

Matching-Adjusted Indirect Comparison of Recombinant Factor IX Albumin Fusion Protein versus Recombinant Factor IX Fc Fusion Protein for Weekly Prophylactic Treatment of Hemophilia B

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Table S1. Baseline characteristics of subjects treated with rFIXFc or rIX-FP before and after adjustment for two to four key prognostic factors.

<i>Annualized bleeding rate, annualized spontaneous bleeding rate, and annualized joint bleeding rate</i>						
Variables adjusted		rFIXFc	rFIX-FP			
		None n = 63	None n = 56	Two Factors ^a ESS ^d = 55.7	Three Factors ^b ESS ^d = 49.8	Four Factors ^c ESS ^d = 43.1
Disease severity, n (%)	1-2 IU/dL	13 (20.6)	13 (23.2)	11.5 (20.6)	10.9 (20.6)	10.3 (20.6)
	<1 IU/dL	50 (79.4)	43 (76.8)	44.3 (79.4)	41.9 (79.4)	39.4 (79.4)
Age, y, mean (SD)		32.3 (13.9)	32.9 (14.1)	32.3 (14.1)	32.3 (14.1)	32.3 (14.1)
Prior FIX regimen, n (%)	On-demand	29 (46.8) ^e	18 (32.1)		24.7 (46.8)	23.2 (46.8)
	Prophylaxis	33 (53.2) ^e	38 (67.9)		28.1 (53.2)	26.4 (53.2)
BMI, kg/m ² , mean (SD)		24.8 (5.4)	23.4 (4.3)			24.8 (5.4)
Geographic region, n (%)	Europe/North America	39 (61.9)	36 (64.3)			
	Other	24 (38.1)	20 (35.7)			
<i>Proportion of patients without bleeding events, no spontaneous bleeds events, and no joint bleeding events</i>						
		n = 63	n = 59	ESS ^d = 58.9	ESS ^d = 53.8	ESS ^d = 49.8
Disease severity, n (%)	1-2 IU/dL	13 (20.6)	13 (22.0)	12.1 (20.6)	11.4 (20.6)	10.8 (20.6)
	<1 IU/dL	50 (79.4)	46 (78.0)	46.7 (79.4)	44.0 (79.4)	41.6 (79.4)
Age, y, mean (SD)		32.3 (13.9)	33.2 (14.2)	32.3 (14.0)	32.3 (14.1)	32.3 (14.1)
Prior FIX regimen, n (%)	On-demand	29 (46.8) ^e	19 (32.2)		25.9 (46.8)	24.5 (46.8)
	Prophylaxis	33 (53.2) ^e	40 (67.8)		29.5 (53.2)	27.9 (53.2)
BMI, kg/m ² , mean (SD)		24.8 (5.4)	23.5 (4.3)			24.8 (5.4)
Geographic region, n (%)	Europe/North America	39 (61.9)	39 (66.1)			
	Other	24 (38.1)	20 (33.9)			

Note: Binary and continuous baseline characteristics are presented as n (%) and mean (SD), respectively. Due to missingness in individual patient data for the PROLONG-9FP trial on rIX-FP, the ESS for annualized bleeding rate, annualized spontaneous bleeding rate, and annualized joint bleed rate differed from the outcomes on the percentage of subjects with no bleeding events, no spontaneous bleeding events, and no joint bleeding events.

^a Two factor multivariable analyses adjusted for disease severity and age.

^b Three factor multivariable analyses adjusted for disease severity, age, and prior FIX regimen.

^c Four factor multivariable analyses adjusted for disease severity, age, prior FIX regimen, and BMI.

^d ESS is calculated as the sum of patient weights squared divided by the sum of squared patient weights. In the adjusted analyses, number of patients in each category of disease severity and prior FIX regimen are calculated as the sum of patient weights, and therefore do not sum to the ESS.

^e Prior FIX regimen was unknown in one patient in the rFIXFc population, and percentages were calculated based on patients with complete data.

BMI, body mass index; dL, deciliter; ESS, effective sample size; FIX, factor IX; IU, international unit; kg, kilogram; m², square-metre; rFIXFc, recombinant factor IX Fc fusion protein; rIX-FP, recombinant factor IX albumin fusion protein; SD, standard deviation; y, years.

Table S2. Summary of efficacy outcomes for subjects treated with rFIXFc and rIX-FP before and after adjustment for two to four key prognostic factors.

Variables adjusted		rFIXFc	rIX-FP			
		None	None	Two Factors ^a	Three Factors ^b	Four Factors ^c
		n = 63	n = 56	ESS ^d = 55.7	ESS ^d = 49.8	ESS ^d = 43.1
ABR	RR (95% CI) Point estimate P-value	- 3.12 -	0.56 (0.35, 0.91) 1.75 P = 0.0199	0.57 (0.32, 0.98) 1.76 P = 0.0439	0.69 (0.34, 1.39) 2.15 P = 0.2970	0.75 (0.32, 1.75) 2.35 P = 0.5095
AjBR	RR (95% CI) Point estimate P-value	- 2.26 -	0.61 (0.37, 1.01) 1.38 P = 0.0564	0.61 (0.35, 1.06) 1.38 P = 0.0789	0.75 (0.39, 1.47) 1.70 P = 0.4047	0.82 (0.37, 1.82) 1.84 P = 0.6178
AsBR	RR (95% CI) Point estimate P-value	- 1.65 -	0.39 (0.22, 0.72) 0.65 P = 0.0023	0.38 (0.22, 0.67) 0.63 P = 0.0009	0.42 (0.24, 0.76) 0.70 P = 0.0040	0.42 (0.22, 0.82) 0.69 P = 0.0107
		n = 63	n = 59	ESS ^d = 58.9	ESS ^d = 53.8	ESS ^d = 49.8
No bleeding events	OR (95% CI) Point estimate P-value	- 0.230 -	3.25 (1.50, 7.03) 0.492 P = 0.0028	3.30 (1.51, 7.20) 0.496 P = 0.0027	2.92 (1.31, 6.51) 0.465 P = 0.0089	3.24 (1.41, 7.45) 0.491 P = 0.0057
No spontaneous bleeding events	OR (95% CI) Point estimate P-value	- 0.410 -	3.56 (1.71, 7.39) 0.712 P = 0.0009	3.65 (1.74, 7.66) 0.717 P = 0.0006	3.13 (1.45, 6.76) 0.685 P = 0.0037	3.47 (1.56, 7.73) 0.707 P = 0.0023
No joint bleeding events	OR (95% CI) Point estimate P-value	- 0.344 -	2.59 (1.27, 5.30) 0.576 P = 0.0092	2.62 (1.27, 5.39) 0.579 P = 0.0092	2.23 (1.05, 4.71) 0.539 P = 0.0362	2.41 (1.10, 5.26) 0.559 P = 0.0274

Note: RR <1 and OR >1 indicate results in favor of rIX-FP. Due to missingness in individual patient data for the PROLONG-9FP trial on rIX-FP, the ESS for annualized bleeding rate, annualized spontaneous bleeding rate, and annualized joint bleed rate differed from the outcomes on the proportion of patients without bleeding events, spontaneous bleeding events, and joint bleeding events.

^a Two factor multivariable analyses adjusted for disease severity and age.

^b Three factor multivariable analyses adjusted for disease severity, age, and prior FIX regimen.

^c Four factor multivariable analyses adjusted for disease severity, age, prior FIX regimen, and BMI.

^d ESS is calculated as the sum of patient weights squared divided by the sum of squared patient weights.

ABR, annualized bleeding rate; AjBR, annualized joint bleeding rate; AsBR, annualized spontaneous bleeding rate; CI, confidence interval; ESS, effective sample size; OR, odds ratio; RR, rate ratio; rFIXFc, recombinant factor IX Fc fusion protein; rIX-FP, recombinant factor IX albumin fusion protein.