PO047

Patient characteristics in FREEDOM, a study evaluating physical activity and joint health in patients with haemophilia A receiving efanesoctocog alfa prophylaxis

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CONCLUSIONS

- **Early signs of impaired joint health were detected in most patients at study baseline in spite of low ABRs.**
- **The recruited population mostly comprises patients younger than 45 years (80%) with 27% being <18 years; all were on prophylaxis prior to enrolment (SHL FVIII [23.7%], EHL FVIII [72.0%], both [4.3%]).**

INTRODUCTION

- Efanesoctocog alfa is a first-in-class, high sustained factor VIII (FVIII) replacement therapy (also known as ultra-long half-life FVIII) designed to overcome the von Willebrand factor-imposed half-life ceiling.[1]

AIM

- We report baseline data from FREEDOM (NCT05817812),[2] a prospective phase 3b study assessing physical activity and joint health in patients with severe haemophilia A on efanesoctocog alfa prophylaxis.

METHODS

- FREEDOM is an open label, single arm study that has enrolled participants across Europe.
- Eligibility criteria include previously treated patients ≥12 years of age with severe haemophilia A who have received prophylaxis for at least 12 months prior to enrolment.
- Following a screening visit, there was a run-in period of 30–45 days with previous treatment (physical activity levels data collected here; **Figure 1**).
  - Data on bleeds in the last six months and prior prophylaxis in the last 12 months were then collected at a baseline visit.
- Joint health was assessed within 14 days after baseline using:
  - Magnetic resonance imaging (MRI; International Prophylaxis Study Group [IPSG] MRI scale);[3]
  - Haemophilia Early Arthropathy Detection with Ultrasound (HEAD-US);[4]
  - Haemophilia Joint Health Score (HJHS).[5]
- Patient-reported outcomes and physical activity were also evaluated (data not shown).
- Participants will then receive once-weekly efanesoctocog alfa prophylaxis (50 International Units [IU]/kg) for 24 months.

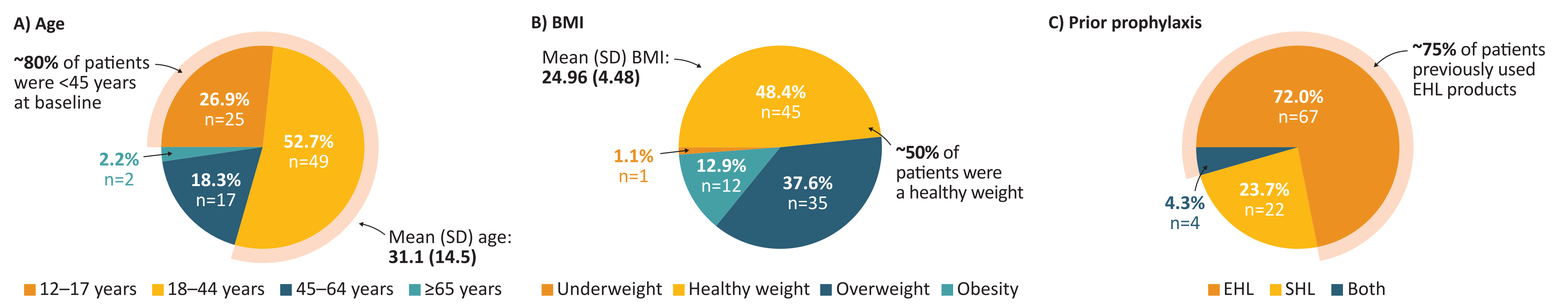
RESULTS

- A total of 93 patients were enrolled across 32 sites in 14 European countries (**Figure 2**).
- Mean (standard deviation [SD]) age was 31.1 (14.5) years; proportions of patients across age categories are presented in **Figure 3A**.
- Mean (SD) body mass index (BMI) was 24.96 (4.48) kg/m^2; proportions of patients across BMI categories are presented in **Figure 3B**.
- Patients received prophylaxis with standard half-life (SHL) FVIII (23.7%), extended half-life (EHL) FVIII (72.0%) or both (4.3%) prior to enrolment (**Figure 3C**).
- Mean (SD) weekly injection frequency and weekly factor consumption was 3.5 (1.4) and 107.6 (46.0) IU/kg, respectively, in patients who received SHL-FVIII (n=26; **Figure 4A**), and 2.4 (1.1) and 94.8 (50.2) IU/kg in patients who received EHL-FVIII (n=70; **Figure 4B**).
- In the 6 months prior to enrolment, mean/median (IQR) annualised bleeding rate (ABR) and joint ABR were 1.32/0.0 (0.0–2.01) and 1.04/0.0 (0.0–0.0), respectively (**Figure 5**).
  - 65.6% of patients had zero bleeds and 75.3% had zero joint bleeds.
- Sixteen target joints were recorded, in seven patients (**Figure 6A**); 97 impaired joints were recorded, in 32 patients (**Figure 6B**).
- Median (IQR) total IPSG MRI scale (n=75), HEAD-US (n=92) and HJHS (n=87) was 8.0 (2.0–19.0), 6.5 (0.0–14.0) and 6.0 (1.0–17.0), respectively (**Figures 7, 8 and 9**).

Figure 1: FREEDOM Study design

Figure 2: Participating countries with ≥1 patient enrolled

Figure 3: Age, BMI and prior prophylaxis (N=93)



BMI categories are age dependent. Underweight: for adults, BMI <18.5; for adolescents, BMI <-2SD, where SD is the SD from WHOs growth reference data for that age.[6] Healthy weight: for adults, BMI 18.5–<25; for adolescents, −2SD ≥ BMI <+1SD. Overweight: for adults, BMI 25–<30; for adolescents, +1SD ≤ BMI ≤+2SD. Obese: for adults, BMI >30; for adolescents, BMI >+2SD.

Figure 4: Mean weekly injection frequency and factor consumption

A) SHL

Weekly injection frequency (n=26)
Mean (SD): **3.5 (1.4)**
Median (IQR): **3.0 (3.0–3.5)**

Weekly factor consumption (IU/kg; n=26)
Mean (SD): **107.6 (46.0)**
Median (IQR): **105.0 (84.0–134.9)**

B) EHL

Weekly injection frequency (n=70)
Mean (SD): **2.4 (1.1)**
Median (IQR): **2.2 (2.0–3.0)**

Weekly factor consumption (IU/kg; n=70)
Mean (SD): **94.8 (50.2)**
Median (IQR): **86.2 (62.4–112.7)**

Patients who received both EHL and SHL products are included in both groups.

Figure 5: ABR and joint ABR (n=93)

ABR
Mean (SD): **1.32 (2.96)**
Median (IQR): **0.0 (0.0–2.01)**

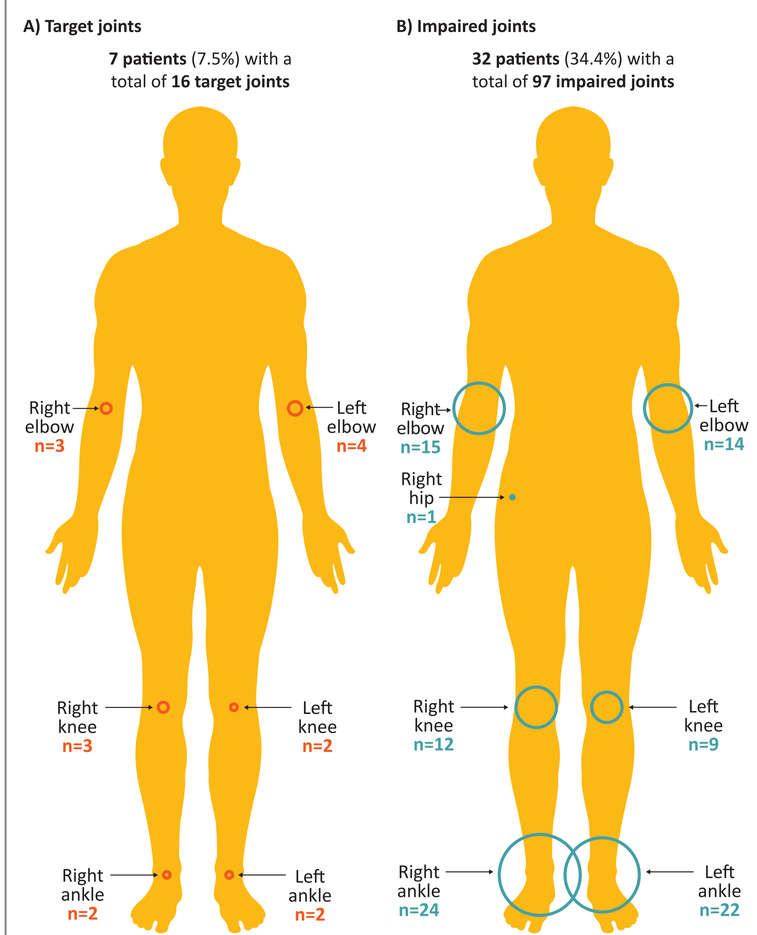
Joint ABR
Mean (SD): **1.04 (2.92)**
Median (IQR): **0.0 (0.0–0.0)**

65.6% of patients had **zero bleeds** (n=61/93)

75.3% of patients had **zero joint bleeds** (n=70/93)

Bleed data are as reported during the 6-month period prior to enrolment.

Figure 6: Target joints and impaired joints

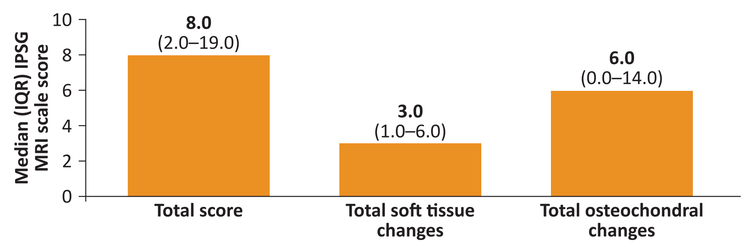


Target joints, n (%) (N=93)				
0	1	2	3	>3
86 (92.5)	3 (3.2)	2 (2.2)	0	2 (2.2)

Impaired joints, n (%) (N=93)				
0	1	2	3	>3
61 (65.6)	8 (8.6)	7 (7.5)	3 (3.2)	14 (15.1)

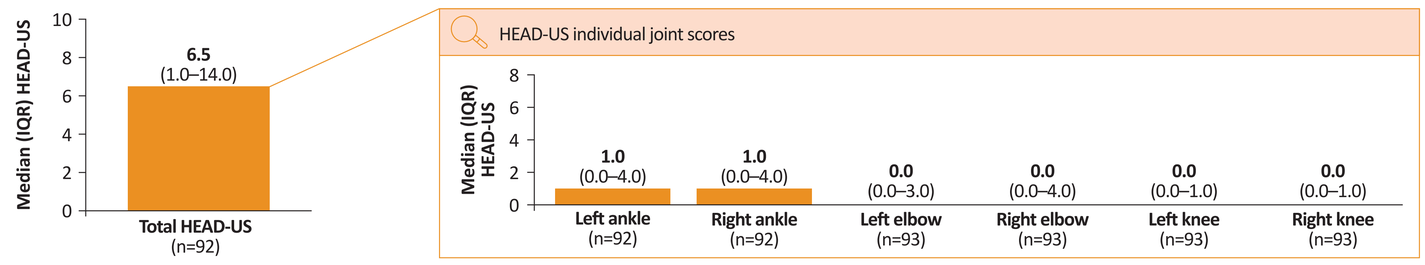
Target joints were defined as ≥3 spontaneous bleeds into a single joint within a consecutive 6-month period. Where there were ≤2 bleeds into the joint within a consecutive 12-month period, the joint was no longer considered a target joint.[7] Impaired joints were defined as any joint that had persistent functional or structural abnormalities, considered clinically relevant by the investigator, with or without bleedings. Multiple responses from each patient were allowed.

Figure 7: IPSG MRI scale scores (n=75)



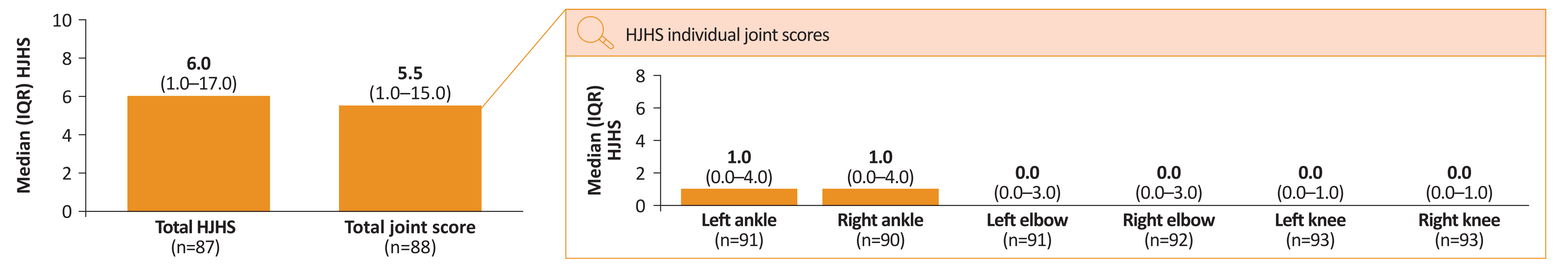
Total IPSG MRI scale score ranges from 0–102. Total soft tissue changes score ranges from 0–54. Total osteochondral changes score ranges from 0–48.

Figure 8: HEAD-US scores



Total HEAD-US ranges from 0–48. HEAD-US individual joint scores range from 0–8.

Figure 9: HJHS



Total HJHS (including global gait) ranges from 0–124; total joint score (not including global gait) ranges from 0–120. HJHS individual joint scores range from 0–20.

References

1. von Drygalski A, et al. *N Engl J Med* 2023;388:310–8; **2.** ClinicalTrials.gov (NCT05817812); **3.** Lundin B, et al. *Haemophilia* 2012;18:962–70; **4.** Martinoli C, et al. *Thromb Haemost* 2013;109:1170–9; **5.** St-Louis J, et al. *Res Pract Thromb Haemost* 2022;6:e12690; **6.** World Health Organization. Growth Reference Data for 5–19 Years. Available at: www.who.int/tools/growth-reference-data-for-5to19-years/indicators/bmi-for-age [Accessed 05 December 2024]; **7.** Blanchette VS, et al. *J Thromb Haemost* 2014;12:1935–9.

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Abbreviations

ABR: annualised bleeding rate; **BMI:** body mass index; **EHL:** extended half-life; **FVIII:** factor VIII; **HEAD-US:** Haemophilia Early Arthropathy Detection with Ultrasound; **HJHS:** Haemophilia Joint Health Score; **IPSG:** International Prophylaxis Study Group; **IQR:** interquartile range; **IU:** International Unit; **MRI:** magnetic resonance imaging; **SD:** standard deviation; **SHL:** standard half-life; **WHO:** World Health Organization.

Acknowledgements

Hemophilia Joint Health Score 2.1©, The Hospital for Sick Children, Centre Hospitalier Universitaire Sainte Justine, the Regents of the University of Colorado, Karolinska Hospital, University Medical Center Utrecht, 2009. Used under license by The Hospital for Sick Children. We thank the patients and investigators who participated in the study. The authors acknowledge Nick Fulcher, PhD, Sobi and Alicia Mack, PharmD, Sanofi for publication coordination. The authors also acknowledge Yasha Najafi, MSc, Costello Medical, London, UK for medical writing and editorial assistance, and Ellie Denham of Costello Medical, Manchester, UK for design assistance, funded by Sobi. Sobi and Sanofi reviewed and provided feedback on the poster. This research is funded by Sobi.

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