PO050

Physical Activity and Efficacy in Patients with Severe Haemophilia A Treated with Efanesoctocog Alfa: 12-Month Interim Results from FREEDOM

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CONCLUSIONS

- **Patients with severe haemophilia A in FREEDOM had higher physical activity levels at baseline, assessed using an activity tracker and the International Physical Activity Questionnaire, than patients in other haemophilia clinical trials and the general haemophilia population.[1–5]**
- **These high physical activity levels were maintained over the first 12 months of efanesoctocog alfa prophylaxis, with patients having highly effective bleed control and a large proportion having no treated bleeds.**

INTRODUCTION

- Efanesoctocog alfa is a first-in-class, high-sustained FVIII replacement therapy (also known as ultra-long half-life FVIII) designed to overcome the von Willebrand factor-imposed half-life ceiling.[6]
- FREEDOM (NCT05817812) is a Phase 3b study evaluating joint health and physical activity in patients with severe haemophilia A receiving efanesoctocog alfa prophylaxis for 24 months.[7]

AIM

- To report 12-month interim bleed, physical activity and safety data from FREEDOM.

METHODS

Study design

- Patients aged ≥12 years with severe haemophilia A, who previously received any prophylactic FVIII replacement therapy, will receive once-weekly efanesoctocog alfa (50 IU/kg) for 24 months in FREEDOM (**Figure 1**).
- Physical activity data were collected in FREEDOM using a wearable activity tracker (Fitbit) and the self-reported International Physical Activity Questionnaire (IPAQ; long form).[8]

Activity tracker

- Activity tracker data were collected 30–45 days pre-baseline (run-in period) and throughout the study, and were normalised according to patients' wear time.
- The activity tracker was to be worn for ≥8 hours daily, between 06:00–23:00, on at least 12 days per month (including ≥1 weekend day).
- Data are shown as the proportion of total wear time categorised as either light activity (1.5–2.9 MET; e.g. walking) or moderate–vigorous activity (≥3.0 MET; e.g. running).

IPAQ

- The IPAQ was completed by patients at enrolment and every 6 months, and assessed physical activity for the prior 7 days across four domains.
- The sums of all domain scores were converted into metabolic equivalent of task (MET)-minutes per week to quantify energy expenditure.
- Total IPAQ scores, as well as scores categorised into low, moderate and high activity,[8] are reported.

Bleeds

- Annualised bleeding rates and proportions of patients with zero bleeds are reported up to 12 months.

Safety

- Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs) and TEAEs leading to death or study discontinuation are reported.

Statistical analysis

- Mean change from baseline in activity tracker data, mean IPAQ scores and mean change from baseline in IPAQ were calculated using a mixed model for repeated measures.
  - For activity tracker data, mean daily minutes were used as the response, with absolute values of response, age, joint status (assessed using HEAD-US Synovitis), body mass index and visit used as fixed effects, and tracker wear time used as a covariate.
  - For IPAQ data, total scores were used as the response, with baseline age, joint status (assessed using HEAD-US Synovitis), body mass index and visit used as fixed effects.
  - An unstructured covariance matrix was used to account for within-patient correlation.
- Physical activity and bleed data are reported up to 12 months (interim data cut-off: 21 July 2025).
- Safety data are reported up until the same interim data cut-off; since this date is the day of the last patient's 12-month visit, most patients had >12 months of follow-up.

RESULTS

Baseline characteristics

- In total, 93 patients were enrolled across 32 sites in 14 European countries.
  - At Month 12, 2 out of 93 patients had discontinued; 1 due to patient withdrawal and 1 due to use of a treatment listed in the exclusion criteria.
- Baseline characteristics (**Table 1**) have been described in detail previously.[9]

Bleeding rates

- Mean (SD) and median (IQR) annualised bleeding rates (ABRs) were 0.3 (0.9) and 0.0 (0.0–0.0) at Month 12, respectively (n=93; **Figure 2**).
- The proportion of patients with zero treated bleeds at Month 12 was 83.9% (n=93).
  - The proportion of patients with zero treated bleeds during Months 1–6 was 89.2% (n=83), and 88.2% (n=82) during Months 7–12.
- Overall, 15 patients reported 27 treated bleeds over 12 months.
  - Eleven bleeds were traumatic and 16 were spontaneous.

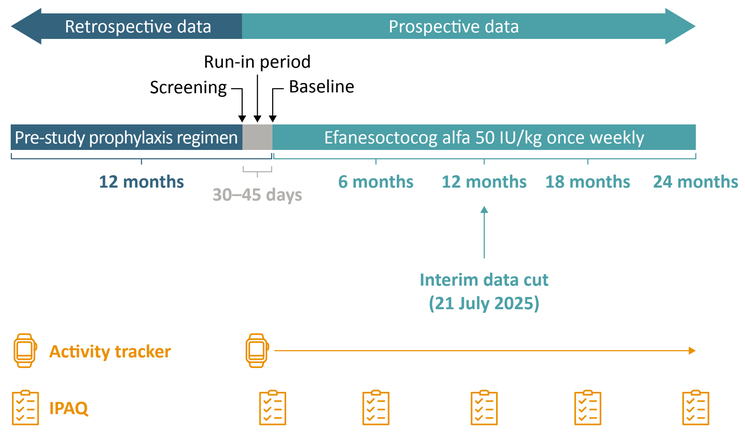
Physical activity levels

- According to activity tracker data, physical activity levels were stable from baseline to Month 12 (**Figure 3**).
- According to the IPAQ, patient-reported physical activity levels were high at baseline (high: 75.9%; moderate: 22.9%; low: 1.2%; n=83) and were maintained at Month 6 (high: 77.5%; moderate: 20.2%; low: 2.2%; n=89) and Month 12 (high: 71.8%; moderate: 23.5%; low: 4.7%; n=85).
- Total IPAQ scores were similarly high at baseline, Month 6 and Month 12 (**Figure 4**).
  - The estimated mean (95% CI) change from baseline to Month 6 was –406 (–1,257; 446) MET minutes/week and from baseline to Month 12 was –504 (–1,333; 326) MET minutes/week; the 95% CIs are wide and include zero, suggesting no evidence of a change in IPAQ scores over the first year of treatment.

Safety

- Mean (SD) duration of treatment was 16.8 (2.8) months.
- No new safety findings were reported in this analysis (**Table 2**).
  - One TESAE was considered related to efanesoctocog alfa (superficial thrombus in the setting of a pre-existing venous malformation).
  - There were no TEAEs leading to death or study discontinuation.

Figure 1: FREEDOM study design



The IPAQ was completed at enrolment and every 6 months thereafter; activity tracker data were collected 30–45 days pre-baseline and throughout the study.

Table 1: Baseline characteristics

	Overall (N=93)
Age (years) at screening, mean (SD)	31.1 (14.5)
Age categories (years), n (%)	
12–17	25 (26.9)
18–44	49 (52.7)
45–64	17 (18.3)
≥65	2 (2.2)
BMI (kg/m²), median (range)	24.5 (16.2; 41.9)
Type of prior prophylaxis, n (%)[a]	
EHL	67 (72.0)
SHL	22 (23.7)
Both EHL and SHL	4 (4.3)

[a] Type of prior prophylaxis only includes treatments taken within the 12-month period prior to enrolment.

Figure 2: Annualised bleeding rates at 12 months

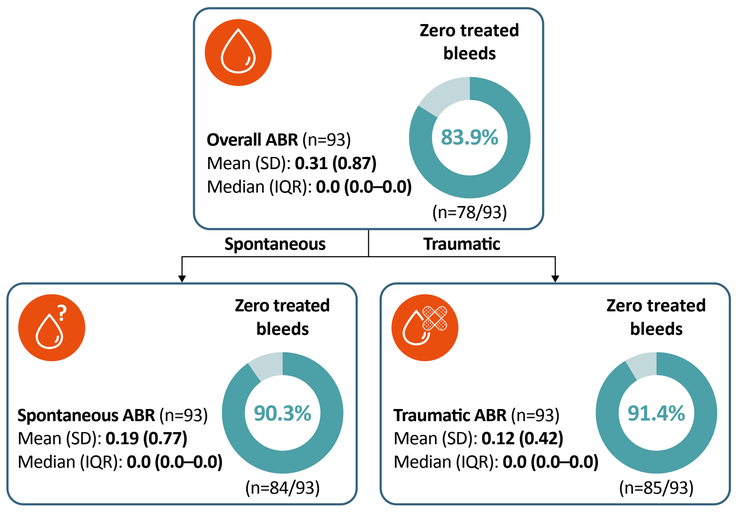
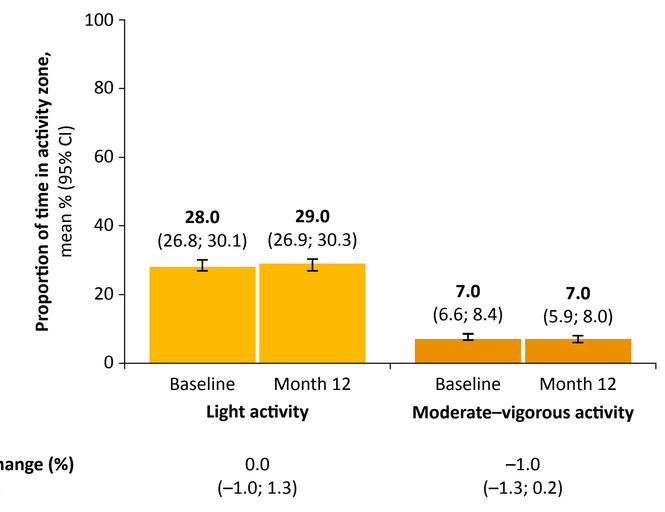
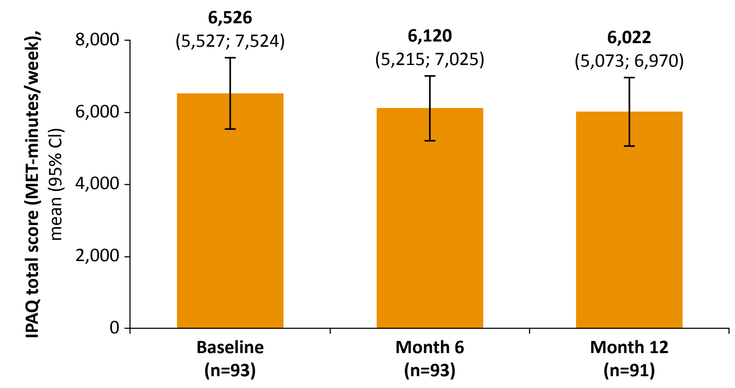


Figure 3: Tracker-recorded activity levels (n=81)



	Light activity	Moderate–vigorous activity
Mean change (%) (95% CI)	0.0 (–1.0; 1.3)	–1.0 (–1.3; 0.2)

Figure 4: IPAQ total score over time



	Baseline (n=93)	Month 6 (n=93)	Month 12 (n=91)
Mean change (95% CI)	–	–406 (–1,257; 446)	–504 (–1,333; 326)

Mean change values are derived from patients with valid assessments at both baseline and Month 6 (n=93) and baseline and Month 12 (n=91).

Table 2: Safety outcomes

n (%)	Overall (N=93)
Patients with ≥1 TEAE[a]	67 (72.0)
Patients with ≥1 related TEAE[b]	5 (5.4)
Patients with ≥1 TESAE	6 (6.5)
Patients with ≥1 related TESAE[c]	1 (1.1)
Patients with TEAEs leading to death	0
Patients with TEAEs leading to study discontinuation	0

[a] The most common TEAEs (n [%]) were arthralgia (15 [16.1%]), nasopharyngitis (13 [14.0%]) and headache (9 [9.7%]); **[b]** Five TEAEs were considered related to efanesoctocog alfa (arthralgia, myalgia, misuse of drug delivery system, headache and eye pain); **[c]** One TESAE was considered related to efanesoctocog alfa (superficial thrombus in the setting of a pre-existing venous malformation).

References

1. den Uijl I, et al. *Blood Transfus* 2013;11:364–9; **2.** Versloot O, et al. *Haemophilia* 2019;25:244–51; **3.** Taylor S, et al. *Haemophilia* 2020;26:718–25; **4.** Astermark J, et al. *Haemophilia* 2025;0:1–12; **5.** Matlary RED, et al. *Haemophilia* 2023;29:900–9; **6.** von Drygalski A, et al. *N Engl J Med* 2023;388:310–8; **7.** ClinicalTrials.gov (NCT05817812); **8.** Craig CL, et al. *Med Sci Sports Exerc* 2003;35;1381–95; **9.** Astermark J, et al. EAHAD 2025; Poster PO047.

Abbreviations

ABR: annualised bleeding rate; **BMI:** body mass index; **CI:** confidence interval; **EHL:** extended half-life; **FVIII:** factor VIII; **HEAD-US:** Hemophilia Early Arthropathy Detection with Ultrasound; **IPAQ:** International Physical Activity Questionnaire; **IQR:** interquartile range; **MET:** Metabolic Equivalent of Tasks; **SD:** standard deviation; **SHL:** standard half-life; **TEAE:** treatment-emergent adverse event; **TESAE:** treatment-emergent serious adverse event.

Disclosures

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