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Interim Analysis of Joint Outcomes in Adult and Adolescent Patients With Severe Hemophilia A Receiving Efanesoctocog Alfa During the Phase 3 XTEND-ed Long-Term Extension Study

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Presentation Learning Objectives

At the conclusion of this presentation, participants will be able to:

- Understand that **once-weekly efanesoctocog alfa prophylaxis (50 IU/kg)** was associated with **improvement or maintenance of joint health** in adults and adolescents (≥12 years) with severe hemophilia A in the Phase 3 **XTEND-ed** long-term extension study
- Recognize **efanesoctocog alfa** as a first-in-class, high-sustained factor VIII (HSF) replacement therapy for the treatment of hemophilia A

Efanesoctocog Alfa Is a First-in-Class FVIII Replacement Designed to Provide High-Sustained FVIII Activity Levels

- **Hemophilic arthropathy** and **chronic joint pain** from repeated **bleeding episodes** may occur in people with **hemophilia A** despite treatment with standard-of-care prophylaxis[1-4]

- In the XTEND-1 study (NCT04161495), once-weekly efanesoctocog alfa 50 IU/kg prophylaxis achieved **high-sustained factor levels** in the **normal to near-normal range** (>40%) for the majority of the week[5]
- Once-weekly efanesoctocog alfa prophylaxis provided **highly effective bleed protection** with clinically meaningful improvements in physical health, pain, and **joint health**[5]
- Efanesoctocog alfa was well tolerated, with no development of inhibitors[5-8]

FVIII, factor VIII.

1. Manco-Johnson M, et al. *J Thromb Haemost*. 2017;15(11):2115-2124. 2. Oldenburg J, et al. *Blood*. 2015;125(13):2038-2044. 3. Nijdam A, et al. *Haemophilia*. 2016;22(6):852-858.
4. Srivastava A, et al. *Haemophilia*. 2020;26 Suppl 6:1-158. 5. von Drygalski A, et al. *N Engl J Med*. 2023;388(4):310-318. 6. Konkle BA, et al. *N Engl J Med*. 2020;383(11):1018-1027.
7. Lissitchkov T, et al. *Blood Adv*. 2022;6(4):1089-1094. 8. ALTUVIIIO Package Insert. https://www.altuviiio.com/assets/pdf/ALTUVIIIO-Prescribing-Information.pdf. Accessed April 11, 2023.

Aim

To describe the **impact of once-weekly efanesoctocog alfa prophylaxis** on **long-term joint health** in **adult and adolescents** (≥12 years old) with hemophilia A from XTEND-1 who continued to the XTEND-ed long-term extension study (NCT04644575)

Outcomes

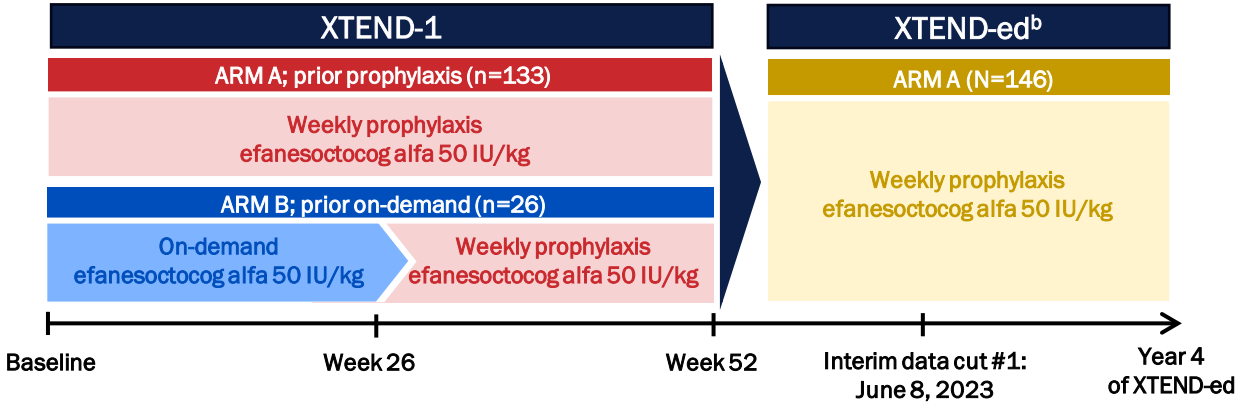
HJHS

Target joint resolution

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score.

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

- Participants from XTEND-1 who rolled over into XTEND-ed
- Severe hemophilia A (<1 IU/dL endogenous FVIII activity)[a]
- Previous treatment with any recombinant and/or plasma-derived FVIII, or cryoprecipitate



Primary endpoint

- The occurrence of inhibitor development[c]

Secondary endpoints

- Annualized bleed rates (ABRs)
- Treatment of bleeding episodes
- Joint health (target joint status, HJHS)

FVIII, factor VIII; HJHS, Hemophilia Joint Health Score.
[a]Or a documented genotype known to produce severe hemophilia A. [b]XTEND-ed began in February 2021. [c]Inhibitor development was evaluated using the Nijmegen-modified Bethesda assay at the central laboratory. Inhibitor development was defined as an inhibitor result of ≥0.6 BU/mL and confirmed by a second test result from a separate sample drawn 2–4 weeks following the date of the original sample.

Key Patient Demographics and Characteristics of Adults and Adolescents in XTEND-ed

A total of **146 patients** enrolled in **XTEND-1** rolled over into **Arm A of XTEND-ed** and are included in this interim **analysis**

Mean (SD) **treatment duration in XTEND-ed** was 82.5 (14.3) weeks

	Overall (N=146)
Sex, n (%)	
Male	145 (99.3)
Female	1 (0.7)
Age	
Mean (SD)	37.0 (15.1)
Median (range)	37.0 (13–74)
Age group, years, n (%)	
12–17 years	21 (14.4)
18–64 years	120 (82.2)
≥65 years	5 (3.4)
Race, n (%)	
White	100 (68.5)
Black or African American	4 (2.7)
Asian	27 (18.5)
Other	2 (1.4)
Not reported, not collected	13 (8.9)
Weight, kg	
Mean (SD)	78.0 (19.4)
Median (IQR)	77.3 (33.9–132.8)

Data cutoff date June 8, 2023.
IQR, interquartile range; SD, standard deviation.

All Target Joints[a] Resolved in Participants Receiving Prophylaxis for ≥12 Months

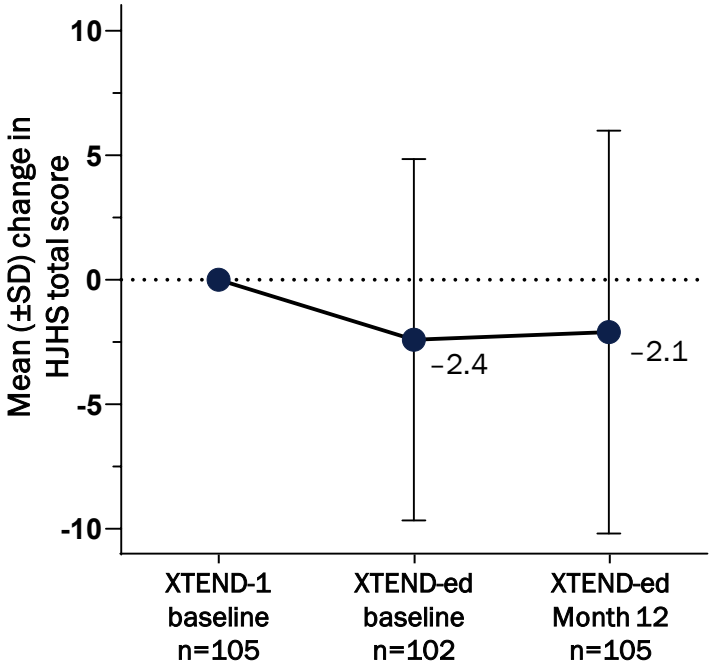
At **baseline**, there were **140 target joints** among 45 participants

At **1 year, all target joints (n=132) had resolved**[b] in participants exposed for ≥12 consecutive months (n=43)[c]

Target joint resolution[b] among participants on prophylaxis for ≥12 months[c]

Data cutoff date June 8, 2023.
[a]A target joint was defined as a major joint (eg, hip, elbow, wrist, shoulder, knee, or ankle) into which ≥3 spontaneous bleeding episodes occurred in a consecutive 6-month period. [b]Target joint resolution was assessed according to the International Society on Thrombosis and Hemostasis criteria, defined as ≤2 bleeding episodes in the target joint over 12 months of continuous exposure. [c]Two participants had exposure to prophylaxis of <52 weeks and did not qualify for target joint evaluation.

Improvements in HJHS Total Score Were Sustained Through XTEND-ed Month 12



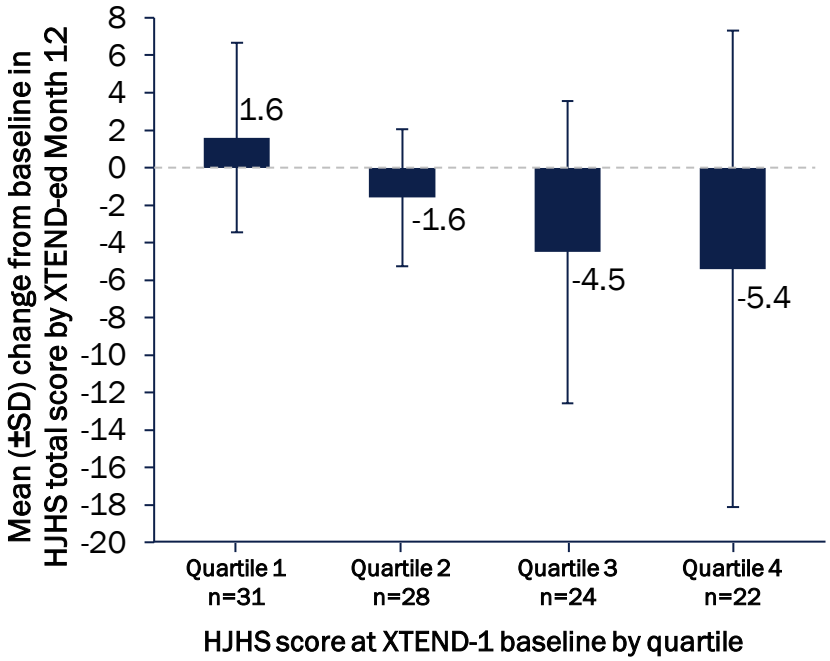
Mean (SD) HJHS total score (0–124) in Arm A by XTEND-ed Month 12		
XTEND-1 baseline	XTEND-ed baseline	XTEND-ed Month 12
18.5 (18.0) n=105	15.6 (16.5) n=102	16.4 (17.3) n=105

Mean (SD) change from XTEND-1 baseline to XTEND-ed Month 12 in **HJHS total score** was **-2.1** (8.1) (n=105)

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score; LOCF, last observation carried forward; SD, standard deviation.
Higher HJHS scores denote worse joint health. An HJHS total score can be calculated if all 48 individual item scores (8 domains × 6 joints, total joint score) and the gait score were present. HJHS assessments within 2 weeks after a joint or muscle bleed are excluded. Joint scores post joint surgeries are replaced using the LOCF method.

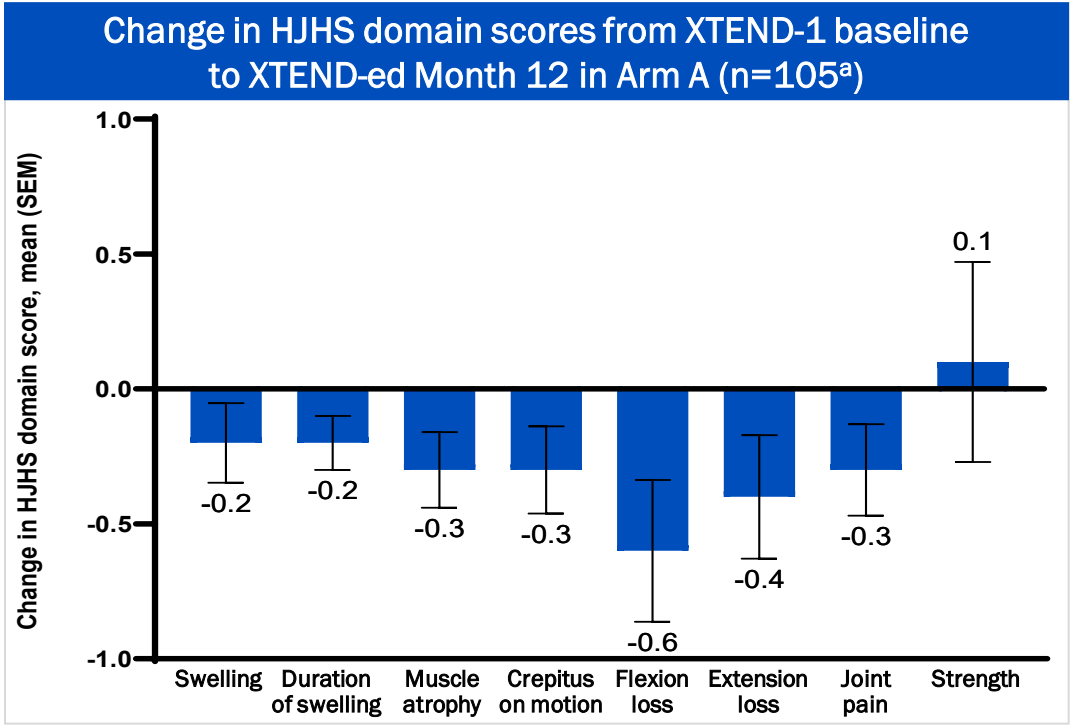
Greatest Improvements in HJHS Total Score by XTEND-ed Month 12 Were Observed Among Those With the Highest HJHS at XTEND-1 Baseline

XTEND-1 baseline HJHS quartile	XTEND-1 baseline (mean [SD] HJHS total score per quartile)	XTEND-ed Month 12 (mean [SD] HJHS total score per baseline quartile)
HJHS ≤4 (Quartile 1)	1.2 (1.5) n=31	2.8 (5.4) n=31
HJHS >4 to ≤19 (Quartile 2)	10.0 (4.4) n=28	8.4 (6.3) n=28
HJHS >19 to ≤32 (Quartile 3)	26.3 (3.9) n=24	21.8 (8.2) n=24
HJHS >32 (Quartile 4)	45.3 (14.2) n=22	40.0 (18.4) n=22



Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score; LOCF, last observation carried forward; SD, standard deviation.
Higher HJHS scores denote worse joint health. An HJHS total score can be calculated if all 48 individual item scores (8 domains × 6 joints, total joint score) and the gait score were present. HJHS assessments within 2 weeks after a joint or muscle bleed are excluded. Joint scores post joint surgeries are replaced using the LOCF method.

Improvements Were Observed in Most HJHS Domain Scores From XTEND-1 Baseline to XTEND-ed Month 12



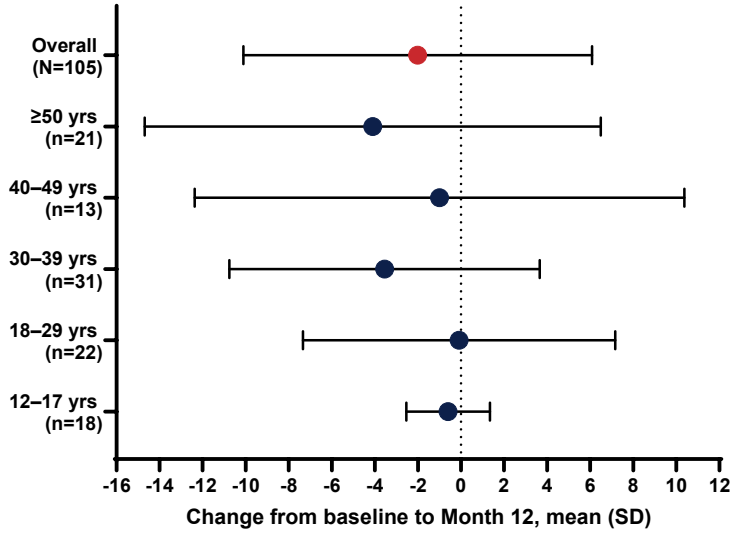
The **HJHS domain with the greatest mean improvement** from XTEND-1 baseline to XTEND-ed Month 12 was **flexion loss**

The mean (SD) **global gait score remained the same** at XTEND-ed Month 12 (1.6 [1.6]; n=126) as at XTEND-1 baseline (1.7 [1.6]; n=144)

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score; LOCF, last observation carried forward; SD, standard deviation; SEM, standard error of the mean.
Higher HJHS scores denote worse joint health. An HJHS total score can be calculated if all 48 individual item scores (8 domains × 6 joints, total joint score) and the gait score were present. HJHS assessments within 2 weeks after a joint or muscle bleed are excluded. Joint scores post joint surgeries are replaced using the LOCF method.
[a]Includes patients who had HJHS at both baseline and XTEND-ed Month 12.

Greatest Improvements in Joint Health Were Observed in Participants ≥50 Years of Age by XTEND-ed Month 12

Change in HJHS total score from XTEND-1 baseline to Week 52[a] Arm A prophylaxis by age group at XTEND-ed Month 12



	HJHS at XTEND-1 baseline, mean (SD)	HJHS at XTEND-ed Month 12, mean (SD)	Change from baseline to XTEND-ed Month 12, mean (SD)[a]
Overall	18.5 (18.0) n=105	16.4 (17.3) n=105	−2.1 (8.1) n=105
≥50 y	38.8 (19.1) n=21	34.7 (21.3) n=21	−4.1 (10.6) n=21
40–49 y	26.7 (14.4) n=13	25.7 (16.2) n=13	−1.0 (11.4) n=13
30–39 y	18.9 (12.8) n=31	15.4 (10.8) n=31	−3.6 (7.2) n=31
18–29 y	7.5 (9.2) n=22	7.4 (7.9) n=22	−0.1 (7.3) n=22
12–17 y	1.9 (3.0) n=18	1.3 (2.2) n=18	−0.6 (1.9) n=18

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score; SD, standard deviation.
[a]Includes only patients with HJHS measurements at both timepoints.

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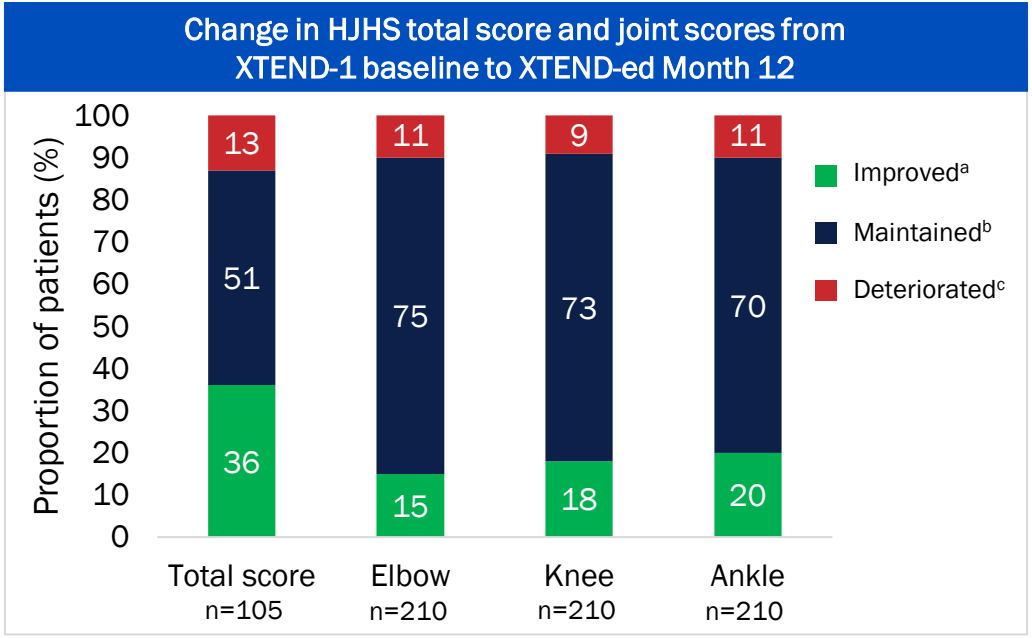
Most Participants Improved or Maintained Their Joint Health During XTEND-ed



Most patients improved (36%) or **maintained** (51%) their **total HJHS** and scores **across individual joints** from baseline to XTEND-ed Month 12

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score.
[a]Defined as a decrease of ≥4 points for total score, or ≥2 points for individual joint scores.[1] [b]Defined as changes between -3 and +3 points for total score, or between -1 and +1 for individual joints.[1]
[c]Defined as an increase of ≥4 points for total score, or ≥2 for individual joints scores.[1]
[1]Kuijlaars IAR, et al. *Haemophilia*. 2017;23(6):934-940.

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Conclusions

All target joints were resolved in participants receiving ≥12 months efanesoctocog alfa prophylaxis

Improvements to total HJHS during XTEND-1 were maintained at XTEND-ed Month 12

Patients with worse baseline HJHS had the greatest improvements in HJHS total score at XTEND-ed Month 12 from XTEND-1 baseline

Most patients improved or maintained their total HJHS from XTEND-1 baseline with once-weekly efanesoctocog alfa (50 IU/kg) prophylaxis
- Over one-third improved their HJHS score
- Over one-half maintained their score

Interim results from XTEND-ed indicate once-weekly efanesoctocog alfa 50 IU/kg prophylaxis is associated with improvement or maintenance of joint health in adults and adolescents (≥12 years) through 12 months of treatment in XTEND-ed

Data cutoff date June 8, 2023.
HJHS, Hemophilia Joint Health Score.

Thank you

to the study participants, their families,
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