Real-World Effectiveness and Usage of Recombinant Factor IX Fc: Final Data from the B-MORE Study

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CONCLUSIONS

- **Real-world data from the B-MORE study confirm the effectiveness of recombinant factor IX Fc fusion protein (rFIXFc) and demonstrate that rFIXFc prophylaxis can reduce injection frequency and factor consumption while improving/maintaining bleed protection, compared with standard half-life prophylaxis.**

INTRODUCTION

- Extended half-life (EHL) recombinant factor IX Fc fusion protein (rFIXFc) has an established efficacy and safety profile for the treatment of people with hemophilia B (PwHB) across all ages.[1–4] However, there is a need for more real-world data.
- B-MORE (NCT03901755) was a 24-month, prospective, non-interventional study evaluating the real-world effectiveness and usage of rFIXFc in PwHB across Europe and the Middle East.[5]

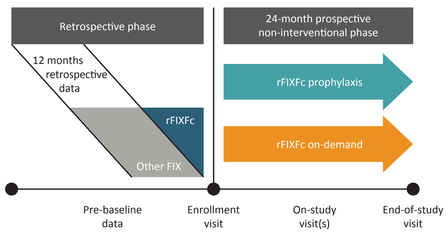
AIM

- To describe final data from the B-MORE study for PwHB treated with rFIXFc.

METHODS

- Eligible PwHB, including both previously treated and untreated PwHB, were prescribed rFIXFc on-demand or prophylaxis prior to or at B-MORE study enrollment (**Figure 1**).
- Twelve-month retrospective data on previous FIX (as available), baseline characteristics, and follow-up on rFIXFc (from retrospective and prospective periods) are reported.
- Annualized endpoints included PwHB with ≥6 months treatment only.

Figure 1: B-MORE study design



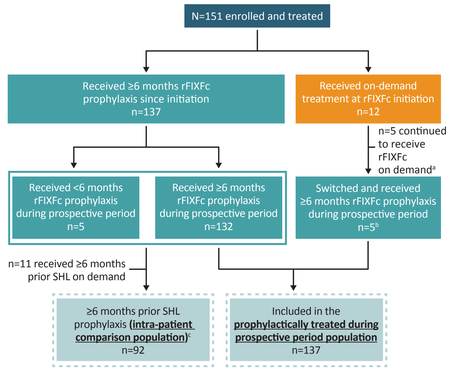
Retrospective period of 12 months is only applicable to previously treated patients. PwHB could switch between rFIXFc treatment regimens (on-demand and prophylaxis) throughout the study.

RESULTS

Patients

- B-MORE enrolled 151 PwHB from 29 centers; 137 PwHB received rFIXFc prophylaxis for ≥6 months during the prospective period (**Figure 2**).
- Baseline characteristics of these 137 PwHB are shown in **Table 1**.
  - Median (range) age was 22.3 (1–81) years.

Figure 2: Patient flow diagram



[a]n=7 patients switched to rFIXFc prophylaxis; n=5 continued to receive on-demand treatment. [b]1 patient was excluded due to multiple treatment regimen switches between rFIXFc on demand and rFIXFc prophylaxis; 1 patient was excluded due to receiving rFIXFc prophylaxis for less than 6 months during the prospective period. [c]9 were previously untreated patients; 3 patients had no prior treatment in the 12 months prior to rFIXFc initiation; 3 patients received prior EHL treatment; 9 patients had prior rFIXFc treatment as investigational medicinal product only; 10 patients had <6 months prior SHL treatment on the same treatment regimen.

Table 1: Patient demographics and baseline characteristics

n (%), unless otherwise stated	Prophylactically treated PwHB during the prospective period (N=137)
Age (years), median (IQR) [range]	22.3 (8.6–43.0) [1–81]
<18 years	65 (47.4)
Gender, male	134 (97.8)
BMI (kg/m²), median (IQR) [n]	22.6 (17.7–26.9) [120]
Hemophilia severity	
Severe	112 (81.8)
Moderate	25 (18.2)
Mild	0
Type of prior FIX treatment ≤12 months before rFIXFc initiation[a]	
Only plasma-derived product	28 (20.4)
Only recombinant product	85 (62.0)
Only rFIXFc[b]	9 (6.6)
Plasma-derived and recombinant product	1 (0.7)
Recombinant product and rFIXFc[b]	1 (0.7)
Previously untreated patients[c]	11 (8.0)
Patients without treatment ≤12 months prior to rFIXFc initiation[d]	2 (1.5)
Relevant comorbidities at enrollment[e]	
Yes	40 (29.2)
No	94 (68.6)
Missing	3 (2.2)
History of inhibitors	1 (0.7)

Percentages may not sum to 100 due to rounding. Baseline characteristics are reported for PwHB who received ≥6 months rFIXFc prophylaxis during the prospective period. [a]Out of the 137 PwHB included, 3 (2.2%) PwHB were treated with prior EHL FIX products other than rFIXFc and 112 (81.8%) PwHB were treated with prior SHL FIX products only. [b]rFIXFc given as investigational medicinal product. [c]Previously untreated patients who have not received any prior FIX treatment. [d]Previously treated patients without treatment ≤12 months prior to rFIXFc initiation. [e]Relevant comorbidities included clinically significant renal, liver, and cardiovascular disease, HIV, HCV (PCR positive), clinical depression, non-hemophilic acute or chronic medical conditions causing mobility/joint problems, other coagulation disorder(s) in addition to hemophilia, and other clinically relevant comorbidities.

Annualized bleeding rate and FIX usage (prospective period)

- Mean (range) treatment duration on rFIXFc prophylaxis was 22.4 (7.3–30.0) months.
- The primary endpoints, annualized bleeding rate (ABR), annualized injection frequency, and annualized factor consumption, are shown in **Table 2**.
- The proportion of PwHB with zero bleeds for consecutive periods of 6 months ranged from 63.0–80.4% (**Table 3**).

Table 2: ABRs and factor usage during the prospective period (primary endpoints)

	Prophylactically treated PwHB during the prospective period (N=137)		
	Annualized bleeding rate	Annualized injection frequency	Annualized factor consumption (IU/kg/year)
Mean (SD)	0.91 (1.4)	51.8 (12.8)	2,538 (801)
Median (IQR)	0.45 (0.0–1.2)	52.5 (52.2–52.6)	2,443 (2,022–2,970)
Range	0.0–9.1	26.2–121.8	1,057–5,220

Primary endpoints (prospective period) are reported for PwHB treated with ≥6 months rFIXFc prophylaxis during the prospective period.

Table 3: Proportion of PwHB with zero bleeds during the prospective period

	Proportion of PwHB with zero bleeds by time period, n (%)[a]			
Duration of rFIXFc treatment during the prospective period	Months from enrollment			
	0–6	>6–12	>12–18	>18–24
≥6 months (N=137)	98 (71.5)	N/A	N/A	N/A
≥12 months (N=131)	94 (71.8)	83 (63.4)	N/A	N/A
≥18 months (N=119)	84 (70.6)	75 (63.0)	88 (73.9)	N/A
≥24 months (N=46)	36 (78.3)	29 (63.0)	34 (73.9)	37 (80.4)

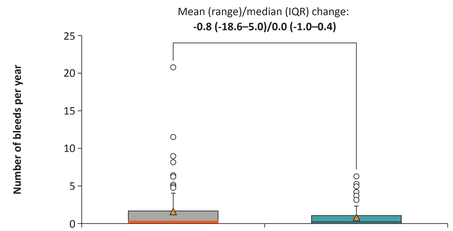
Proportion of zero bleeds assessed for consecutive periods of 6 months from baseline to 24 months. [a]Percentages are calculated according to the N values for each 6 month period.

Intrapatient comparison (prior SHL FIX prophylaxis versus rFIXFc prophylaxis)

- An intrapatient analysis was conducted in 92 PwHB with ≥6 months prior SHL FIX prophylaxis (**Figure 2**).
- Baseline characteristics of the intrapatient comparison population were similar to the prophylactically treated during prospective period population (data not shown).
- Mean (range) treatment duration was 11.5 (6.4–12.0) months with prior SHL prophylaxis and 40.6 (9.8–83.3) months since rFIXFc prophylaxis to end of study.
- Compared with prior SHL FIX prophylaxis, treatment with rFIXFc prophylaxis showed improved/maintained protection from bleeds, reduced injection frequency and reduced factor consumption (**Figure 3A–C**).

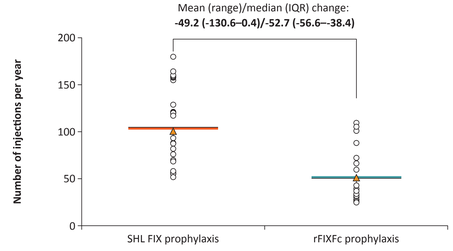
Figure 3: Intrapatient comparison of ABRs and factor usage with prior SHL FIX prophylaxis versus rFIXFc prophylaxis (N=92)

A) ABR



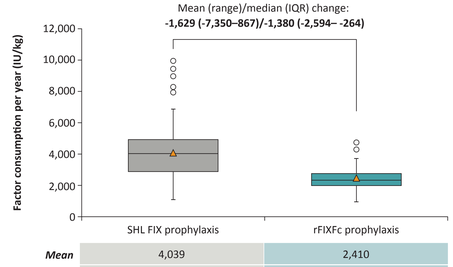
	SHL FIX prophylaxis	rFIXFc prophylaxis
Mean	1.6	0.8
Median (IQR)	0.0 (0.0–1.7)	0.3 (0.0–1.1)
Range	0.0–21.0	0.0–6.0

B) Annualized injection frequency



	SHL FIX prophylaxis	rFIXFc prophylaxis
Mean	101.0	51.8
Median (IQR)	105.1 (104.1–105.1)	52.3 (50.5–52.5)
Range	52.2–183.1	27.6–112.2

C) Annualized factor consumption[a]



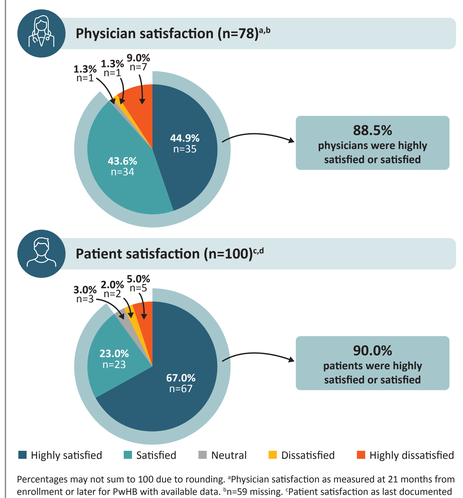
	SHL FIX prophylaxis	rFIXFc prophylaxis
Mean	4,039	2,410
Median (IQR)	3,940 (2,859–4,887)	2,311 (1,967–2,747)
Range	1,066–9,788	947–4,789

Some outlier data points may overlap. Outlier values are defined as more than 1.5 times the interquartile range above the upper quartile or 1.5 times the interquartile range below the lower quartile. Figures show means (orange triangles) and IQR (box boundaries); ends of whiskers represent the largest and smallest values excluding the outliers; thick red lines indicate equal medians/quartiles; circles represent outliers. [a]N=91.

Treatment satisfaction

- For PwHB who received ≥6 months rFIXFc prophylaxis from initiation with available data, most physicians (88.5%; n=69/78) and PwHB (90.0%; n=90/100) were satisfied or highly satisfied with rFIXFc prophylaxis (**Figure 4**).

Figure 4: Patient and physician treatment satisfaction in PwHB treated prophylactically since rFIXFc initiation (N=137)



Percentages may not sum to 100 due to rounding. [a]Physician satisfaction as measured at 21 months from enrollment or later for PwHB with available data. [b]n=59 missing. [c]Patient satisfaction as last documented for PwHB with available data. [d]n=37 missing.

Safety

- No inhibitor development or serious adverse events related to rFIXFc were reported.

References

1. Powell JS, et al. *N Engl J Med* 2013;369:2313–23; **2.** Fischer K, et al. *Lancet Haematol* 2017;4:e75–82; **3.** Pasi KJ, et al. *Haemophilia* 2020;26:e262–71; **4.** Nolan B, et al. *Blood Adv* 2021;5:2732–9; **5.** ClinicalTrials.gov (NCT03901755).

Disclosures

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Abbreviations

ABR: annualized bleeding rate; **BMI:** body mass index; **EHL:** extended half-life; **FIX:** factor IX; **HCV:** hepatitis C virus; **HIV:** human immunodeficiency virus; **IQR:** interquartile range; **IU:** international unit; **kg:** kilogram; **N/A:** not applicable; **PCR:** polymerase chain reaction; **rFIXFc:** recombinant factor IX Fc fusion protein; **SD:** standard deviation; **SHL:** standard half-life.

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