Treatment of Bleeding Episodes With Efanesoctocog Alfa in Children: XTEND-ed Second Interim Analysis

Lynn Malec,[1,2] Christoph Königs,[3] Amy Dunn,[4] Manuel Carcao,[5] Bulent Zulfikar,[6] Ruben Berrueco,[7] Simon Brown,[8] Umer Khan,[9] Sriya Gunawardena,[10] Graham Neill,[11] Lydia Abad-Franch,[12] Linda Bystrická,[12] Sophie Susen[13]

1. Versiti Blood Research Institute, Milwaukee, WI, USA; 2. Medical College of Wisconsin, Milwaukee, WI, USA; 3. Goethe University Frankfurt, University Hospital, Frankfurt, Germany; 4. Nationwide Children's Hospital/Ohio State University, Columbus, OH, USA; 5.The Hospital for Sick Children, Toronto, ON, Canada; 6. Istanbul University Oncology Institute, Inherited Bleeding Disorders Center, Istanbul, Turkey; 7. Hospital Sant Joan de Déu, Barcelona, Spain; 8. Queensland Children's Hospital, Queensland Haemophilia Centre, South Brisbane, QLD, Australia; 9. Sanofi, Cambridge, MA, USA; 10. Sanofi, Bridgewater, NJ, USA; 11. Sanofi, Reading, United Kingdom; 12. Sobi, Basel, Switzerland; 13. Centre Hospitalier Universitaire de Lille, Université de Lille, Lille, France

International Society on Thrombosis and Hemostasis; 21–25 June 2025, Washington

Disclosures

Lynn Malec reports consultancy/advisory board expenses from CSL Behring, Genentech, Novo Nordisk, Sanofi, Sobi, Spark Therapeutics, and Takeda and speaker's bureau fees from CSL Behring and Sanofi.

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

Introduction

Despite advances in treatment for people living with hemophilia, **bleeding episodes can persist**, negatively affecting health and quality of life[1,2]

Efanesoctocog alfa is a first-in-class high-sustained factor VIII (FVIII) replacement therapy designed to **decouple recombinant FVIII from endogenous von Willebrand factor**[3,4]

The **Phase 3 XTEND-Kids**[a] study showed once-weekly efanesoctocog alfa was well tolerated and provided highly effective bleed protection in children aged <12 years with severe hemophilia A[5]

Patients completing XTEND-Kids were eligible to continue once-weekly efanesoctocog alfa prophylaxis in Arm A of the **long-term extension study, XTEND-ed**[a]

[a]XTEND-Kids: NCT04759131; XTEND-ed: NCT04644575.

1. Gooding R, et al. *J Blood Med.* 2021;12:209-20. 2. Gualtierotti R, et al. *J Thromb Haemost.* 2021;19:2112-21. 3. Konkle BA, et al. *N Engl J Med.* 2020;383:1018-27. 4. Lissitchkov T, et al. *Blood Adv.* 2022;6:1089-94.
5. Malec L, et al. N Engl J Med 2024;391:235–46.

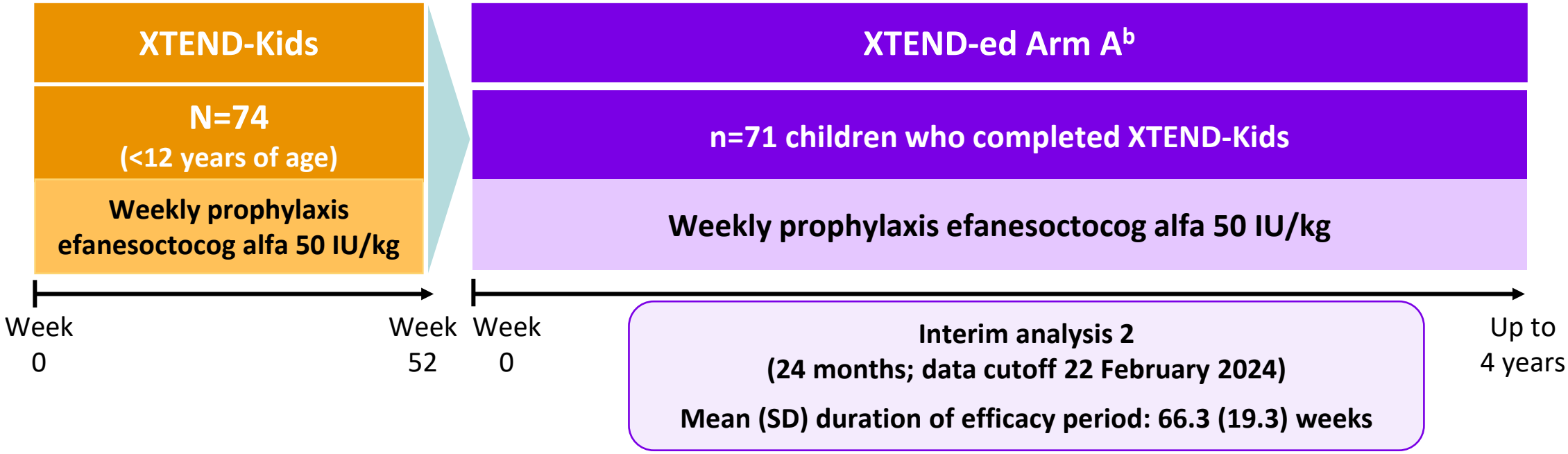
Objective

To report the **efficacy and safety of efanesoctocog alfa** for treating bleeds in children aged <12 years after **2 years** of follow-up[a] in XTEND-ed

[a]Second interim analysis. Data cutoff: 22 February 2024. The XTEND-ed study commenced in February 2021.

XTEND Clinical Trial Program

Previously treated children (aged <12 years old at enrollment) with severe hemophilia A[a] and who completed the XTEND-Kids trial could roll over to Arm A of XTEND-ed



Patients provided informed consent; the study was approved by applicable review boards. [a]<1 IU/dL endogenous FVIII activity or a documented genotype known to produce severe hemophilia A. [b]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.
FVIII, factor VIII; IU, international units; SD, standard deviation.

Methods

Methods

- Per protocol, bleeding episodes were to be treated with a single injection of 50 IU/kg efanesoctocog alfa
- Additional doses could be administered every 2–3 days, if needed
- Model-based ABRs were derived from a negative binomial model of treated bleeding episodes

Study endpoints

- Number, type, and location of treated bleeding episodes
- ABRs, model-based ABRs
- Assessment of hemostatic response[a]
- Safety and tolerability

Data cutoff: 22 February 2024

[a]Patient assessment of response 72 hours after the initial treatment using the 4-point International Society on Thrombosis and Haemostasis scale; scores ranged from excellent, good, moderate, to none.
ABR, annualized bleed rate; IU, international units.

Patient Demographics and Clinical Characteristics

	Age <6 years[a] (n=35)	Age 6 to <12 years[a] (n=36)	Overall (N=71)
Age at XTEND-ed enrollment, years[a]			
Mean (SD)	5.3 (1.4)	10.1 (2.3)	7.7 (3.1)
Sex, n (%)			
Male	35 (100)	36 (100)	71 (100)
Weight, kg			
Median (range)	17.5 (11.4–25.7)	32.9 (17.2–66.5)	22.1 (11.4–66.5)
Race, n (%)			
White	25 (71.4)	27 (75.0)	52 (73.2)
Black or African American	1 (2.9)	2 (5.6)	3 (4.2)
Asian	4 (11.4)	4 (11.1)	8 (11.3)
Other	3 (8.6)	0	3 (4.2)
Not reported	2 (5.7)	3 (8.3)	5 (7.0)

At data cutoff, **52 patients** were continuing the study, 18 patients had completed the study, and 1 patient had discontinued (withdrew consent)

[a]Age refers to the age at screening for the parent study (patients were assigned to the appropriate age cohort [<6 years or 6 to <12 years] at baseline of the parent study [XTEND-Kids]).
SD, standard deviation.

ABRs for Treated Bleeds by Age Group and Type

	Age <6 years[a] (n=35)	Age 6 to <12 years[a] (n=36)	Overall (N=71)
Duration of efficacy period[b] (weeks) Median (range)	58.4 (31.1–96.6)	69.6 (8.0–100.6)	66.3 (8.0–100.6)
Total number of treated bleeds	26	35	61
Model-based[c] mean (95% CI) ABRs			
Total treated bleeds	0.64 (0.41–0.99)	0.70 (0.43–1.12)	0.67 (0.48–0.93)
Spontaneous treated bleeds	0.07 (0.02–0.23)	0.04 (0.01–0.16)	0.06 (0.02–0.13)
Traumatic treated bleeds	0.46 (0.23–0.91)	0.48 (0.29–0.79)	0.46 (0.31–0.70)

A total of **61** bleeding episodes were treated; **overall mean ABR** was **0.67; median ABR** was **0**

[a]Age refers to the age at screening for the parent study. [b]The efficacy period is defined as the treatment regimen period, which is from the first injection in Arm A in XTEND-ed to the day of the last dose of study drug in Arm A in XTEND-ed, excluding periods of surgery/rehabilitation (minor and major), and large injection intervals (>28 days). [c]Estimated using a negative binomial model with the total number of treated bleeds during the efficacy period as the response variable and log-transformed efficacy period duration (in years) as an offset variable.
ABR, annualized bleed rate; CI, confidence interval.

ABRs for Treated Bleeds by Age Group and Location

	Age <6 years[a] (n=35)	Age 6 to <12 years[a] (n=36)	Overall (N=71)
Duration of efficacy period[b] (weeks) Median (range)	58.4 (31.1–96.6)	69.6 (8.0–100.6)	66.3 (8.0–100.6)
Model-based[c] mean (95% CI) ABRs			
Joint	0.18 (0.08–0.40)	0.39 (0.22–0.70)	0.29 (0.18–0.48)
Muscle	NC	0.08 (0.02–0.27)	0.07 (0.03–0.17)
Internal	0.13 (0.04–0.48)	0.02 (0–0.14)	0.07 (0.02–0.23)
Skin/mucosa	0.22 (0.10–0.48)	0.17 (0.06–0.46)	0.20 (0.11–0.36)

ABRs were **low** regardless of age group or location; all median ABRs were 0

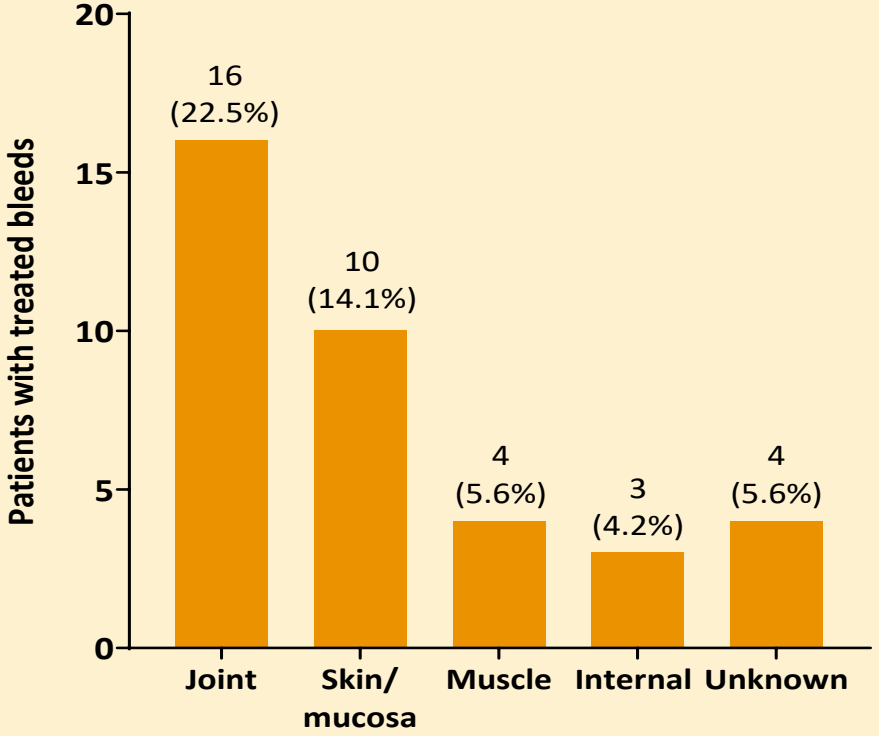
[a]Age refers to the age at screening for the parent study. [b]The efficacy period is defined as the treatment regimen period, which is from the first injection in Arm A in XTEND-ed to the day of the last dose of study drug in Arm A in XTEND-ed, excluding periods of surgery/rehabilitation (minor and major), and large injection intervals (>28 days). [c]Estimated using a negative binomial model with the total number of treated bleeds during the efficacy period as the response variable and log-transformed efficacy period duration (in years) as an offset variable.
ABR, annualized bleed rate; CI, confidence interval; NC, not calculated.

Number and Location of Treated Bleeds in Year 1 of XTEND-ed

Number of treated bleeds per patient

	1–12 months (n=71)
Mean (SD)	0.66 (1.08)
Number per patient, n (%)	
0	**45 (63.4)**
1	14 (19.7)
2	5 (7.0)
3	6 (8.5)
4	0
5	1 (1.4)
>5	0

Location of treated bleeds[a]



During the **first year of treatment**, **63.4%** of patients had **0 bleeds**
Most bleeds occurred in **joints** and **skin/mucosa**

[a]Patients having bleeds in more than one location are counted in each location.
SD, standard deviation.

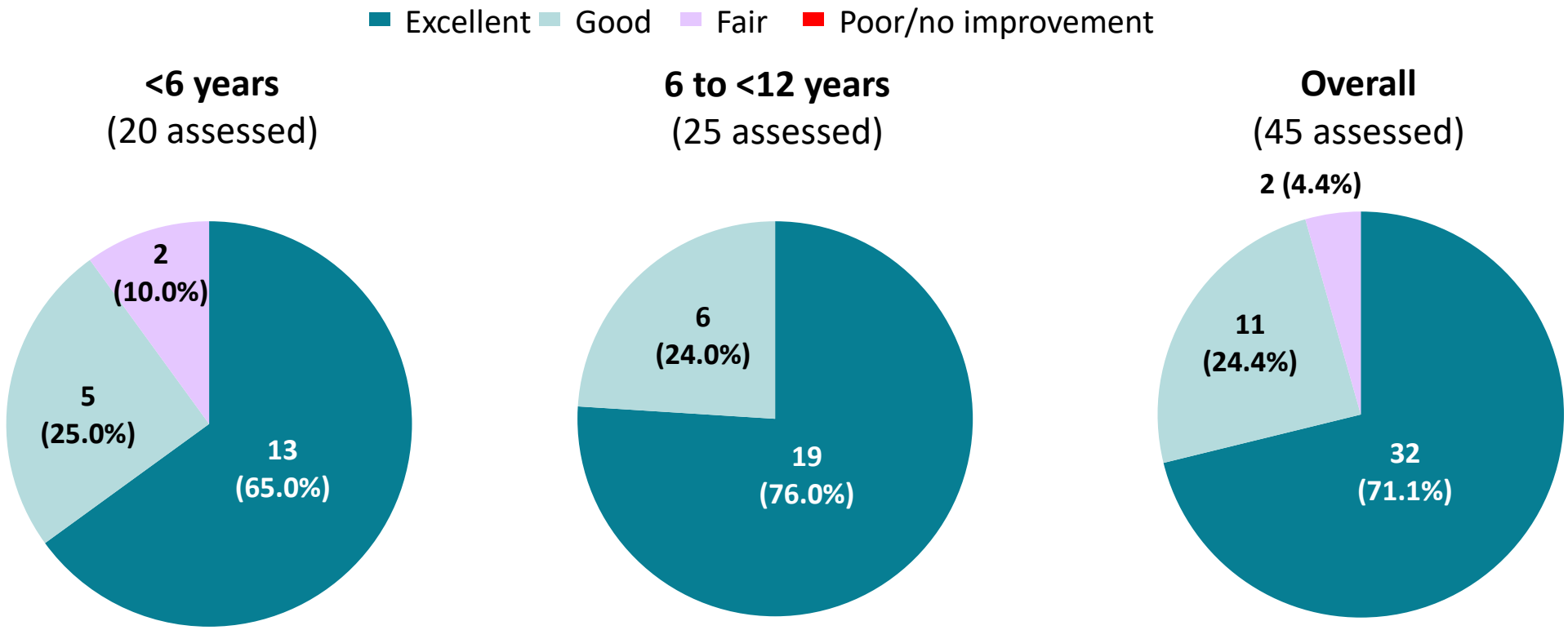
Reported Number of Injections to Treat a Bleeding Episode

	Age <6 years (n=35)	Age 6 to <12 years (n=36)	Overall (N=71)
Dose per injection, IU/kg Mean (SD)	52.0 (7.8)	50.0 (7.5)	50.8 (7.6)
Total dose, IU/kg Mean (SD)	59.6 (23.2)	59.0 (23.8)	59.2 (23.3)
Injections per bleed, n (%)[a]			
1	24 (92.3)	30 (85.7)	54 (88.5)
2	1 (3.8)	4 (11.4)	5 (8.2)
3[b]	1 (3.8)	0	1 (1.6)
4[c]	0	1 (2.9)	1 (1.6)

A single efanesoctocog alfa injection **resolved 88.5%** of bleeds

[a]All injections given from the initial sign of a bleed, until the last date/time within the bleed window are counted. [b]Three injections were required to treat a traumatic bleed in the right knee; response to the first injection was good; the second and third injections were administered 3 and 6 days after the bleed. [c]Two injections were given as pre-emptive treatment for head trauma following a motor vehicle accident; however, each injection was recorded in duplicate, and the error was not noted prior to the data cutoff (this will be rectified for the final data set).
IU, international units; SD, standard deviation.

Patient/Caregiver Assessment of Hemostatic Response at 72 Hours Postbleed[a]



Hemostatic response was rated **excellent/good** for **95.6% of bleeds**

[a]Only the first injection was evaluated.

Safety Outcomes

No inhibitor development was reported
Efanesoctocog alfa prophylaxis and treatment of bleeds **was well tolerated**

	<6 years (n=35)	6 to <12 years (n=36)	Overall (N=71)
Patients with ≥1 TEAE, n (%)	25 (71.4)	30 (83.3)	55 (77.5)
Patients with ≥1 related TEAE, n (%)	0	1 (2.8)[a]	1 (1.4)
Patients with ≥1 TESAE, n (%)	2 (5.7)	2 (5.6)	4 (5.6)
Patients with ≥1 related TESAE, n (%)	0	0	0
TEAEs leading to death, n (%)	0	0	0
TEAEs leading to treatment discontinuation, n (%)	0	0	0

[a]Two treatment-related TEAEs occurred in 1 patient (Injection-related reaction; headache).
The table includes adverse events that occurred on the day the surgical/rehabilitation period started but not those that occurred during a major surgical/rehabilitation period.
TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Conclusions

Once-weekly efanesoctocog alfa (50 IU/kg) continues to provide **highly effective bleed protection** in children with severe hemophilia A in XTEND-ed, as evidenced by a **low ABR** and a high proportion of patients with **zero bleeds**

A **single 50 IU/kg dose** of efanesoctocog alfa

- Provides highly effective treatment of bleeding episodes in children with severe hemophilia A, **regardless of age, bleed type, or location**
- Resolved **88.5%** of bleeding episodes

Efanesoctocog alfa was **well tolerated**; there were **no reports of inhibitor development**

ABR, annualized bleed rate; IU, international units.

The authors would like to thank the patients, their families, and the study investigators