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Change in Hemophilia Joint Health Score (HJHS) During the Phase 3 XTEND-1 Study of Efanesoctocog Alfa in Patients With Severe Hemophilia A

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Disclosure for Christoph Königs

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Disclosures:

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Efanesoctocog Alfa: A New Class of FVIII Replacement

Despite therapeutic advances, **joint bleeds still occur**, which can lead to **hemophilic arthropathy** and **joint pain,** impacting QoL and limiting everyday life[1-4]

Efanesoctocog alfa is a new class of factor VIII replacement therapy designed to **overcome the VWF-imposed half-life ceiling**[5,6]

In the Phase 3 XTEND-1 study, once-weekly efanesoctocog alfa achieved **high sustained factor levels** in the normal to near-normal range (≥40%) for the majority of the week and provided **superior bleed protection** compared with prior factor prophylaxis[7]

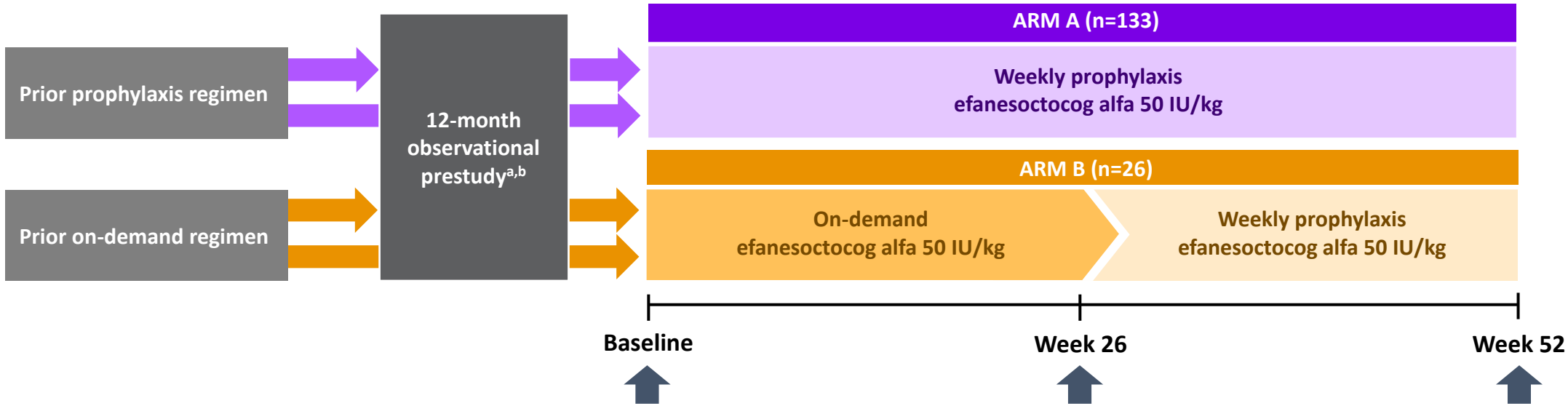
FVIII, factor VIII; QoL, quality of life; VWF, von Willebrand factor.

1. Olivieri M, et al. *Haemophilia.* 2012;18:369-374. 2. Gooding R, et al. *J Blood Med.* 2021;12:209-220. 3. Gualtierotti R, et al. *J Thromb Haemost.* 2021;19:2112-2121. 4. Warren BB, et al. *Blood Adv.* 2020;4(11):2451-2459.
5. Chhabra ES, et al. *Blood.* 2020;135(17):1484-1496. 6. Konkle BA, et al. *N Engl J Med.* 2020;383(11):1018-1027. 7. von Drygalski A, et al. *N Engl J Med.* 2023;388(4):310-318.

Objective

To evaluate changes in joint health in participants from the XTEND-1 study using the Hemophilia Joint Health Score (HJHS)

XTEND-1 Was an Open-Label, Multicenter, Phase 3 Study of Efanesoctocog Alfa in People with Hemophilia A[1,2]



Key eligibility criteria:

- Adults and adolescents (≥12 years) with severe hemophilia A
- Previous treatment with any recombinant and/or plasma-derived FVIII, or cryoprecipitate for ≥150 EDs

Hemophilia Joint Health Score (HJHS) v2.1:

- Joint health was evaluated using the HJHS at baseline, Week 26, and Week 52
- The HJHS total score consists of the total joint score and gait score
- For the total joint score, 6 joints (left and right ankle, elbow, and knee) were scored according to 8 HJHS domains
- Gait was scored based on walking and climbing stairs
- Higher HJHS scores indicate worse joint health

Efanesoctocog alfa is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.
EDs, exposure days; FVIII, factor VIII; HJHS, Hemophilia Joint Health Score.
[a]Prospective prestudy is Study 242HA201/OBS16221. [b]A total of 92 participants rolled over from the observational prestudy into XTEND-1, including 82 patients into Arm A and 10 into Arm B.
1. Clinicaltrials.gov NCT04161495. 2. von Drygalski A, et al. *N Engl J Med.* 2023;388(4):310-318.

Demographics for Participants With HJHS Total Score Assessed at Week 52

	Arm A (n=110)	Arm B (n=22)
Age, years		
Mean (SD)	32.4 (14.6)	42.7 (12.0)
Median (range)	31.5 (12–67)	39.0 (23–68)
Age group, n (%)[a]		
12–17 years	22 (20.0)	0
18–64 years	87 (79.1)	21 (95.5)
≥64 years	1 (0.9)	1 (4.6)
Race, n (%)[a]		
Asian	27 (24.6)	0
Black or African American	3 (2.7)	0
White	54 (49.1)	22 (100)
Other	24 (21.8)	0
Not reported	2 (1.8)	0
BMI group, n (%)[a]		
<25	52 (47.3)	8 (36.4)
≥25–<30	40 (36.4)	7 (31.8)
≥30	18 (16.4)	6 (27.3)
Not reported	0	1 (4.5)[b]

BMI, body mass index; HJHS, Hemophilia Joint Health Score; SD, standard deviation.
[a]Percentages are based on the total number of participants in the column. [b]BMI not reported for 1 participant as height was not recorded.

Improvements in HJHS Total Score Were Observed From Baseline to Week 52 in Both Arm A and Arm B

	Mean (SD) HJHS total score in Arm A and Arm B[a]			
	Baseline	Week 26	Week 52	Change from baseline to Week 52[b]
Arm A (52 weeks prophylaxis)	18.1 (18.4) n=116	17.4 (18.4) n=115	16.5 (17.6) n=110	–1.5 (6.4) n=107
Arm B (26 weeks on-demand then 26 weeks prophylaxis)	26.3 (13.2) n=25	23.7 (14.3) n=11	21.1 (13.1) n=22	–4.1 (8.7) n=22

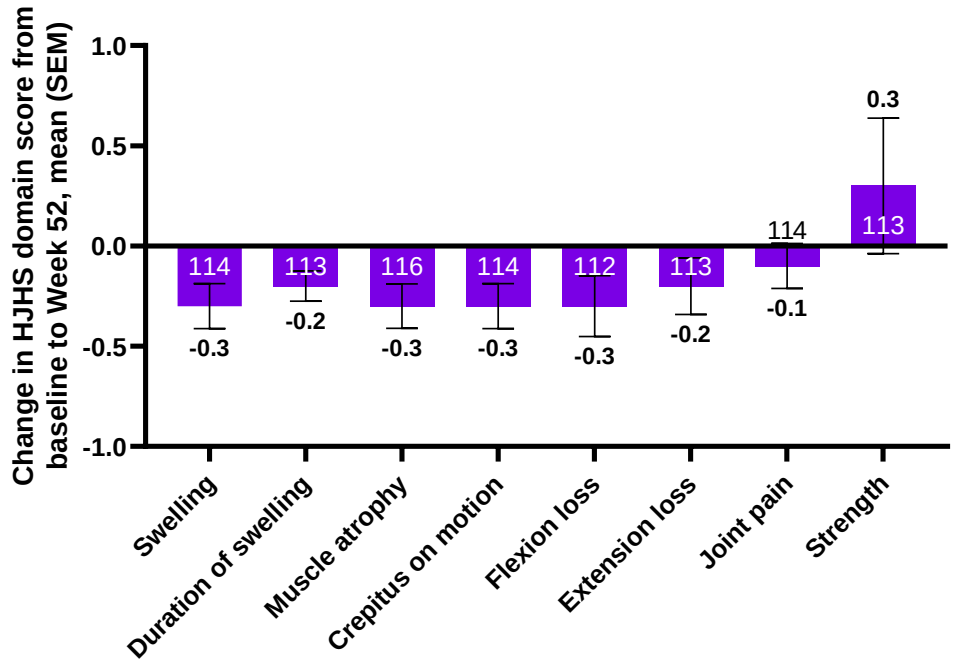
LS mean (95% CI) **change from baseline to Week 52** was **–1.54** (–2.70, –0.37), n=107, *P*=0.0101[1,c]

Mean (95% CI) **change from baseline to Week 52** was **–4.1** (–7.94, –0.25), n=22, *P*=0.0382[d]

CI, confidence interval; HJHS, Hemophilia Joint Health Score; LS, least squares; SD, standard deviation.
[a]HJHS assessments within 2 weeks after a joint or muscle bleed were excluded. Joint scores post joint surgeries were replaced using the last observation carried forward method. Assessments during other major surgical periods were excluded. HJHS total score was calculated if all 48 individual item scores (8 domains x 6 joints) and the gait score were present. [b]Change from baseline to Week 52 data only includes patients with HJHS measurements at both timepoints. [c]Change from baseline to Week 52 was estimated using a mixed-effect model with repeated measures with visit as a fixed effect, and baseline HJHS total score as covariate. [d]95% CI of mean and *P*-value obtained using paired t-test. 1. von Drygalski A, et al. *N Engl J Med.* 2023;388(4):310-318.

Improvements Were Observed in Most HJHS Domain Scores From Baseline to Week 52 in Arm A

Change in HJHS domain scores from baseline to Week 52 in Arm A prophylaxis[a-c]



In Arm A, the **HJHS domains with greatest mean improvement** from baseline to Week 52 were **swelling, muscle atrophy, crepitus on motion, and flexion loss**

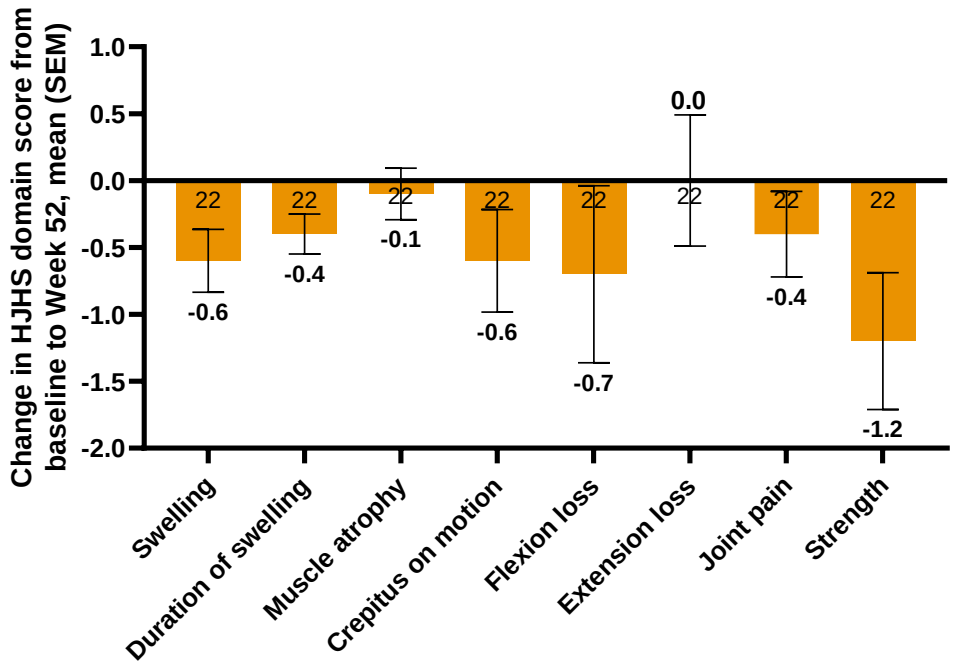
Mean (SD) change from baseline to Week 52 in HJHS **total joint score** was **–1.4** (6.2); n=108[d]

Mean (SD) change from baseline to Week 52 in HJHS **gait score** was **–0.1** (0.8); n=120[e]

HJHS, Hemophilia Joint Health Score; SD, standard deviation; SEM, standard error of the mean.
[a]HJHS assessments within 2 weeks of a joint or muscle bleed were excluded. Joint scores post joint surgeries were replaced using the last observation carried forward method. Assessments during other major surgical periods were excluded. [b]HJHS domains are assessed on the following ranges of scores: swelling (0–3); duration of swelling (0 or 1); muscle atrophy (0–2); crepitus on motion (0–2); flexion loss (0–3); extension loss (0–3); joint pain (0–2); strength (0–4). [c]The domain score was calculated if all 6 joints for each domain were present. [d]The HJHS total joint score was calculated if all 48 individual item scores (8 domains × 6 joints) were present. [e]Global gait is assessed on a range from 0–4.

Improvements Were Observed in Most HJHS Domain Scores From Baseline to Week 52 in Arm B

Change in HJHS domain scores from baseline to Week 52 in Arm B (on-demand to prophylaxis)[a-c]



In Arm B, the **HJHS domains with greatest mean improvement** from baseline to Week 52 were **swelling, duration of swelling, crepitus on motion, flexion loss, joint pain, and strength**

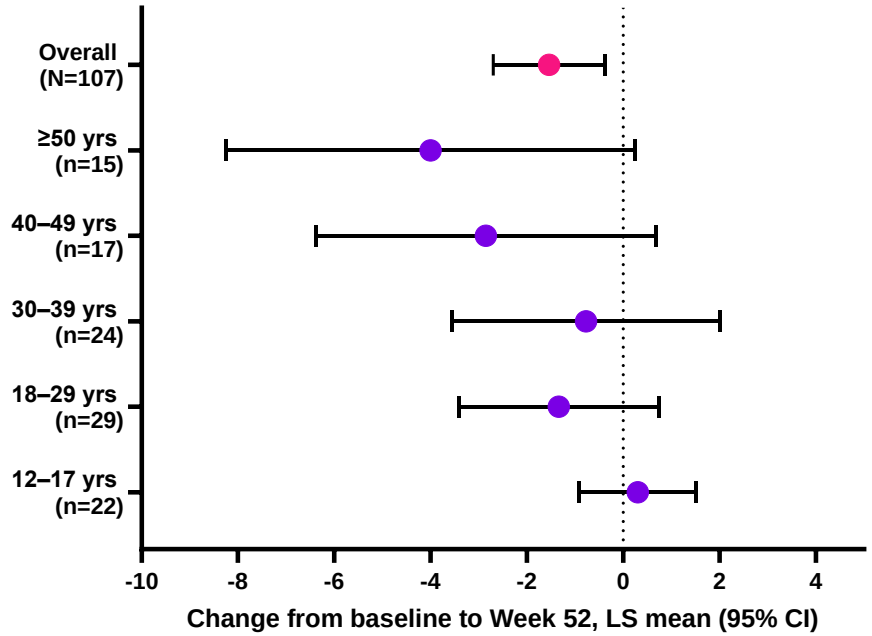
Mean (SD) change from baseline to Week 52 in HJHS **total joint score** was **–3.9** (8.6); n=22[d]

Mean (SD) change from baseline to Week 52 in HJHS **gait score** was **–0.2** (0.5); n=23[e]

HJHS, Hemophilia Joint Health Score; SD, standard deviation; SEM, standard error of the mean.
[a]HJHS assessments within 2 weeks of a joint or muscle bleed were excluded. Joint scores post joint surgeries were replaced using the last observation carried forward method. Assessments during other major surgical periods were excluded. [b]HJHS domains are assessed on the following ranges of scores, swelling (0–3); duration of swelling (0 or 1); muscle atrophy (0–2); crepitus on motion (0–2); flexion loss (0–3); extension loss (0–3); joint pain (0–2); strength (0–4). [c]The domain score was calculated if all 6 joints for each domain were present. [d]The HJHS total joint score was calculated if all 48 individual item scores (8 domains × 6 joints) were present. [e]Global gait is assessed on a range from 0–4.

Greater Improvements in Joint Health Were Observed in Participants in Arm A With Increased Age and Higher HJHS Total Score at Baseline

Change in HJHS total score from baseline to Week 52[a,b]
Arm A prophylaxis by age group



	HJHS at baseline, mean (SD)	HJHS at Week 52, mean (SD)	Change from baseline to Week 52, LS mean (95% CI)[a,b]
Overall	18.1 (18.4) n=116	16.5 (17.6) n=110	–1.54 (–2.70, –0.37) n=107; *P*=0.0101
≥50 yrs	41.1 (19.6) n=17	37.1 (21.7) n=15	–4.00 (–8.25, 0.25) n=15; *P*=0.0634
40–49 yrs	27.7 (14.0) n=19	26.4 (12.3) n=17	–2.85 (–6.39, 0.69) n=17; *P*=0.1071
30–39 yrs	21.6 (15.6) n=27	20.7 (16.1) n=26	–0.77 (–3.55, 2.01) n=24; *P*=0.5733
18–29 yrs	7.7 (9.9) n=30	6.5 (8.2) n=30	–1.34 (–3.42, 0.74) n=29; *P*=0.1990
12–17 yrs	2.9 (5.5) n=23	3.3 (7.2) n=22	0.30 (–0.91, 1.51) n=22; *P*=0.6104

CI, confidence interval; HJHS, Hemophilia Joint Health Score; LS, least squares; SD, standard deviation.
[a]LS mean (95% CI), and *P*-value estimated by mixed-effect model with repeated measures with visit as a fixed effect, and baseline HJHS as covariate. [b]Includes only patients with HJHS measurements at both timepoints.

Greater Improvements in Joint Health Were Observed in Participants in Arm A Who Were Older and Had a Higher BMI

	Demographics and baseline characteristics of participants in Arm A who had a change from baseline to Week 52 of ≥4 / <4 or of ≥2 / <2 points in HJHS total score				
	HJHS total score reduced by ≥4 points (n=24)	**HJHS total score reduced by <4 points (n=83)**	**HJHS total score reduced by ≥2 points (n=38)**	**HJHS total score reduced by <2 points (n=69)**	**Overall population in Arm A (N=107)**
Age, years					
Mean (SD)	35.5 (13.3)	31.5 (15.1)	36.2 (13.7)	30.3 (15.0)	32.4 (14.8)
Median (range)	35.5 (14–59)	29.0 (12–67)	35.5 (12–64)	28.0 (12–67)	31.0 (12–67)
Age group, n (%)[a]					
12–17 years	1 (4.2)	21 (25.3)	2 (5.3)	20 (29.0)	22 (20.6)
18–64 years	23 (95.8)	61 (73.5)	36 (94.7)	48 (69.6)	84 (78.5)
≥64 years	0	1 (1.2)	0	1 (1.5)	1 (0.9)
BMI, kg/m^2					
Mean (SD)	26.4 (4.6)	24.6 (4.9)	25.9 (4.8)	24.5 (4.9)	25.0 (4.9)
Median (range)	26.1 (18–35)	25.0 (15–40)	25.7 (16–35)	24.9 (15–40)	25.2 (15–40)
BMI group, n (%)[a]					
<25	9 (37.5)	42 (50.6)	15 (39.5)	36 (52.2)	51 (47.7)
≥25–<30	9 (37.5)	31 (37.4)	15 (39.5)	25 (36.2)	40 (37.4)
≥30	6 (25.0)	10 (12.1)	8 (21.1)	8 (11.6)	16 (15.0)

BMI, body mass index; HJHS, Hemophilia Joint Health Score; SD, standard deviation.
[a]Percentages are based on the total number of participants in the column.

Conclusions

Significant improvements in joint health were observed **within 1 year of starting efanesoctocog alfa** treatment in both study arms

There was a trend of **greater improvement in joint health** observed in **older participants,** those with a **higher BMI,** and those with **poorer joint health at baseline**

These data suggest that **once-weekly efanesoctocog alfa prophylaxis** may **improve joint health** in adults and adolescents with severe hemophilia A and **offer benefits above current standard of care FVIII prophylaxis**

BMI, body mass index; FVIII, factor VIII.