Web-Based Supplementary Materials for 'Characteristics and Treatment Patterns of Patients with Haemophilia B Receiving Recombinant Coagulation Factor IX'

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Table S1. Patient characteristics based on medical chart review.

Demographics and Clinical Characteristics		Treatment Patterns	
Inhibitors, *n* (%)		**Prescribed weekly infusion for prophylaxis, cases (%)#**	642 (100.00%)
Yes	0 (0.00%)	≤1/week	174 (27.10%)
Transient	0 (0.00%)	1–2/week	287 (44.70%)
No	129 (99.23%)	2–3/week	136 (21.18%)
Unknown	1 (0.77%)	3–4/week	23 (3.58%)
Arthropathy, *n* (%)		> 4/week	22 (3.43%)
Yes	72 (55.38%)	**Changes of prophylactic dose, *n* (%)**	*n* = 126
No	58 (44.62%)	Yes	99 (78.57%)
Arthropathy site, *n* (%)		No	27 (21.43%)
Knee joints, *n* (%) Yes	36 (27.69%)	**Reasons for changing in prophylaxis, cases (%)#**	*n* = 572
No	94 (72.31%)	Lack of preventive effect	17 (2.97%)
Ankle joints, *n* (%) Yes	58 (44.62%)	Increased activity	0 (0.00%)
No	72 (55.38%)	Acute stage after surgery	4 (0.70%)
Elbow joints, *n* (%) Yes	34 (26.15%)	Subacute stage after surgery	23 (4.02%)
No	96 (73.85%)	Salivitis	0 (0.00%)
Shoulder joints, *n* (%) Yes	4 (3.08%)	Acute phase after severe bleeding	0 (0.00%)
No	126 (96.92%)	Others	518 (90.56%)
Hip joints, *n* (%) Yes	10 (7.69%)	Unknown	14 (2.45%)
No	120 (92.31%)		
Other joints, *n* (%) Yes	2 (1.54%)		
No	128 (98.46%)		
HIV, *n* (%)			
Positive	6 (4.62%)		
Negative	115 (88.46%)		
Hepatitis B, *n* (%)			
Acute	0 (0.00%)		
Chronic	3 (2.31%)		
Recovery after infection	3 (2.31%)		
No	108 (83.08%)		
Unknown	16 (12.31%)		

Table S2. Detailed Average dose and factor consumption.

(A) All							
	Mild (*n* = 2)	**Moderate (*n* = 23)**	**Severe (*n* = 105)**	***P*-Value**	**Extended Half-Life (*n* = 8)**	**Standard Half-Life (*n* = 75)**	***P*-value‡**
Prophylactic dose (IU/kg/week)				0.212			<0.001
n	2	20	104		8	118	
Mean ± SD†	91.47 ± 48.18	78.80 ± 24.42	87.59 ± 26.99		45.55 ± 10.18	89.02 ± 25.34	
Factor consumption (IU/kg/week)				0.013			<0.001
n	2	23	105		8	122	
Mean ± SD†	80.03 ± 28.85	61.75 ± 34.09	83.99 ± 26.59		45.92 ± 11.20	82.23 ± 28.53	
***(B)* Prophylactic Treatment**							
	Mild (*n* = 0)	**Moderate (*n* = 4)**	**Severe (*n* = 43)**	***P*-Value**	**Extended Half-Life (*n* = 0)**	**Standard Half-Life (*n* = 47)**	***P*-Value ‡**
Prophylactic dose (IU/kg/week)				0.619			-
n	0	4	43		0	47	
Mean ± SD†	-	104.38 ± 16.10	106.78 ± 13.35		-	106.58 ± 13.42	
Factor consumption (IU/kg/week)				0.38			-
n	0	4	43		0	47	
Mean ± SD†	-	100.17 ± 14.84	105.49 ± 11.37		-	105.04 ± 11.60	
***(C)* Non-prophylactic treatment**							
	Mild (*n* = 2)	**Moderate (*n* = 19)**	**Severe (*n* = 62)**	***P*-value**	**Extended half-life (*n* = 8)**	**Standard half-life (*n* = 75)**	***P*-value†**
Prophylactic dose (IU/kg/week)				0.753			<0.001
n	2	16	61		8	71	
Mean ± SD	91.47 ± 48.18	72.40 ± 22.03	74.06 ± 25.99		45.55 ± 10.18	77.39 ± 24.72	
Factor consumption (IU/kg/week)				0.097			0.01
n	2	19	62		8	75	
Mean ± SD†	80.03 ± 28.85	53.66 ± 31.41	69.07 ± 23.76		45.92 ± 11.20	67.93 ± 26.64	

Abbreviations: SD, standard deviation. † P-values are calculated using the Mann–Whitney *U* test.

Table S3. Detailed Adherence variables The patient survey was conducted once, and patients were asked about their experiences over the course of a month. The means and standard deviations were calculated for continuous variables, while frequencies and percentages were calculated for categorical variables.

Variables of Patients' Adherence	
Injection administrator, *n* (%)	
Patient	80 (61.54%)
Protector	33 (25.38%)
Physician	17 (13.08%)
Prescribed treatment regimen, *n* (%)	
Prophylaxis	79 (60.77%)
On-demand 1†	10 (7.69%)
On-demand 2†	5 (3.85%)
Prophylaxis and On-demand 1	28 (21.54%)
Prophylaxis and On-demand 2	6 (4.62%)
Others	2 (1.54%)
Treatment regimen switch, *n* (%)	
Yes	7 (5.38%)
No	123 (94.62%)
Switch type, *n* (%)	*n* = 7
On-demand to prophylaxis	4 (57.14%)
Prophylaxis to prophylaxis and on-demand	1 (14.29%)
Others	2 (28.57%)
Bleeding in the past month, *n* (%)	
Yes	49 (37.69%)
Total dose for a month before bleeding (IU/month)	20,046.06 ± 11,024.13
Total number of doses for a month before bleeding (n/month)	5.41 ± 3.20
No	81 (62.31%)
Total dose for the past month (IU/month)	20,991.26 ± 9,393.71
Total number of doses for the past month (n/month)	5.48 ± 2.26

†On-demand 1 represents the on-demand regimen after bleeding, while On-demand 2 represents the on-demand regimen before bleeding.

Table S4. Comparisons of annual bleeding events (ABEs) by demographic and clinical characteristics Mean ± standard deviation represents the mean of ABEs and their standard deviations for each characteristic. The correlation coefficients were calculated with a *p*-value for continuous characteristics, while the p-value was calculated using the methods described below for categorical characteristics.

Characteristics	*n* (%)	Mean ± SD	Correlation coefficients	*P*-value
Age (years)	130 (100.00%)		0.110	0.213†
Gender, *n* (%)				-
Male	129 (99.23%)			
Female	1 (0.77%)	3.06 ± 4.73		
Height (cm)	130 (100.00%)	1.00 ± NA	−0.015	0.867†
Weight (kg)	130 (100.00%)		0.031	0.730†
BMI (kg/m²)	130 (100.00%)		0.029	0.740†
Disease duration (months)	117 (90.00%)		0.123	0.185†
Severity, *n* (%)				
Severe	105 (80.15%)			0.636‡
Moderate	23 (17.56%)			
Mild	3 (2.29%)			
Inhibitors, *n* (%)				0.275‡
Yes	0 (0.00%)			
High	0 (0.00%)			
Low	0 (0.00%)	3.08 ± 4.64		
Transient	0 (0.00%)	3.13 ± 5.28		
No	129 (99.23%)	0.50 ± 0.71		
Unknown	1 (0.77%)			
Arthropathy, *n* (%)				0.096§
Yes	72 (55.38%)	-		
No	58 (44.62%)	-		
Unknown	0 (0.00%)	-		
Arthropathy site, *n* (%)		-		
Knee joints, *n* (%)		3.03 ± 4.73		0.080§
Yes	36 (27.69%)	5.00 ± NA		
No	94 (72.31%)			
Ankle joints, *n* (%)				0.222§
Yes	58 (44.62%)	3.68 ± 5.16		
No	72 (55.38%)	2.26 ± 4.00		
Elbow joints, *n* (%)		-		**0.011**§
Yes	34 (26.15%)			
No	96 (73.85%)			
Shoulder joints, *n* (%)				0.307§
Yes	4 (3.08%)	3.75 ± 4.63		
No	126 (96.92%)	2.78 ± 4.74		
Hip joints, *n* (%)				0.846§
Yes	10 (7.69%)	3.41 ± 4.58		
No	120 (92.31%)	2.75 ± 4.83		
Other joints, *n* (%)				0.083§

Yes	2 (1.54%)	4.47 ± 5.22		
No	128 (98.46%)	2.54 ± 4.44		
HIV, *n* (%)				0.481‡
Positive	6 (4.62%)	5.50 ± 6.66		
Negative	115 (88.46%)	2.97 ± 4.65		
Unknown	9 (6.92%)			
Hepatitis B, *n* (%)		3.60 ± 5.32		0.999‡
Chronic	3 (2.31%)	3.00 ± 4.68		
Recovery after infection	3 (2.31%)			
No	108 (83.08%)	11.00 ± 11.31		
Unknown	16 (12.31%)	2.92 ± 4.53		
Factor IX activity level (%)	109 (83.85%)		−0.139	0.151†

Abbreviations: SD, standard deviation

†P-value by Spearman's correlation analysis; ‡p-value by Kruskal–Wallis test; §p-value by Mann–Whitney *U* test

Table S5. Comparisons of annual bleeding events (ABEs) by treatment patterns

Mean ± standard deviation represents the mean of ABEs and their standard deviations for each characteristic. The correlation coefficients were calculated with a p-value for continuous characteristics, while the p-value was calculated using the methods described below for categorical characteristics.

Characteristics	*n* (%)	Mean ± SD	Correlation coefficients	*P*-value
Treatment duration (months)	130 (100.00%)		0.183	**0.037**†
Half-life, *n* (%)				0.269‡
SHL	122 (93.85%)	3.02 ± 4.76		
EHL	8 (6.15%)	3.50 ± 4.24		
Switch	0 (0.00%)	-		
SHL to EHL	0 (0.00%)	-		
EHL to SHL	0 (0.00%)	-		
SHL to EHL to SHL	0 (0.00%)	-		
EHL to SHL to EHL	0 (0.00%)	-		
Treatment regimen, *n* (%)				**<0.001**‡
Prophylaxis	47 (36.15%)	1.47 ± 2.91		
Non-prophylaxis	83 (63.85%)	3.94 ± 5.29		
Prophylactic dose (IU/kg/week)	*n* = 126		−0.264	**0.003**†
On-demand dose (IU/kg)	*n* = 64		−0.338	**0.006**†
Change of dose in prophylaxis, *n* (%)				0.528‡
Yes	99 (78.57%)	3.06 ± 4.70		
No	27 (21.43%)	2.19 ± 3.75		
Factor consumption (IU/kg/week)	130 (100.00%)		−0.206	**0.019**†
Prophylaxis	66 (50.77%)		−0.224	0.071†
On-demand 1§	3 (2.31%)		0.500	1.000†
On-demand 2§	1 (0.77%)		-	-
Prophylaxis and On-demand 1	60 (46.15%)		−0.086	0.511†
Treatment duration (months)	130 (100.00%)		0.183	**0.037**†

Abbreviations: SD, standard deviation; SHL, standard half-life; EHL, extended half-life

†*P*-value by Spearman's correlation analysis; ‡*p*-value by Mann–Whitney *U* test

§On-demand 1 represents the on-demand regimen after bleeding, while On-demand 2 represents the on-demand regimen before bleeding

Table S6. Comparisons of annual bleeding events (ABEs) by patients' adherence based on patient survey Mean ± standard deviation represents the mean of ABEs and their standard deviations for each characteristic. The correlation coefficients were calculated with a p-value for continuous characteristics, while the p-value was calculated using the methods described below for categorical characteristics.

Characteristics	*n* (%)	Mean ± SD	Correlation coefficients	*P*-value
Injection administrator, *n* (%)				0.449†
Patient	80 (61.54%)	3.69 ± 5.36		
Protector	33 (25.38%)	2.39 ± 3.83		
Physician	17 (13.08%)	1.29 ± 1.31		
Prescribed treatment regimen, *n* (%)				**0.001†**
Prophylaxis	79 (60.77%)	2.09 ± 3.86		
On-demand 1¶	10 (7.69%)	7.70 ± 7.51		
On-demand 2¶	5 (3.85%)	2.40 ± 1.67		
Prophylaxis and On-demand 1¶	28 (21.54%)	4.04 ± 5.01		
Prophylaxis and On-demand 2¶	6 (4.62%)	3.33 ± 5.85		
Others	2 (1.54%)	4.50 ± 3.54		
Treatment regimen switch, *n* (%)				0.237‡
Yes	7 (5.38%)	4.57 ± 6.58		
No	123 (94.62%)	2.96 ± 4.61		
Switch type, *n* (%)				0.619†
Prophylaxis to On-demand 1¶	0 (0.00%)	-		
Prophylaxis to On-demand 2¶	0 (0.00%)	-		
On-demand 1** to Prophylaxis	4 (57.14%)	6.75 ± 8.42		
On-demand 2** to Prophylaxis	0 (0.00%)	-		
Prophylaxis to Prophylaxis and On-demand	1 (14.29%)	1.00 ± NA		
On-demand to Prophylaxis and On-demand	0 (0.00%)	-		
Others	2 (28.57%)	2.00 ± 1.41		
Bleeding in the past month, *n* (%)				**<0.001‡**
Yes	49 (37.69%)	5.31 ± 5.96		
Total dose for a month before bleeding (IU/month)			–0.115	0.431§
Total number of doses for a month before bleeding (n/month)			–0.095	0.517§
No	81 (62.31%)	1.68 ± 3.09		
Total dose for the past month (IU/month)			–0.111	0.325§
Total number of doses for the past month (n/month)			–0.107	0.342§
Adherence status, *n* (%)				0.063‡
Adherent	97 (74.62%)	2.75 ± 4.52		
Non-adherent	33 (25.38%)	3.91 ± 5.22		
Number of non-adherents	33 (25.38%)		–0.126	0.486§
Types of non-adherence, *n* (%)	*n* = 33			
Overdose injection per administration				0.333‡
Yes	12 (36.36%)	5.17 ± 6.75		

	No	21 (63.64%)	3.19 ± 4.13	
Under-dose injection per administration				0.959‡
	Yes	5 (15.15%)	4.20 ± 6.22	
	No	28 (84.85%)	3.86 ± 5.15	
Over-frequent administration				0.089‡
	Yes	9 (27.27%)	7.44 ± 7.43	
	No	24 (72.73%)	2.58 ± 3.46	
Under-frequent administration				0.237‡
	Yes	19 (57.58%)	2.79 ± 3.82	
	No	14 (42.42%)	5.43 ± 6.52	
Reasons for non-adherence, *n* (%)		*n* = 33		
Lack of time				0.517‡
	Yes	7 (21.21%)	2.86 ± 3.58	
	No	26 (78.79%)	4.19 ± 5.61	
Too frequent administration				0.504‡
	Yes	3 (9.09%)	4.33 ± 4.16	
	No	30 (90.91%)	3.87 ± 5.37	
Feel worsening of the disease				**0.009**‡
	Yes	5 (15.15%)	11.00 ± 7.97	
	No	28 (84.85%)	2.64 ± 3.46	
Feel getting better of the disease				**0.029**‡
	Yes	2 (6.06%)	15.00 ± 0.00	
	No	31 (93.94%)	3.19 ± 4.51	
Occurrence of bleeding				0.359‡
	Yes	13 (39.39%)	5.46 ± 6.79	
	No	20 (60.61%)	2.90 ± 3.75	
Too expensive				0.220‡
	Yes	1 (3.03%)	9.00 ± NA	
	No	32 (96.97%)	3.75 ± 5.22	
Forgetfulness				0.327‡
	Yes	4 (12.12%)	1.00 ± 0.00	
	No	29 (87.88%)	4.31 ± 5.46	
Lack of dosage				-
	Yes	0 (0%)	-	
	No	33 (100%)	3.91 ± 5.22	
Tiredness from injections				0.115‡
	Yes	12 (36.36%)	2.08 ± 2.84	
	No	21 (63.64%)	4.95 ± 6.00	
Others				0.475‡
	Yes	5 (15.15%)	4.40 ± 4.16	
	No	28 (84.85%)	3.82 ± 5.45	

†*P*-value by Kruskal–Wallis test; ‡*p*-value by Mann–Whitney *U* test; §*p*-value by Spearman's correlation analysis

¶On-demand 1 represents the on-demand regimen after bleeding, while On-demand 2 represents the on-demand regimen before bleeding

Table S7. Univariate analysis of annual bleeding events (ABEs) with negative binomial regression.

	Coefficients	S.E	Exponential estimates (95% CI)	*P*-value
Treatment regimen				
Non-prophylaxis	ref			
Prophylaxis	−0.987	0.292	0.373 (0.212–0.667)	**0.001**
Patients' adherence				
Non-adherent	ref			
Adherent	−0.351	0.321	0.704 (0.364–1.293)	0.274
Age (years)	0.015	0.008	1.015 (0.997–1.033)	**0.072**
Gender				
Female	ref			
Male	1.119	1.816	3.062 (0.012–106.336)	0.538
Height (cm)	0.003	0.009	1.003 (0.985–1.018)	0.752
Weight (kg)	0.003	0.007	1.003 (0.987–1.017)	0.724
BMI (kg/m²)	0.010	0.033	1.011 (0.944–1.082)	0.750
Disease duration (months)	0.002	0.001	1.002 (1.000–1.004)	**0.064**
Severity				
Severe	ref			
Moderate	0.017	0.369	1.018 (0.511–2.206)	0.962
Mild	−1.817	1.467	0.163 (0.006–5.219)	0.216
Arthropathy				
Yes	ref			
No	−0.488	0.283	0.614 (0.353–1.075)	**0.085**
Arthropathy site				
Knee joints				
No	ref			
Yes	0.301	0.313	1.351 (0.744–2.561)	0.337
Ankle joints				
No	ref			
Yes	0.216	0.284	1.241 (0.712–2.182)	0.447
Elbow joints				
No	ref			

Yes	0.565	0.313	1.759 (0.971–3.341)	**0.071**
Shoulder joints				
No	ref			
Yes	0.617	0.796	1.853 (0.498–13.630)	0.438
Hip joints				
No	ref			
Yes	0.182	0.527	1.200 (0.470–3.901)	0.730
Other joints				
No	ref			
Yes	1.326	1.085	3.765 (0.724–85.193)	0.222
HIV				
Negative	ref			
Positive	0.892	0.645	2.439 (0.815–11.277)	0.167
Unknown	−0.073	0.557	0.929 (0.343–3.228)	0.895
Hepatitis B				
No	ref			
Chronic	−0.662	0.987	0.516 (0.092–6.118)	0.503
Recovery after infection	−0.662	0.987	0.516 (0.092–6.118)	0.503
Unknown	−0.335	0.438	0.716 (0.320–1.821)	0.445
Factor IX activity level (%)	−0.011	0.012	0.989 (0.969–1.015)	0.371
Treatment duration (months)	0.003	0.001	1.003 (1.000–1.005)	**0.024**
Half-life				
Standard half-life	ref			
Extended half-life	0.149	0.586	1.160 (0.415–4.416)	0.800
Factor consumption (1,000 IU/kg/week)	−0.879	0.479	0.415 (0.164–1.017)	**0.066**
Injection administrator				
Patient	ref			
Protector	−0.432	0.328	0.649 (0.347–1.266)	0.188
Physician	−1.047	0.449	0.351 (0.150–0.893)	**0.020**
Treatment regimen switch				
No	ref			
Yes	0.435	0.614	1.545 (0.534–6.442)	0.479
Bleeding in the past month				
No	ref			

Yes	1.151	0.267	3.160 (1.885–5.387)	**<0.001**

Abbreviations: S.E, standard error; CI, confidence interval

Table S8. Multiple analyses of annual bleeding events with negative binomial regression.

		Coefficients	S.E	Exponentiated Estimates (95% CI)	*P*-Value
Treatment regimen					
	Non-prophylaxis	ref			
	Prophylaxis	−0.9590	0.379	0.3830 (0.182–0.805)	**0.011**
Patients' adherence					
	Non-adherent	ref			
	Adherent	−0.352	0.310	0.703 (0.383–1.292)	0.257
Age (years)		0.011	0.011	1.011 (0.989–1.033)	0.341
BMI (kg/m²)		−0.039	0.037	0.961 (0.894–1.033)	0.285
Severity					
	Severe	ref			
	Moderate	−0.013	0.428	0.987 (0.426–2.284)	0.975
	Mild	−1.934	1.484	0.145 (0.008–2.650)	0.193
Arthropathy					
	Yes	ref			
	No	−0.513	0.346	0.599 (0.304–1.179)	0.138
Treatment duration (months)		0.001	0.002	1.001 (0.998–1.005)	0.542
Half-life					
	Standard half-life	ref			
	Extended half-life	0.336	0.634	1.400 (0.404–4.847)	0.596
Factor consumption (1,000 IU/kg/week)		−0.107	0.623	0.899 (0.265–3.051)	0.864
Injection administrator					
	Patient	Ref			
	Protector	0.096	0.401	1.101 (0.502–2.415)	0.810
	Physician	−0.325	0.470	0.722 (0.287–1.816)	0.489

Abbreviations: S.E, standard error; CI, confidence interval.

Table S9. Multiple analyses of monthly bleeding events with generalised linear mixed model and a negative binomial distribution. In this analysis, 'dose before' refers to the total prescribed dose in the previous month, while 'dose' refers to the total prescribed dose in the month in which the bleeding event occurred.

		Coefficients	S.E	Exponentiated Estimates (95% CI*)	*P*-Value
Treatment regimen					
	Non-prophylaxis	ref			
	Prophylaxis	−0.456	0.357	0.634 (0.315–1.275)	0.201
Dose (100 IU/kg)		−0.367	0.068	0.693 (0.606–0.792)	**<0.001**
Dose before (100 IU/kg)		−0.013	0.043	0.987 (0.906–1.074)	0.759
Patients' adherence					
	Non-adherent	ref			
	Adherent	−0.373	0.329	0.689 (0.361–1.313)	0.257
Age (years)		0.005	0.012	1.005 (0.981–1.030)	0.663
BMI (kg/m²)		−0.023	0.039	0.977 (0.906–1.055)	0.560
Severity, *n* (%)					
	Severe	ref			
	Moderate	−0.201	0.446	0.818 (0.341–1.963)	0.653
	Mild	−1.503	1.581	0.222 (0.010–4.931)	0.342
Arthropathy, *n* (%)					
	Yes	ref			
	No	−0.489	0.381	0.613 (0.290–1.294)	0.199
Treatment duration (months)		0.002	0.002	1.002 (0.998–1.006)	0.333
Half-life					
	Standard half-life	ref			
	Extended half-life	0.193	0.638	1.213 (0.347–4.236)	0.763
Injection administrator					
	Patient	ref			
	Protector	0.210	0.430	1.233 (0.531–2.863)	0.625
	Physician	−0.224	0.501	0.800 (0.300–2.133)	0.655

Abbreviations: S.E, standard error; CI, confidence interval.