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

Christoph Königs[1*], Annette von Drygalski[2], Cedric Hermans[3], Barbara A. Konkle[4], Paul Van der Valk[5], Liane Khoo[6], Nobuaki Suzuki[7], Liqi Feng[8], Umer Khan[9], Linda Bystrická[10], Jennifer Dumont[9], Elena Santagostino[10], Lara Mamikonian[9], Robert Klamroth[11]

[1]Department of Pediatrics and Adolescent Medicine, Goethe University, Frankfurt, University Hospital, Frankfurt, Germany; [2]Division of Hematology/Oncology, Department of Medicine, University of California, San Diego, CA, USA; [3]Division of Haematology, Haemostasis and Thrombosis Unit, Saint-Luc University Hospital, Université Catholique de Louvain, Brussels, Belgium; [4]Washington Center for Bleeding Disorders and the University of Washington, Seattle, WA, USA; [5]Centre for Benign Haematology, Thrombosis and Haemostasis, Van Creveldkliniek, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands; [6]Institute of Haematology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia; [7]Department of Transfusion Medicine, Nagoya University Hospital, Aichi, Japan; [8]Sanofi, Shanghai, China; [9]Sanofi, Cambridge, MA, USA ; [10]Sobi, Basel, Switzerland; [11]Vivantes Klinikum, Friedrichshain, Berlin, Germany.

*presenting author

Author disclosures

Disclosures for: Dr. Christoph Königs

Conflict	Disclosure - if conflict of interest exists
Research Support to Goethe University	Bayer Vital GmbH, Biotest, CSL Behring, Intersero, Novo Nordisk, Pfizer, Roche/Chugai, Sanofi/Sobi, and Takeda.
Honoraria	Personal fees from Bayer Vital GmbH, CSL Behring, Novo Nordisk, Pfizer, Roche/Chugai, Sanofi/Sobi, and Takeda.

Opening remarks and purpose of presentation

- Efanesoctocog alfa
  - First-in-class FVIII replacement[1-3]
  - Activity is 3-4x longer than other FVIII therapies[1-3]
- XTEND-1 Phase 3 Results[4]
  - 50 IU/kg weekly maintained FVIII ≥40% most of week
  - Effective bleed protection
  - Improved physical health & joints
  - Well tolerated; no inhibitors

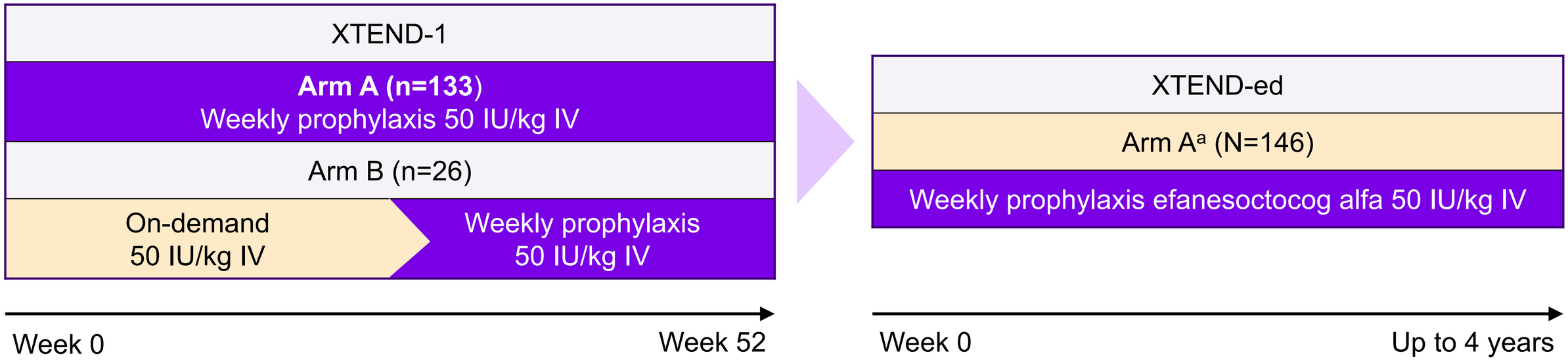
PURPOSE To study if once-weekly efanesoctocog alfa protects or improves joint health in adults & adolescents (≥12 years) with severe haemophilia A over ~3 years of treatment.

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.

Who could take part in the study?

Participants ≥12 years with severe haemophilia A (<1% FVIII activity or known gene mutation) who completed XTEND-1 study

Figure 1. XTEND clinical trial program



Joint health (target joint status, HJHS) was a secondary endpoint

[a]Participants who completed XTEND-1 continued into XTEND-ed Arm A, receiving weekly injections of efanesoctocog alfa (50 IU/kg) for up to 4 years.
Data cutoff date: February 22, 2024
FVIII, factor VIII; HJHS, Hemophilia Joint Health Score; IU, international unit; IV, intravenous.

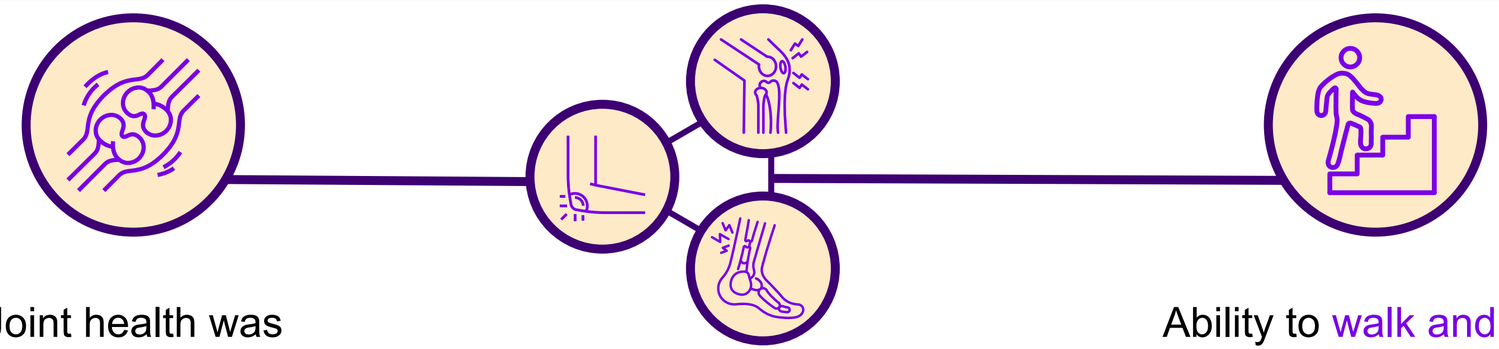
What were the characteristics of participants included in XTEND-ed (Arm A)?

146 participants continued from XTEND-1 to XTEND-ed,

115 had joint health data available for analysis, covering approximately **3 years of continuous treatment** (median 170.5 weeks).

- **115 (all male)** participants with joint health data
- Average (mean) age: **35.6 years**
- **Average age at start of first treatment:** 4.8 years
- **Average number of joint bleeds in the year before the study:** 6.2 (based on 104 participants with available data)
- **Had no joints with repeated bleeds at start of study:** 80 out of 115 (70%)

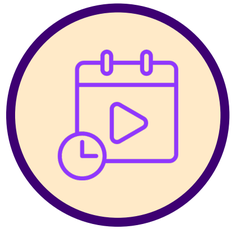
How was joint health measured?



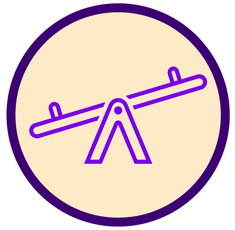
Joint health was assessed using HJHS version 2.1

Six joints were evaluated

Ability to walk and climb stairs was also assessed



Joint health assessment
At study initiation*
At 12 months
At 24 months



Lower HJHS score=better joint health
(scores range from 0 to 124)

A meaningful improvement = decrease of ≥4 points

A meaningful worsening = an increase of ≥4 points

A score change between −3 and +3 points was considered unchanged

*At the start of the XTEND-1 and XTEND-ed studies.
HJHS, Hemophilia Joint Health Score.

Did joint health improve over 3 years of treatment?

At the Start of study

Average joint health score:

19.7 out of 124

Participants with repeated joint bleeds averaged 42.5 years; those without averaged 32.5 years

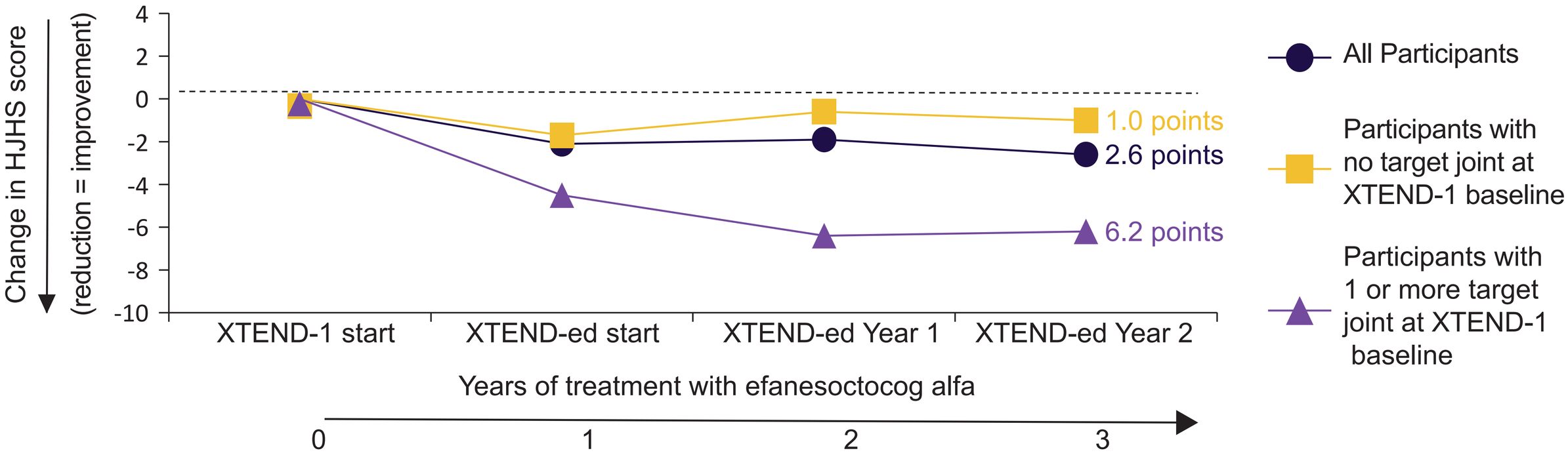
After 3 years of weekly treatment

The average joint health score improved to 17.1 (an improvement of 2.6 points)

The greatest improvements were seen in swelling and range of movement

Participants with repeated joint bleeds improved 6.2 points on average; those without improved 1.0 point

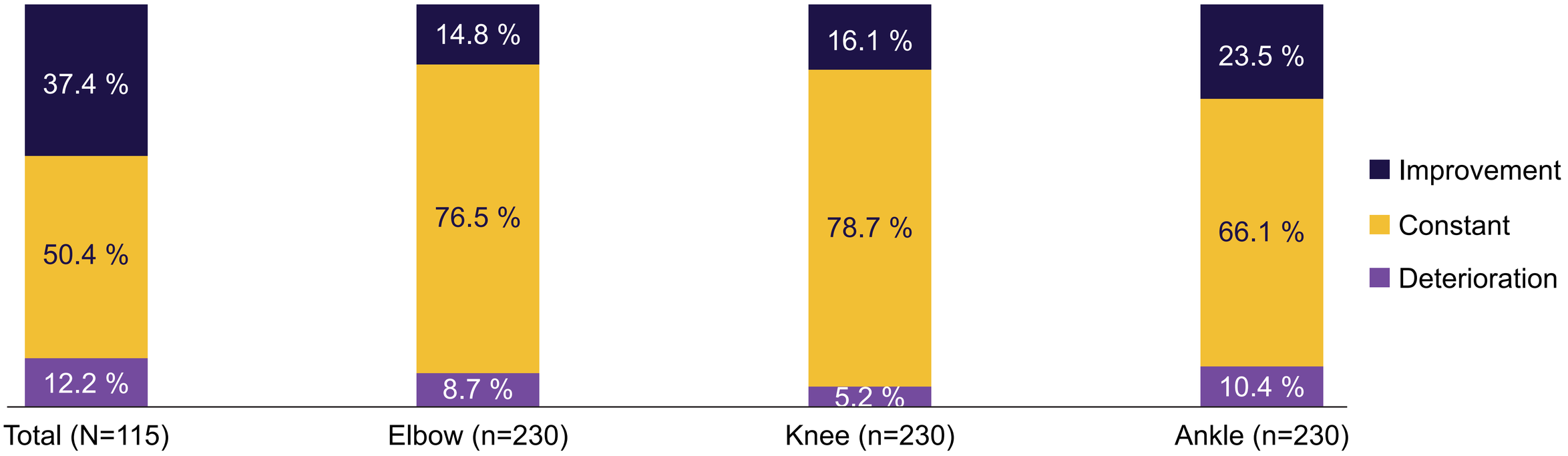
Did joint health improve over 3 years of treatment?



Target joint: a major joint with repeated bleeds (≥3 spontaneous bleeds in a 6-month period)

How many participants improved, remained the same, or worsened?

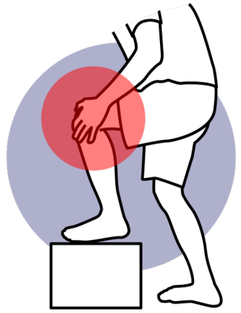
Joint health score improved or remained the same in **88%** of participants (N=115)

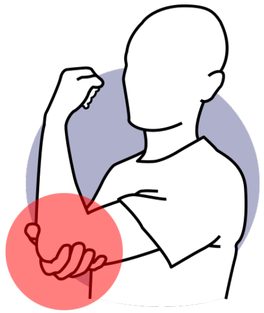


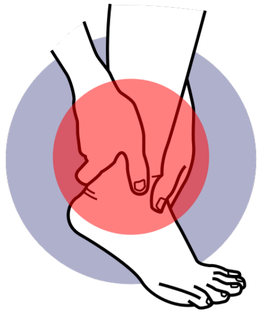
Improved/worsened HJHS scores were defined by decreases/increases of ≥4 points; an unchanged (or constant) HJHS score was defined by a change in score of between -3 and +3 points.
BL, baseline; HJHS, Hemophilia Joint Health Score; SD, standard deviation.

Did treatment help participants who already had joint damage?

Participants with the most joint damage at the start (score >32) showed the greatest improvement.





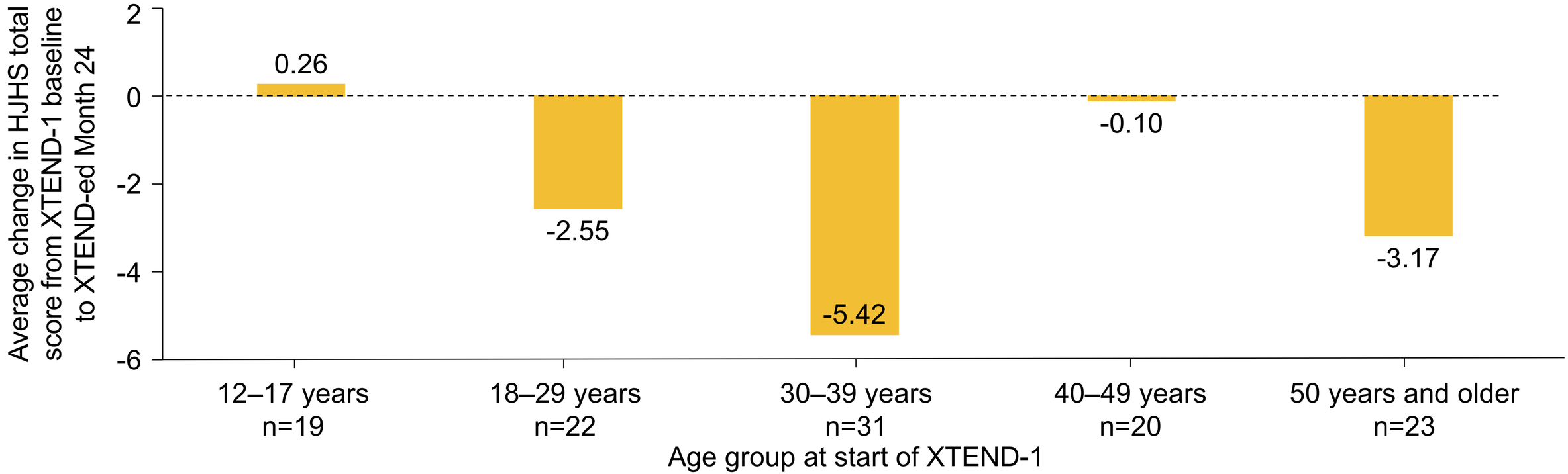


HJHS Score Range per Quartile	Average Improvement
≤4	0.1 points
>4 to 19	2.1 points
>19 to 32	3.5 points
>32	4.6 points

Quartile: Represents total dataset divided into four equal parts (i.e. each group represents 25%)

How did joint health improvement vary across age groups?

Largest joint health improvements by Month 24 were in participants aged 30-39 years, followed by those ≥50 years



HJHS, Hemophilia Joint Health Score.

Summary of key points - What do the findings mean?

Joint health improvements from the XTEND-1 study (12 months) were sustained through 24 months in XTEND-ed

Once-weekly efanesoctocog alfa (50 IU/kg) improved or maintained joint health in most participants:

- 37% (43/115 participants) showed a meaningful improvement
- 50% (58/115 participants) maintained their joint health score

The greatest improvements were seen in those with the worst baseline joint health (HJHS >32 or presence of target joints)

Thank you

- The authors would like to thank the participants and their caregivers for their time and participation in the study
- The authors were responsible for all content and editorial decisions, and received no honoraria related to the development of this presentation
- The authors would like to thank the study investigators for their contributions
- This study was sponsored by Sanofi and Sobi; and they reviewed and provided feedback

Originally presented as a poster at The International Society on Thrombosis and Haemostasis (ISTH) 2025 Congress; June 21–25, 2025; Washington, DC.
Coordination of the development of this presentation, facilitation of author discussion and critical review were provided by Monique Bidell, PharmD, CMPP (Sanofi) and Nick Fulcher, PhD, CMPP (Sobi). Sanofi and Sobi personnel reviewed this presentation. Medical writing support for the development of this presentation was provided by Divya Sadhna, M.Pharm, Sanofi.