT04759131 (accessed January 2026);
3. ClinicalTrials.gov. XTEND-ed. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04644575 (accessed January 2026)

XTEND-ed: an Ongoing, Multicentre, Open-label Study of the Long-term Safety and Efficacy of Efanesoctocog Alfa



Primary endpoint:

- Occurrence of inhibitor development

Secondary endpoints:

- ABRs
- Treatment of bleeding episodes
- Safety and tolerability

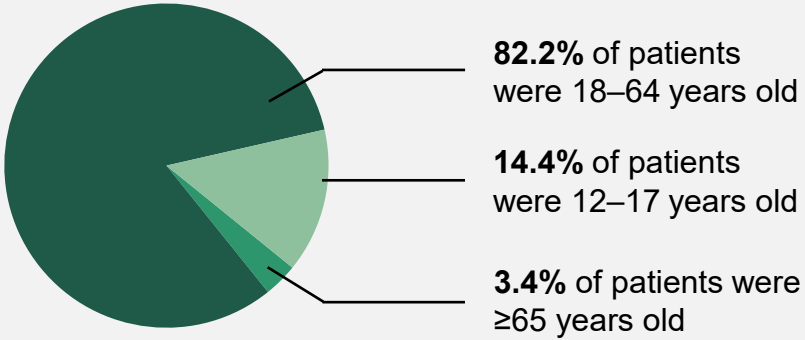
ABR, annualised bleed rate

1. ClinicalTrials.gov. XTEND-1. Available at: https://clinicaltrials.gov/study/NCT04161495 (accessed January 2026); 2. ClinicalTrials.gov. XTEND-Kids. Available at: https://clinicaltrials.gov/study/NCT04759131 (accessed January 2026);
3. ClinicalTrials.gov. XTEND-ed. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04644575 (accessed January 2026)

Patient Demographics in XTEND-ed

Adults and adolescents (n=146)

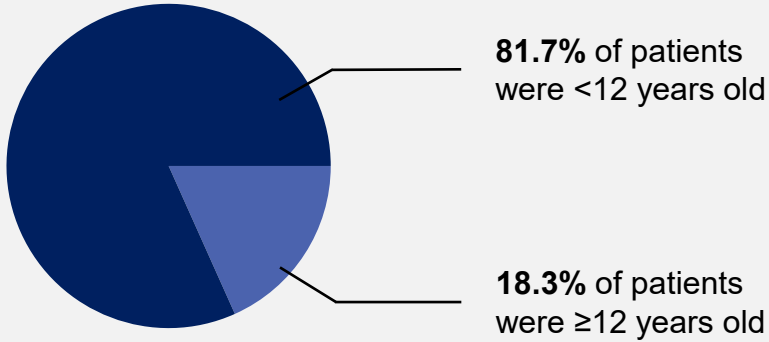
Age at enrolment in XTEND-ed, years



- Median age was **37** (range: 13–74) years
- Median weight was **77.3** (range: 33.9–132.8) kg
- All patients except one are male

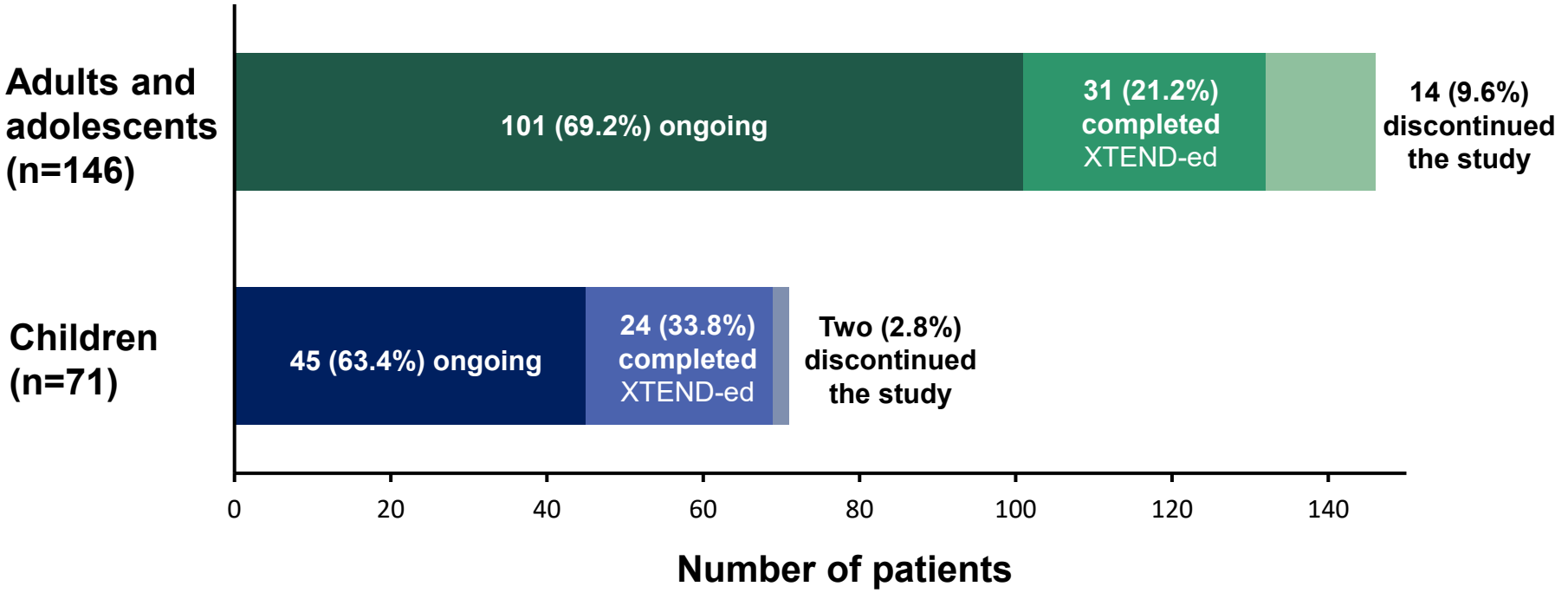
Children (n=71)

Age at enrolment in XTEND-ed, years



- Median age was **7** (range: 2–13) years
- Median weight was **22.1** (range: 11.4–66.5) kg
- All patients are male

Patient follow-up in XTEND-ed*



*The number of patients in XTEND-ed has been decreasing as efanesoctocog alfa becomes commercially available

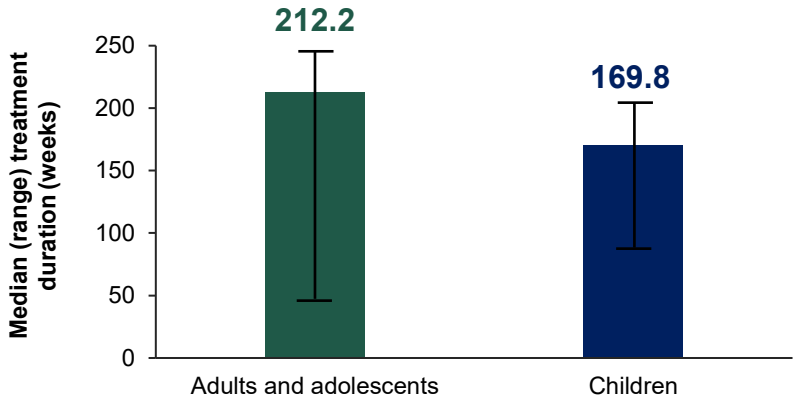
No FVIII Inhibitors Developed With Efanesoctocog Alfa During the XTEND-ed Study

The incidence of inhibitor formation for previously treated patients with severe haemophilia A was:

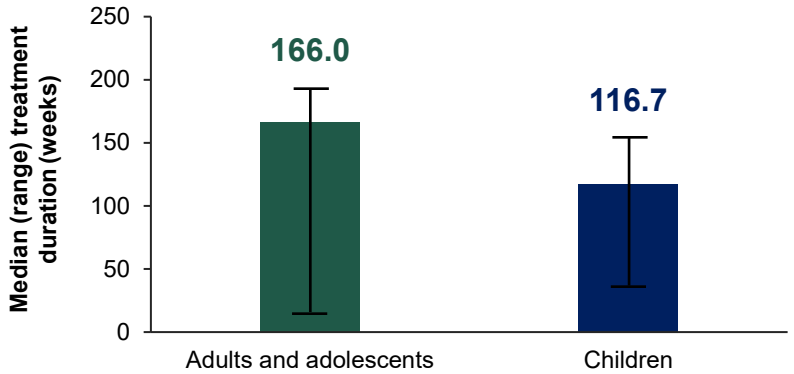
0.0 **Adults and adolescents**
(95% CI: 0.0–2.5)

0.0 **Children**
(95% CI: 0.0–5.1)

Treatment duration from parent study baseline



Treatment duration in XTEND-ed



- **Mean exposure days** during XTEND-ed were **156.4** for **adults** and **adolescents** and **103.5** for **children**
- **Total patient-years** followed were **429.6** for **adults and adolescents** and **139.5** for **children**
- **In XTEND-ed, mean total number of injections per patient** were **157.1** for **adults** and **adolescents** and **103.9** for **children**

Data cut: 21 February 2025
CI, confidence interval; FVIII, factor VIII

Low Bleed Rates (ABR <1) Were Maintained With Weekly Efanesoctocog Alfa Prophylaxis in XTEND-ed

Adults and adolescents

Over a median of **166.0 weeks** in XTEND-ed, the mean model-based **ABR for treated bleeds** was:

0.60

This is consistent with the low ABR in XTEND-1 (**0.71**)[1]

Mean **model-based spontaneous ABR** during XTEND-ed was:

0.20

Children

Over a median of **116.7 weeks** in XTEND-ed, the mean model-based **ABR for treated bleeds** was:

0.64

This is consistent with the low ABR in XTEND-Kids (**0.61**)[2]

Mean **model-based spontaneous ABR** during XTEND-ed was:

0.08

Data cut: 21 February 2025
ABR, annualised bleed rate
1. von Drygalski A *et al. N Engl J Med* 2023;388:310–8; 2. Malec L *et al. N Engl J Med* 2024;391:235–46

Low Bleed Rates (ABR <1) Were Maintained With Weekly Efanesoctocog Alfa Prophylaxis in XTEND-ed

Adults and adolescents

Duration	Evaluable patients*	Overall bleeds		Spontaneous bleeds	
		Mean ABR	SD	Mean ABR	SD
Day 1 – Month 6	146	**0.64**	1.62	**0.19**	0.76
Months 6–12	144	**0.76**	1.54	**0.30**	0.83
Months 12–18	141	**0.65**	1.64	**0.23**	0.76
Months 18–24	138	**0.58**	1.58	**0.23**	0.69
Months 24–30	132	**0.43**	1.06	**0.12**	0.54
Months 30–36	123	**0.52**	2.17	**0.14**	0.71

Children

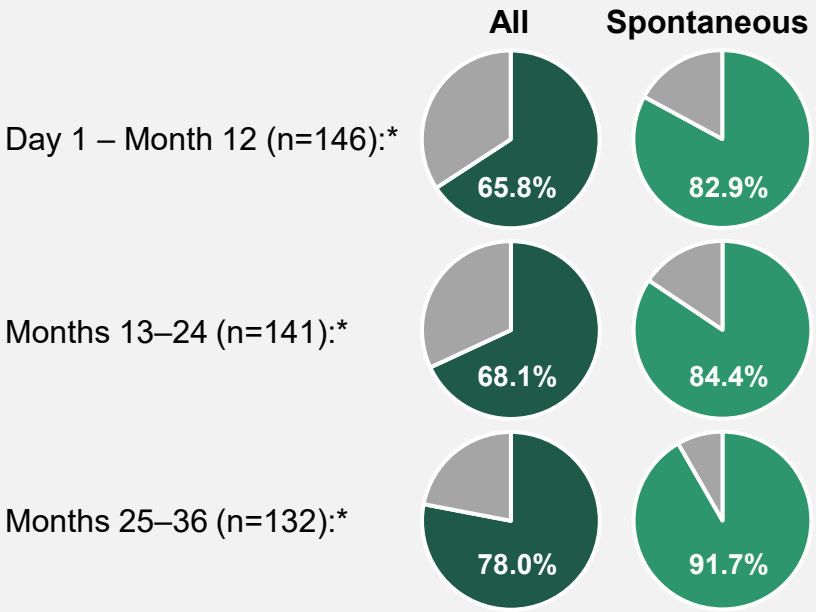
Duration	Evaluable patients*	Overall bleeds		Spontaneous bleeds	
		Mean ABR	SD	Mean ABR	SD
Day 1 – Month 6	71	**0.65**	1.47	**0.06**	0.33
Months 6–12	70	**0.72**	1.56	**0.06**	0.34
Months 12–18	62	**0.43**	0.99	**0.04**	0.28
Months 18–24	50	**0.68**	1.12	**0.04**	0.28

Data cut: 21 February 2025
*N numbers represent the number of patients with an efficacy period. Latter periods have not been completed by all patients and data may change
ABR, annualised bleed rate; SD, standard deviation

Percentage of Participants With Zero Bleeds Remained High With Long-Term Weekly Prophylaxis With Efanesoctocog Alfa

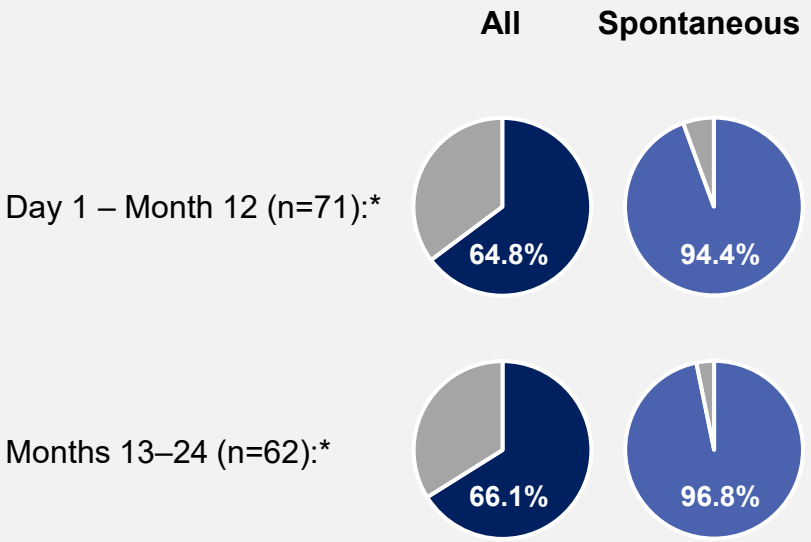
Adults and adolescents

Percentage with zero bleeds by 12-month intervals



Children

Percentage with zero bleeds by 12-month intervals

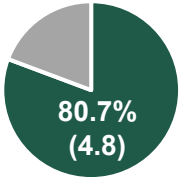


Data cut: 21 February 2025
*N numbers represent the number of patients with an efficacy period. Latter periods have not been completed by all patients and percentages may change

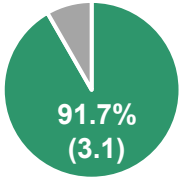
Percentage of Patients With Zero Bleeds Remained High With Long-Term Weekly Efanesoctocog Alfa Prophylaxis

Adults and adolescents

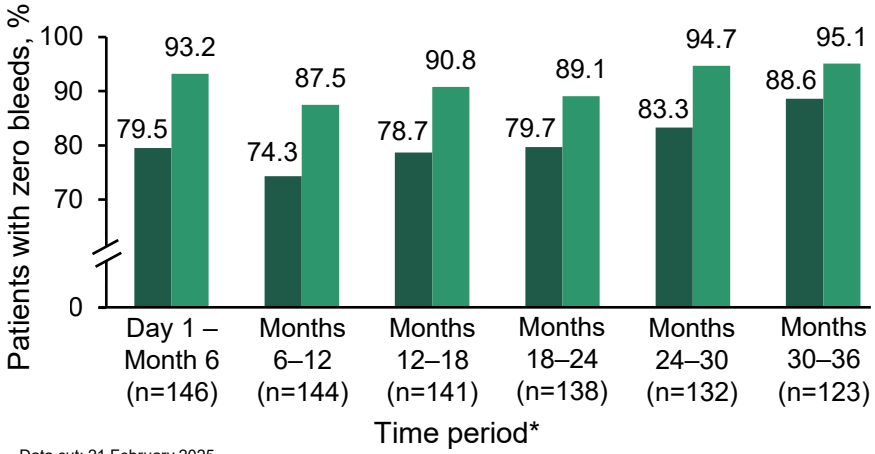
All bleeds:



Spontaneous bleeds:

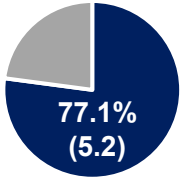


Mean (SD) percentage with **zero bleeds** per 6-month interval

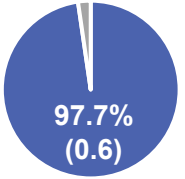


Children

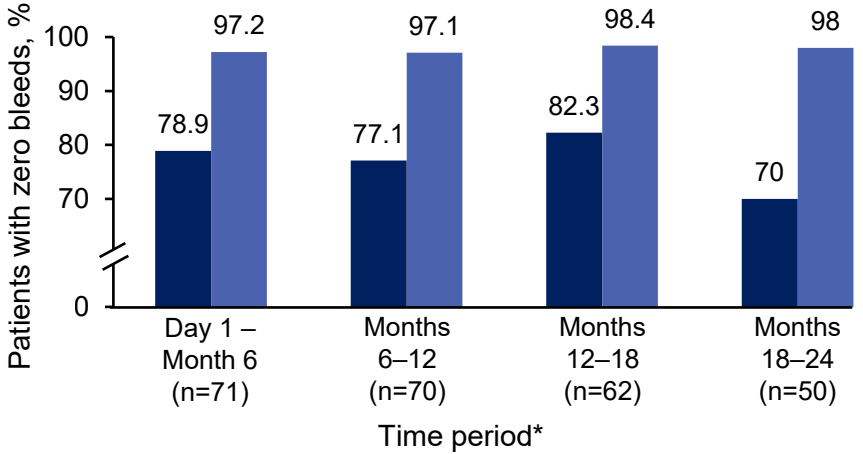
All bleeds:



Spontaneous bleeds:



Mean (SD) percentage with **zero bleeds** per 6-month interval



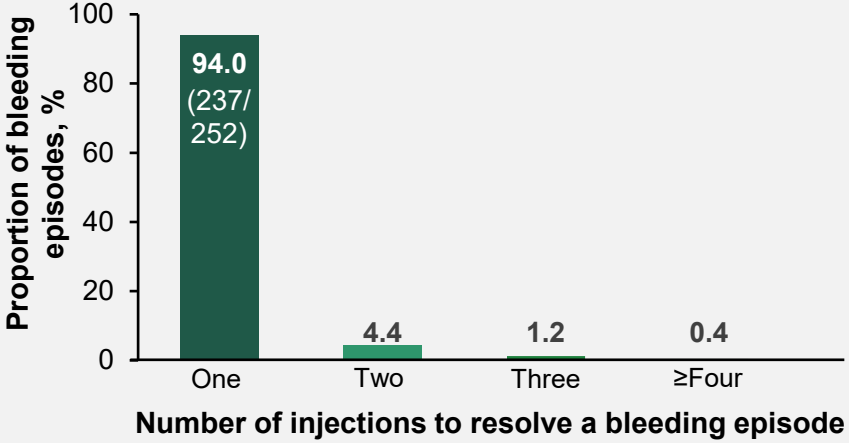
Data cut: 21 February 2025

*During each 6-month period, N numbers represent the number of patients with an efficacy period. Latter periods have not been completed by all patients and percentages may change

SD, standard deviation

Efanesoctocog Alfa Remains Highly Effective for the Treatment of Bleeding Episodes in XTEND-ed

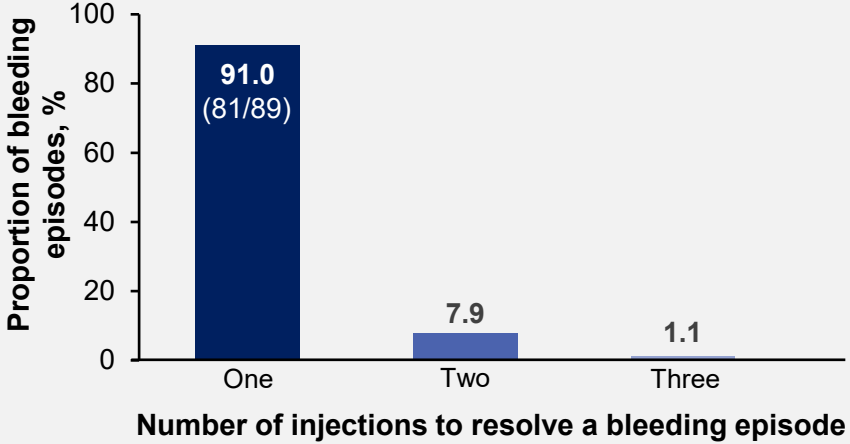
Adults and adolescents



87.8% (**173/197**) of injections with an evaluation were assessed as **excellent** or **good** by patients

Mean dose (SD), IU/kg:
- Per injection: **45.1** (9.6)
- Total: **49.2** (24.6)

Children



94.1% (**64/68**) of injections with an evaluation were assessed as **excellent** or **good** by patients

Mean dose (SD), IU/kg:
- Per injection: **50.5** (9.4)
- Total: **56.0** (19.6)

Data cut: 21 February 2025
SD, standard deviation

Efanesoctocog Alfa Treatment was Well Tolerated, With No Related Serious Adverse Events

	Adults and adolescents (n=146)	Children (n=71)
Total number of TEAEs, n	762	427
Patients with ≥1 TEAE, n (%)	126 (86.3)	60 (84.5)
Patients with ≥1 related TEAE, n (%)	2 (1.4)	2 (2.8)
Total number of TESAEs, n	52	7
Patients with ≥1 TESAE, n (%)	29 (19.9)	7 (9.9)
Patients with ≥1 related TESAE, n (%)	0 (0.0)	0 (0.0)
TEAEs leading to death, n (%)	2 (1.4)	0
TEAEs leading to treatment discontinuation, n (%)	3 (2.1)	0

All treatment-related TEAEs in adults and adolescents were resolved:
- Facial paralysis
- Coagulation FVIII level decreased

The two deaths were unrelated to efanesoctocog alfa

All TEAEs leading to treatment discontinuation in adults and adolescents were unrelated to efanesoctocog alfa treatment:
- Femur fracture (received prohibited concomitant medication)
- Deep vein thrombosis following surgical repair of femur fracture
- Subarachnoid haemorrhage following aortic dissection repair

All treatment-related TEAEs in children were resolved:
- Asthma
- Post-infusion pain and headache

Data cut: 21 February 2025
FVIII, factor VIII; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event

Conclusions

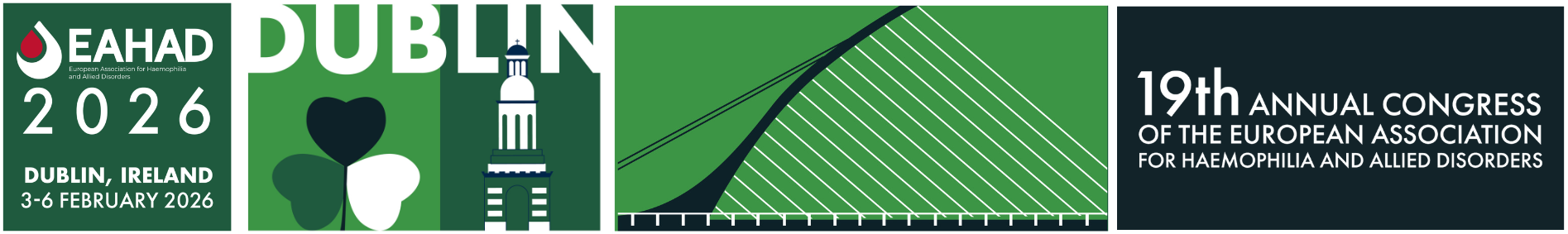
In previously treated patients with severe haemophilia A, there was **no development of FVIII inhibitors** with efanesoctocog alfa

Mean **ABRs** remained **low** (<1)

Mean percentage of patients with **zero spontaneous bleeding episodes** per 6-month interval was **>90%** in adults, adolescents and children

Long-term, once-weekly efanesoctocog alfa prophylaxis (50 IU/kg) continues to be **well tolerated** and **highly effective** in **adults, adolescents** and **children** with severe haemophilia A

ABR, annualised bleed rate; FVIII, factor VIII



We thank the patients, their families and the study investigators

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