Effectiveness and safety of efmoroctocog alfa (a recombinant factor VIII Fc) across body mass index (BMI) categories: Pooled data from two non-interventional phase 4 studies (A-SURE/PREVENT)

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CONCLUSIONS

- These real-world data from two large observational studies support the use of efmoroctocog alfa (hereinafter referred to as rFVIIIFc) prophylaxis in persons with hemophilia A of all BMI categories.
- The numerically higher annualized bleeding rates and the observed lower weekly rFVIIIFc consumption in persons with hemophilia A in the overweight and obese groups, compared with the normal BMI group, might suggest the need for dose adjustments in these populations.

BACKGROUND

- Prophylaxis with factor VIII (FVIII) replacement therapy is a widely accepted treatment strategy to reduce the risk of bleeding and chronic arthropathy in persons with severe hemophilia A (HA).[1]
- Persons with severe HA (FVIII levels <1%) require regular ongoing prophylaxis with intravenous FVIII to maintain factor activity levels sufficiently high to reduce the risk of bleeding.[1]
- Persons with mild-to-moderate HA (FVIII levels ≥1–40%) often do not receive regular prophylaxis and there is increasing concern regarding subclinical bleeding in persons with low FVIII activity levels, which can lead to progressive joint damage over time.[1]
- Whilst the debate around the optimum FVIII activity on prophylaxis is ongoing, there is a consensus that raising the FVIII trough levels reduces the risk of bleeding and should be considered in those with mild-to-moderate disease to improve long-term outcomes.[1, 2]
- Efmoroctocog alfa (Elocta®), a recombinant FVIII Fc fusion protein (herein rFVIIIFc), has an extended half-life allowing longer dosing intervals (every 3–5 days), whilst maintaining high FVIII levels, compared to standard half-life (SHL) products.[3, 4]

AIMS

- This post-hoc analysis of two non-interventional, observational studies in Europe assessed real-world outcomes by body mass index (BMI) categories in persons with hemophilia A (PwHA) treated with rFVIIIFc.

METHODS

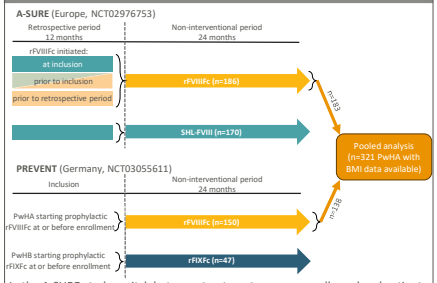
- Data on prophylactic treatment with rFVIIIFc were pooled from the Sobi-sponsored A-SURE (Europe, NCT02976753) and PREVENT (Germany, NCT03055611) phase 4, prospective, observational studies (**Figure 1**).
  - A-SURE evaluated the effectiveness of prophylaxis with rFVIIIFc compared with a matched group receiving prophylaxis with SHL FVIII products.
  - PREVENT evaluated the real-world use of rFVIIIFc.
  - Only variables recorded in the same way in both studies were included.
- Treatment regimens were in line with standard clinical practice.
- PwHA were grouped into underweight, normal, overweight, and obese categories by baseline BMI (**Table 1**).
- Baseline demographics, characteristics, and presence of target joints were assessed.
- Annualized bleeding rates (ABR) and joint bleeding rates (AjBR), length of prospective follow-up, injection frequency, and weekly factor consumption were recorded.
  - In both studies, annualized endpoints were only calculated when there were ≥3 months of prospective follow up.

Table 1. BMI categories

	Adults (≥18 years)	Children/ adolescents (<18 years)
Underweight	<18.5	<-2 SD
Normal	18.5 to <25	–2 SD to <+1 SD
Overweight	25 to <30	+1 SD to <+2 SD
Obese	≥30	≥+2 SD

For children/adolescents, BMI grouping was determined based on number of SDs away from World Health Organization growth reference BMI data for the given age
BMI, body mass index; SD, standard deviation

Figure 1. Overview of the study design for A-SURE and PREVENT and the pooled analysis



In the A-SURE study, switch between treatment groups was allowed and patients with <3 months on initially prescribed treatment were excluded from analysis of annualized endpoints
BMI, body mass index; FVII, factor VIII; PwHA, persons with hemophilia A; PwHB, persons with hemophilia B; rFVIIIFc, recombinant factor VIII Fc; rFIXFc, recombinant factor IX Fc; SHL, standard half-life

RESULTS

Demographics

- A total of 321 PwHA with available BMI data were included in the following groups: n=8 (2.5%), underweight; n=175 (54.5%), normal weight; n=97 (30.2%), overweight; and n=41 (12.8%), obese (**Figure 2**).
  - Baseline demographics/characteristics are summarized in **Table 2**.
- Due to the small sample size, data from the underweight group were not analyzed further.

Figure 2. Baseline weight categories in PwHA from the A-SURE and PREVENT study populations, %(n)

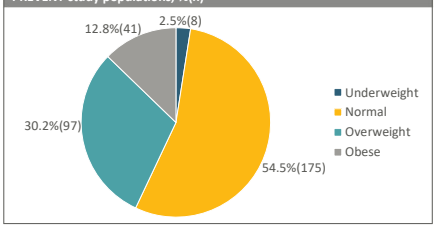


Table 2. Baseline demographics and characteristics by BMI categories

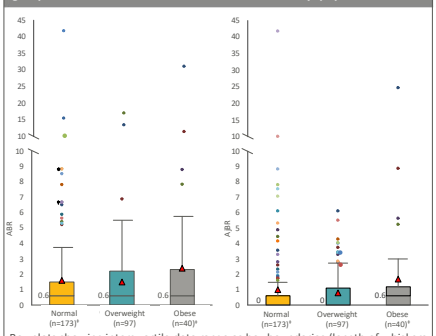
	Underweight (N=8)	Normal (N=175)	Overweight (N=97)	Obese (N=41)
Age, years Mean (SD)	19.6 (11.9)	22.6 (17.1)	33.6 (18.6)	30.2 (20.1)
Children/ adolescents (<18 years), n (%)	3 (37.5)	87 (49.7)	23 (23.7)	16 (39.0)
Adults (≥18 years), n (%)	5 (62.5)	88 (50.3)	74 (76.3)	25 (61.0)
Disease severity, n (%)				
Mild	0	5 (2.9)	0	0
Moderate	1 (12.5)	10 (5.7)	8 (8.2)	3 (7.3)
Severe	7 (87.5)	160 (91.4)	89 (91.8)	38 (92.7)
History of inhibitors, n (%)				
No	7 (87.5)	151 (86.3)	89 (91.8)	33 (80.5)
Yes	1 (12.5)	24 (13.7)	8 (8.2)	8 (19.5)
Type of prophylaxis, n (%)				
Not applicable	0	2 (1.1)	0	0
Primary	4 (50.0)	82 (46.9)	26 (26.8)	18 (43.9)
Secondary	2 (25.0)	57 (32.6)	41 (42.3)	9 (22.0)
Tertiary	1 (12.5)	18 (10.3)	19 (19.6)	9 (22.0)
Unknown	1 (12.5)	16 (9.1)	11 (11.3)	5 (12.2)
Presence of target joint(s), n (%)				
Yes	2 (25.0)	9 (5.1)	11 (11.3)	7 (17.1)
No	5 (62.5)	157 (89.7)	83 (85.6)	34 (82.9)
Missing	1 (12.5)	9 (5.1)	3 (3.1)	0 (0)

Percentages may not add up to 100% due to rounding
BMI, body mass index; IQR, interquartile range; PwHA, persons with hemophilia A; SD, standard deviation

Efficacy

- All groups had similar durations of prospective follow up: median (interquartile range [IQR]) follow-up was 21.0 (19.3–23.9), 21.0 (19.3–24.4), and 20.0 (18.9–22.6) months in the normal, overweight, and obese groups, respectively.
- Total ABRs and AjBRs in the overweight and obese groups were slightly higher compared to the normal BMI group (**Figure 3**).

Figure 3. Prospective follow-up analyses of A) ABR and B) AjBR by BMI group in PwHA from the A-SURE and PREVENT study populations

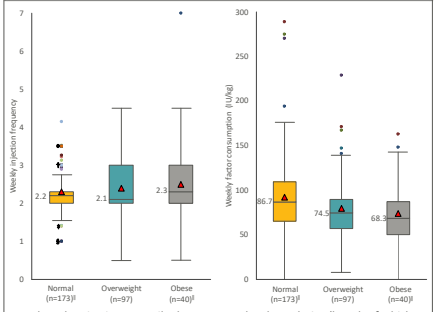


Box plots showing interquartile data range as box boundaries (length of whiskers showing 1.5 x IQR truncated at zero, where applicable), median data (horizontal lines and data labels), and arithmetic means (triangles). Circles denote outliers:
*†n=2
‡Two patients in the normal group and one patient in the obese group were excluded from analysis as they had less than 3 months of prospective follow-up Data were collected during the full prospective observation period (Figure 1)
ABR, annualized bleed rate; AjBR annualized joint bleed rate; BMI, body mass index; IQR, interquartile range; PwHA, persons with hemophilia A

Dosing frequency and factor consumption

- Mean weekly injection frequencies were comparable in all BMI groups (**Figure 4**).
- Mean (SD) weekly factor consumption (IU/kg) was lower with increasing BMI groups (**Figure 4**).

Figure 4. Prospective follow-up analyses of A) weekly injection frequency and B) weekly factor consumption (IU/kg) by BMI group in PwHA from the A-SURE and PREVENT study populations



Box plots showing interquartile data range as box boundaries (length of whiskers showing 1.5 x IQR truncated at zero, where applicable), median data (horizontal lines and data labels), and arithmetic means (triangles). Circles denote outliers:
*n=13, †n=15, ‡n=2, §n=5
‖Two patients in the normal group and one patient in the obese group were excluded from analysis as they had less than 3 months of prospective follow-up Data were collected during the full prospective observation period (Figure 1)
BMI, body mass index; IQR, interquartile range; PwHA, persons with hemophilia A

REFERENCES

1. Srivastava A, et al. Haemophilia. 2020;26(Suppl. 6):1–158.
2. Collins PW, et al. Haemophilia. 2021;27:192–8.
3. Swedish Orphan Biovitrum AB (publ). Elocta® Summary of Product Characteristics 2019.
4. Bioverativ Therapeutics Inc. Eloctate® Prescribing Information, 2021.

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