Joint Health Outcomes with Efanesoctocog Alfa in Adults/Adolescents from XTEND-1 Continuing XTEND-ed

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PB1425

Introduction

- Efanesoctocog alfa is a first-in-class high-sustained factor VIII replacement therapy designed to decouple recombinant factor VIII from endogenous von Willebrand factor to further extend its half-life[1-3]
- The Phase 3 XTEND-1 study[4] (NCT04161495) showed that once-weekly efanesoctocog alfa (50 IU/kg) prophylaxis
  - Achieved high, sustained factor levels in the normal to near-normal range (>40%) for most of the week
  - Provided highly effective bleed protection with clinically meaningful improvements in physical health, pain, and joint health
  - Was well tolerated; no development of inhibitors was detected
- Patients completing XTEND-1 could continue weekly efanesoctocog alfa prophylaxis in the long-term extension study, XTEND-ed (NCT04644575)
- An interim analysis after 1 year of follow-up in XTEND-ed showed that all target joints were resolved in patients receiving ≥12 months of efanesoctocog alfa prophylaxis and that improvements to total Hemophilia Joint Health Score (HJHS) achieved during XTEND-1 were maintained[5]

Objective

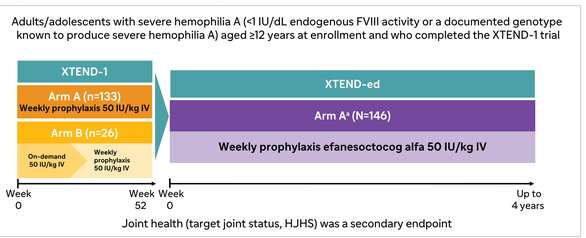
- Report long-term joint health with efanesoctocog alfa in adults/adolescents (aged ≥12 years) over 3 years of weekly prophylaxis treatment, from XTEND-1 baseline through the second interim analysis (Month 24) of XTEND-ed (data cut: February 22, 2024)

Methods

Study design and population

- Patients provided informed consent; the study was approved by applicable review boards
- The XTEND clinical trial program is outlined in **Figure 1**

Figure 1. XTEND clinical trial program



[a]Patients in Arm A will continue to receive efanesoctocog alfa prophylaxis for up to 4 years, unless efanesoctocog alfa is commercially available in their participating country.
FVIII, factor VIII; HJHS, Hemophilia Joint Health Score; IU, international unit; IV, intravenous.

Outcome measures

- Joint health was evaluated at XTEND-1 baseline, and also, at XTEND-ed baseline, Month 12, and Month 24 using HJHS v2.1
- For total joint score, 6 joints (left and right elbows, knees, and ankles) were scored according to 8 HJHS domains, and gait was scored based on walking and climbing stairs
  - HJHS assessments performed within 2 weeks after a joint or muscle bleed were excluded
  - Joint scores following joint surgeries were replaced using the last observation carried forward method
  - Higher HJHS indicates worse joint health, with scores ranging from 0 to 124
- Individual joints (left/right elbows, knees, ankles) were scored according to 8 HJHS domains; gait score ranged from 0 to 4
- Improved/worsened HJHS scores were defined by decreases/increases of ≥4 points; an unchanged (or constant) HJHS score was defined by a change in score of between -3 and +3 points
- A target joint was defined as a major joint (eg, hip, elbow, wrist, shoulder, knee, ankle) in which ≥3 spontaneous bleeding episodes had occurred in a 6-month period; target joint resolution was assessed according to the International Society on Thrombosis and Haemostasis criteria, defined as ≤2 bleeding episodes in the target joint over 12 months of continuous exposure

Results

- A total of 146 adults/adolescents rolled over from XTEND-1 to Arm A of XTEND-ed
  - Median (range) treatment duration and exposure days from XTEND-1 baseline were 170.5 (46.3–192.6) weeks and 121.5 (14–147) days, respectively
- The data presented here represent the 115 patients with joint health data at both XTEND-1 baseline and XTEND-ed Month 24, covering ~3 years of continuous treatment **(Table 1)**

Table 1. Patient demographics and clinical characteristics

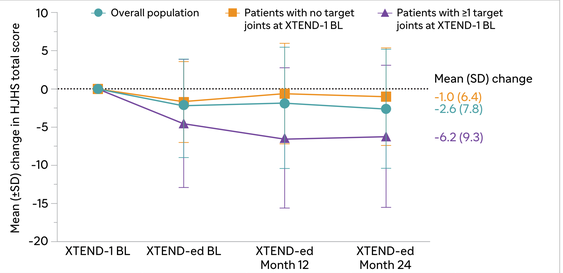
	Patients from XTEND-1 Arm A (n=92)	Patients from XTEND-1 Arm B (n=23)	Overall cohort (N=115)
Male, n (%)	92 (100)	23 (100)	115 (100)
Mean (SD) age (at XTEND-ed enrollment), years	33.6 (14.5)	43.4 (11.9)	35.6 (14.5)
Age category (at XTEND-ed enrollment), n (%)			
12–17 years	19 (20.7)	0	19 (16.5)
18–64 years	71 (77.2)	22 (95.7)	93 (80.9)
≥65 years	2 (2.2)	1 (4.3)	3 (2.6)
Mean (SD) BMI, kg/m²	25.3 (5.1) *(n=92)*	26.6 (5.8) *(n=22)*	25.5 (5.3) *(n=114)*
Mean (SD) age at first prophylaxis treatment, years	3.2 (5.7)	11.4 (15.6)	4.8 (9.2)
Mean (SD) number of joint bleeds in the 12 months prior to XTEND-1	1.6 (2.4) *(n=86)*	27.9 (18.5) *(n=18)*	6.2 (12.7) *(n=104)*
Patients with target joints at BL, n (%)			
0	77 (83.7)	3 (13.0)	80 (69.6)
1	6 (6.5)	1 (4.3)	7 (6.1)
2	2 (2.2)	7 (30.4)	9 (7.8)
3	4 (4.3)	6 (26.1)	10 (8.7)
4	1 (1.1)	2 (8.7)	3 (2.6)
5	1 (1.1)	1 (4.3)	2 (1.7)
6	1 (1.1)	2 (8.7)	3 (2.6)
>6	0	1 (4.3)	1 (0.9)

BL, baseline; BMI, body mass index; SD, standard deviation.

HJHS total and joint scores

- Mean (standard deviation [SD]) total HJHS score was 19.7 (17.9) at XTEND-1 baseline and improved over 3 years of efanesoctocog alfa prophylaxis (mean change, -2.6 [7.8]; **Figure 2**)

Figure 2. Change in HJHS total score from parent study (XTEND-1) baseline to XTEND-ed baseline, Month 12, and Month 24 in patients aged ≥12 years according to target joint status



Mean (SD) HJHS total score (0–124)		XTEND-1 BL N	XTEND-1 BL Mean (SD)	XTEND-ed BL[a] N	XTEND-ed BL[a] Mean (SD)	XTEND-ed Month 12[a] N	XTEND-ed Month 12[a] Mean (SD)	XTEND-ed Month 24 N	XTEND-ed Month 24 Mean (SD)
Overall population	**Total score**	115	19.7 (17.9)	113	16.7 (16.6)	95	16.0 (17.5)	115	17.1 (17.5)
	Change from XTEND-1 BL	–	–	113	-2.6 (6.5)	95	-2.5 (7.9)	115	-2.6 (7.8)
Target joint analysis (performed on patients with data at baseline and Months 12[a] and 24; N=115 patients)									
No target joints at XTEND-1 BL	**Total score**	80	15.8 (18.5)	79	13.5 (16.6)	64	13.6 (19.1)	80	14.8 (18.7)
	Change from XTEND-1 BL	–	–	79	-1.7 (5.3)	64	-0.6 (6.6)	80	-1.0 (6.4)
≥1 target joints at XTEND-1 BL	**Total score**	35	28.6 (12.9)	34	24.2 (14.0)	31	21.1 (12.3)	35	22.5 (13.3)
	Change from XTEND-1 BL	–	–	34	-4.5 (8.4)	31	-6.4 (9.2)	35	-6.2 (9.3)

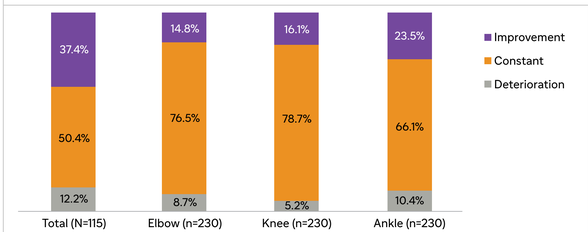
HJHS assessments within 2 weeks after a joint or muscle bleed were excluded. Joint scores following joint surgeries were replaced using the last observation carried forward method. [a]Not all 115 patients had HJHS data at these timepoints.
BL, baseline; HJHS, Hemophilia Joint Health Score; SD, standard deviation.

- At Month 24, the greatest changes (mean [SD]) in domain scores were for flexion loss (-0.4 [2.4]) and swelling (-0.4 [1.8])
- The mean (SD) age of patients with target joints was 42.5 (13.0) years vs 32.5 (14.1) years for those without target joints
- Most patients with target joints at XTEND-1 baseline were in Arm B (n=20/35; 57.1%); only 3 patients (n=3/80; 3.8%) in Arm B had no target joints

Joint health status according to change in HJHS score

- HJHS total score improved or remained constant in 88% of evaluable patients (N=115; **Figure 3**)
- Mean (SD) age at the start of first prophylaxis regimen was 3.2 (5.7) years in Arm A and 11.4 (15.6) years in Arm B

Figure 3. Categorization of joint status according to change in HJHS total and joint scores from XTEND-1 baseline to XTEND-ed Month 24



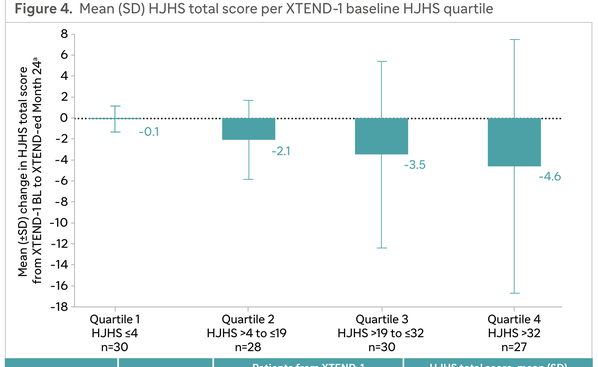
	Overall (N=115) Improvement (n=43)	Constant (n=58)	Deterioration (n=14)
Mean (SD) age at start of first prophylaxis regimen, years	4.9 (7.6)	3.6 (6.9)	9.7 (17.7)
Mean (SD) number of joint bleeds in the 12 months prior to XTEND-1	10.8 (16.0)	1.5 (3.3)	10.3 (18.1)
Patients with target joints at XTEND-1 BL, n (%)	22 (51.2)	8 (13.8)	5 (35.7)

Improved/worsened HJHS scores were defined by decreases/increases of ≥4 points; an unchanged (or constant) HJHS score was defined by a change in score of between -3 and +3 points.
BL, baseline; HJHS, Hemophilia Joint Health Score; SD, standard deviation.

Change in HJHS total score according to baseline HJHS quartile

- The greatest improvements in HJHS total score by XTEND-ed Month 24 were observed among people with the highest HJHS (>32; quartile 4) at XTEND-1 baseline **(Figure 4)**

Figure 4. Mean (SD) HJHS total score per XTEND-1 baseline HJHS quartile



XTEND-1 BL HJHS quartile	Mean (SD) age, years	Patients from XTEND-1 Arm A, n (%)	Patients from XTEND-1 Arm B, n (%)	HJHS total score, mean (SD) XTEND-1 baseline	HJHS total score, mean (SD) XTEND-ed Month 24
Q1	22.3 (9.5)	28 (93.3)	2 (6.7)	1.00 (1.39)	0.90 (1.57)
Q2	30.6 (8.5)	25 (89.3)	3 (10.7)	9.30 (3.66)	7.20 (5.25)
Q3	41.6 (10.6)	21 (70.0)	9 (30.0)	25.80 (4.12)	22.30 (9.28)
Q4	48.8 (12.9)	18 (66.7)	9 (33.3)	44.40 (13.35)	39.80 (15.53)

HJHS total score ranges from 0 to 124. Higher HJHS score denotes worse joint health. [a]Includes patients who had HJHS data at both baseline and XTEND-ed Month 24.
BL, baseline; HJHS, Hemophilia Joint Health Score; Q, quartile; SD, standard deviation.

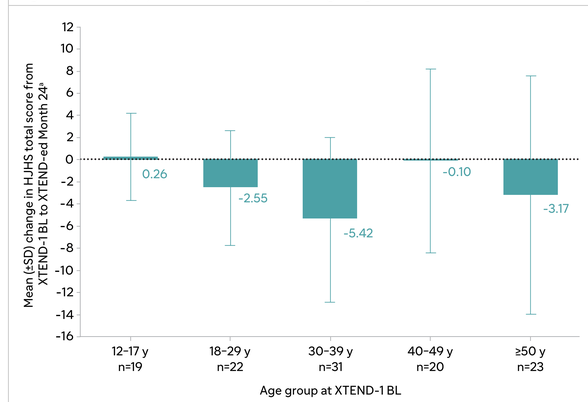
Conclusions

- **The overall improvements in total HJHS score observed after 12 months of treatment in XTEND-1 were maintained at Month 24 of XTEND-ed**
  - **Total HJHS score was improved or maintained with once-weekly efanesoctocog alfa (50 IU/kg) prophylaxis in most patients**
    - **43 of 115 patients (37%) improved their HJHS score**
    - **58 of 115 patients (50%) maintained their score**
- **The greatest improvements were observed in patients with the worst joint health at XTEND-1 baseline, as determined by an HJHS >32 (Quartile 4) or the presence of target joints**

Change in HJHS total score according to baseline age

- The greatest improvements in HJHS total score by XTEND-ed Month 24 were observed among people aged 30 to 39 years, followed by those aged ≥50 years **(Figure 5)**

Figure 5. Mean (SD) HJHS total score according to age



Age group at XTEND-1 BL	HJHS total score, mean (SD) XTEND-1 BL	XTEND-ed Month 24
12–17 years	3.11 (5.82)	3.37 (8.73)
18–29 years	8.86 (10.97)	6.32 (8.16)
30–39 years	20.39 (15.23)	14.97 (14.34)
40–49 years	26.00 (13.88)	25.90 (15.35)
≥50 years	37.30 (18.05)	34.13 (17.88)

HJHS total score ranges from 0 to 124. Higher HJHS score denotes worse joint health. [a]Includes patients who had HJHS data at both baseline and XTEND-ed Month 24.
BL, baseline; HJHS, Hemophilia Joint Health Score; SD, standard deviation.

References

1. Chhabra ES, et al. *Blood*. 2020;135:1484-96.
2. Konkle BA, et al. *N Engl J Med*. 2020;383:1018-27.
3. Lissitchkov T, et al. *Blood Adv*. 2022;6:1089-94.
4. von Drygalski A, et al. *N Engl J Med*. 2023;388:310-18.
5. von Drygalski A, et al. *Res Pract Thromb Haemost*. 2024;8(Suppl 2):e102503.

Disclosures

CK has received personal fees from Bayer Vital GmbH, CSL Behring, Novo Nordisk, Roche/Chugai, Sanofi/Sobi, and Takeda. CK's institution has also received grants from Bayer Vital GmbH, Biotest, CSL Behring, Intersero, Novo Nordisk, Pfizer, Roche/Chugai, Sanofi/Sobi, and Takeda. **AvD** has received fees from BioMarin, Bioverativ/Sanofi-Genzyme, Novo Nordisk, Takeda, and uniQure for participation in industry-sponsored education events and advisory boards. She has received research funding from Bioverativ/Sanofi-Genzyme and Pfizer. She is co-founder and a member of the board of directors of Hematherix Inc. She holds a patent for a super FVa, and she is the inventor and physician lead for the Joint Activity and Damage Examination (JADE) ultrasound measurement tool. JADE is copyrighted through the Office of Innovation and Commercialization at the University of California, San Diego, CA, USA. **CH** has received research funding from Bayer, CSL Behring, Novo Nordisk, Pfizer, Shire/Takeda, and Sobi and honoraria/speakers bureau fees from Bayer, CAF-DCF, CSL Behring, Hoffmann-La Roche, LFB, Novo Nordisk, Octapharma, Pfizer, Regeneron, Sanofi, Shire/Takeda, Sobi, and uniQure. **BAK** has acted as a consultant for Be Biopharma, BioMarin, HC Bioscience, Novo Nordisk, Pfizer, Regeneron, Sanofi, and Takeda and has received research grants from CSL Behring, Pfizer, Sanofi, Takeda, and uniQure. **PVdV** has received consultation fees from Bayer (paid to the institute). **NS** has received honoraria from Bayer, CSL Behring K.K., Chugai, Japan Blood Products Organization, KM Biologics, Novo Nordisk, Pfizer, Sanofi K.K., Takeda, and Yakuhin. **LF, UK, JD,** and **LM** are employees of Sanofi and may hold shares and/or stock options in the company. **LB** and **ES** are employees of Sobi and may hold shares and/or stock options in the company. **RK** has received honoraria and/or been a member of advisory committees for Bayer, BioMarin, Biotest, CSL Behring, Grifols, Novo Nordisk, Octapharma, Pfizer, Roche/Chugai, Sanofi, Shire/Takeda, and Sobi.

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 Helen Jones, PhD, of Envision Pharma Group. The authors thank Emily Ly, PharmD (Sanofi) and Nick Fulcher, PhD, CMPP (Sobi) for publication coordination, Alejandro Fernández (Sanofi) for early guidance on concept, and Meredith Foster (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.

Presented at The International Society on Thrombosis and Haemostasis (ISTH) 2025 Congress; June 21–25, 2025; Washington, DC