Utilization of standard half-life or extended half-life products in members with Hemophilia A prescribed Hemlibra®

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Background

- Prophylaxis with factor or nonfactor products, such as Hemlibra®, is the current standard of care to reduce bleeding events in members with severe hemophilia A
- Despite the efficacy of Hemlibra®, members should always have factor product on-hand for prompt self-management of any breakthrough bleeds
- Treatment of an acute bleed can be accomplished with either standard half-life (SHL) or an extended half-life (EHL) factor product

Objective

- Assess how frequently members with hemophilia A who were prescribed Hemlibra® fill prescriptions for factor products
- Report the percent of members filling prescriptions for SHL and EHL factor products
- Evaluate the annualized bleed rate (ABR) by SHL and EHL
- Report the number of specialty pharmacy (SP) dispenses by SHL and EHL

Methods

- A cohort of hemophilia A members from a large national healthcare payor in the US were observed from 3/31/20 to 3/31/23
- Eligibility criteria included males >18y who received Hemlibra® for at least 6 months and had continuous plan enrollment for at least 6 months after the first Hemlibra® dose
- Annualized bleeding rate (ABR) was defined as the number of bleeding episodes/number of person-years observed
- Factor utilization was defined as the number of SP dispenses/number of person-months observed
- Charlson Comorbidity Index (CCI) was used to adjust for comorbidities
- Student's t and Chi-square tests assessed differences between groups; p-value ≤0.05 was significant

Results

- Mean (standard deviation (SD)) age was 32.2 (10.9) years
- Most members (38/53, 71.7%) filled a factor product; 71.1% (27/38) filled an SHL product
- Members filling factor products had higher comorbidities compared to members not filling factor products (1.7 vs 0.3 p =0.009)
- Overall, the ABR was low with less than 1 (0.95 [95% confidence interval (CI) 0.79-1.13]) bleeding episode per person year
- While prescribed Hemlibra®, the ABR was significantly higher in the SHL (1.02 (0.75-1.36)) group compared to the EHL (0.34 (0.15-0.67)) group (p=0.002)
- There were no differences in SP dispenses between members filling EHL versus SHL products (3.0 (4.0) vs 1.9 (4.7), p=0.5)

Figure 1: Study Inclusion Flowchart

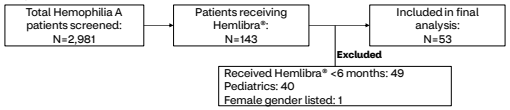

Table 1: Cohort demographics

Variable	Overall N=53	No Factor N = 15 (28.3%)	Factor N = 38 (71.7%)	P-Value
Age, mean (SD)	32.2 (10.9)	31.1 (7.4)	32.6 (12.0)	0.569
Age, median [Q1,Q3]	30.0 [24.0,38.0]	30.0 [25.5,35.5]	30.5 [24.0,38.75]	0.913
Years of observation, mean (SD)	2.6 (1.1)	2.3 (1.1)	2.7 (1.1)	0.225
Years of observation, median [Q1,Q3]	2.8 [1.5,3.6]	2.6 [1.0,3.2]	3.0 [1.7,3.8]	0.112
Years of observation prior to first Hemlibra® dose, mean (SD)	0.88 (0.93)	0.84 (0.96)	0.89 (0.93)	0.863
Years of observation prior to first Hemlibra® dose, median [Q1,Q3]	0.41 [0.1,1.57]	0.37 [0.11,1.40]	0.458 [0.09,1.51]	0.836
Years of observation after first Hemlibra® dose, mean (SD)	1.73 (0.77)	1.46 (0.80)	1.84 (0.75)	0.132
Years of observation after first Hemlibra® dose, median [Q1,Q3]	1.63 [1.01,2.55]	1.12 [0.77,2.24]	1.64 [1.18,2.61]	0.058
New Hemlibra® patient, n (%)*	15 (62.5)	3 (50.0)	12 (66.7)	0.635
Total Hemlibra® fills, mean (SD)	22.4 (12.0)	18.0 (9.3)	24.1 (12.6)	0.062
Total Hemlibra® fills, median [Q1,Q3]	20.0 [13.0,28.0]	14.0 [11.5,21.0]	22.0 [16.25,28.75]	0.051

*29 excluded due to lookback period; SD: Standard Deviation; Q1: first quartile; Q3: third quartile

Table 2: Comorbidities

Variable	Overall	No Factor	Factor	P-Value
Charlson score, mean (SD)	1.3 (2.7)	0.3 (0.6)	1.7 (3.1)	0.009
Charlson score, median [Q1,Q3]	0 [0,1]	0 [0,0]	0 [0,1]	0.333
PVD, n (%)	2 (3.8)		2 (5.3)	1
CVD, n (%)	1 (1.9)		1 (2.6)	1
COPD, n (%)	1 (1.9)	1 (6.7)		0.283
Diabetes, n (%)	2 (3.8)	1 (6.7)	1 (2.6)	0.49
Diabetes with complications, n (%)	1 (1.9)	1 (6.7)		0.283
Renal disease, n (%)	1 (1.9)		1 (2.6)	1
Liver disease (mild), n (%)	6 (11.3)	1 (6.7)	5 (13.2)	0.662
Liver disease, n (%)	1 (1.9)		1 (2.6)	1
AIDS, n (%)	8 (15.1)		8 (21.1)	0.088
Cancer, n (%)	2 (3.8)		2 (5.3)	1

No patients had: Acute MI, history of MI, CHF, dementia, paralysis, ulcers, rheumatic disease, and metastatic cancer; SD: Standard Deviation; Q1: first quartile; Q3: third quartile; PVD: peripheral vascular disease; CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease; AIDS: Acquired immunodeficiency syndrome; MI: myocardial infarction; CHF: congestive heart failure

Table 3: Factor utilization by post-Hemlibra® factor status

Variable	Overall	No Factor	Factor	P-Value
Pre-Hemlibra®				
SHL use, n (%)	16 (30.2)	5 (33.3)	11 (28.9)	0.751
SHL fills, mean (SD)	4.1 (8.7)	4.3 (8.2)	4.0 (9.0)	0.89
EHL use, n (%)	9 (17.0)	2 (13.3)	7 (18.4)	1
EHL fills, mean (SD)	2.5 (11.8)	0.3 (0.9)	3.3 (13.9)	0.196
Post-Hemlibra®				
SHL use, n (%)	27 (50.9)		27 (71.0)	
SHL fills, mean (SD)	2.2 (3.7)		3.0 (4.0)	
EHL use, n (%)	11 (20.8)		11 (28.9)	
EHL fills, mean (SD)	1.4 (4.0)		1.9 (4.7)	

EHL: Extended half-life factor; SHL: Standard half-life factor; SD: standard deviation

Table 4: Factor utilization in utilizers in both periods

	Pre-Hemlibra® N=12	Post-Hemlibra® N=12	P-value
Number factor fills, mean (SD)	21.8 (22.1)	7.6 (7.5)	0.054
Person Months observed, mean (SD)	24.7 (7.0)	19.0 (8.0)	0.077
Factor fills per person month, mean (SD)	0.9 (0.8)	0.4 (0.3)	0.051
Fill rate (Fills per person month)	0.884 (0.78 - 1.0)	0.4 (0.32 - 0.49)	
IRD	-0.485 (-0.63, -0.34)		<0.0001
IRR	0.452 (0.35 - 0.58)		<0.0001

IRD: Incidence rate difference; IRR: Incidence rate ratio ; SD: standard deviation

Table 5: Bleeding events by factor use and period

Variable	Overall	No Factor	Factor	P-Value
Any bleed, n (%)	24 (45.3)	7 (46.7)	17 (44.7)	1
Number of bleeds, mean (SD)	2.5 (5.8)	3.3 (5.6)	2.2 (5.9)	0.528
Any Major bleed, n (%)	13 (24.5)	3 (20.0)	10 (26.3)	0.736
Number of major bleeds, mean (SD)	0.38 (1.0)	0.2 (0.4)	0.45 (1.2)	0.271
Pre-Hemlibra® period				
Any bleed, n (%)	12 (22.6)	4 (26.7)	8 (21.1)	0.722
Number of bleeds, mean (SD)	1.0 (3.2)	1.7 (3.7)	0.7 (2.9)	0.378
Number of major bleeds, mean (SD)	0.07 (0.27)	0.07 (0.26)	0.08 (0.27)	0.879
Hemarthrosis, mean (SD)	0.04 (0.19)	0.0 (0.0)	0.05 (0.23)	0.16
Joint pain, mean (SD)	0.91 (3.0)	1.6 (3.5)	0.6 (2.8)	0.348
Effusion, mean (SD)	0.02 (0.14)	0.07 (0.26)	0.0 (0.0)	0.334
Hemorrhage, mean (SD)	0.02 (0.14)	0.0 (0.0)	0.03 (0.16)	0.324
Post-Hemlibra® period				
Any bleed, n (%)	19 (35.8)	6 (40.0)	13 (34.2)	0.938
Number of bleeds, mean (SD)	1.5 (3.6)	1.6 (3.9)	1.4 (3.5)	0.897
Number of major bleeds, mean (SD)	0.3 (1.0)	0.1 (0.3)	0.4 (1.2)	0.278
Hemarthrosis, mean (SD)	0.2 (0.85)	0.0 (0.0)	0.24 (1.0)	0.152
Joint pain, mean (SD)	1.2 (3.3)	1.5 (4.0)	1.1 (3.1)	0.737
Effusion, mean (SD)	0.04 (0.19)	0.0 (0.0)	0.05 (0.23)	0.16
Hemorrhage, mean (SD)	0.09 (0.35)	0.13 (0.35)	0.08 (0.36)	0.618

SD: Standard Deviation; Q1: first quartile; Q3: third quartile

Table 6: Annualized bleeding rates by factor use and period

Variable	Overall	No Factor	Factor	P-Value
Total Person Years Observed	138. 2	34.5	103.6	
Total Person Years Observed pre-Hemlibra®	46.4	12.6	33.8	
Total Person Years Observed post-Hemlibra®	91.7	21.9	69.8	
Total Bleeds	131	49	82	
ABR	0.95 (0.79-1.12)	1.42 (1.05-1.87)	0.79 (0.63-0.98)	
IRD		-0.627 (-1.00, -0.252)		0.0011
IRR		0.558 (0.387-0.812)		0.0017
Total bleeds pre-Hemlibra®	52	25	27	
ABR	1.12 (0.84-1.47)	1.98 (1.28-2.93)	0.8 (0.53-1.16)	
IRD		-1.19 (-1.87, -0.5)		0.0007
IRR		0.4 (0.22-0.72)		0.0014
Total bleeds post-Hemlibra®	79	24	55	
ABR	0.86 (0.68-1.07)	1.09 (0.7-1.63)	0.79 (0.59-1.03)	
IRD		-0.3 (-0.75 - 0.14)		0.1794
IRR		0.72 (0.44-1.22)		0.1878

ABR: Annualized bleeding rate; IRD: Incidence rate difference; IRR: Incidence rate ratio

Table 7: Annualized bleeding rates by factor type utilized

Variable	Overall	EHL	SHL	p-value
Total Person Years Observed	103.6	31.0	72.6	
Total Person Years Observed post-Hemlibra®	69.8	23.6	46.1	
Total Bleeds	82	10	72	
ABR	0.79 (0.63-0.98)	0.32 (0.15-0.59)	0.99 (0.78 - 1.25)	
IRD		0.67 (0.29-1.04)		0.0005
IRR		3.07 (1.58-6.68)		0.0002
Total bleeds post-Hemlibra®	55	8	47	
ABR	0.79 (0.59-1.03)	0.34 (0.15-0.67)	1.02 (0.75-1.36)	
IRD		0.68 (0.24-1.12)		0.0025
IRR		3.01 (1.41-7.37)		0.0014

ABR: Annualized bleeding rate; IRD: Incidence rate difference; IRR: Incidence rate ratio

Conclusions

- When prescribed Hemlibra®, most members filled a factor product (more filled SHL products than EHL products) and had low ABR
- We observed a higher ABR in those who filled an SHL product versus an EHL product, however the sample size is a limitation of this study as well as other underlying confounders

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