Comparison of Extended to Standard Half-life Factor VIII Therapy in Patients with Hemophilia A on Prophylactic Treatment: A Retrospective Study to Evaluate the Efficacy, Safety, Cost, and Utilization of Treatment

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BACKGROUND

Hemophilia A is a genetic bleeding disorder caused by a deficiency in factor VIII (FVIII). FVIII maintains bleeding homeostasis within the body through its downstream effects on the intrinsic clotting mechanism. The extent of the disease – either mild, moderate, or severe – depends on the amount of available FVIII in the blood. Patients with severe disease (FVIII levels <1%) experience bleeds into joints and muscles which may lead to long-term complications such as pain, joint damage, or joint replacements.[1]

Treatment of hemophilia A involves replacing FVIII through either on-demand or prophylactic infusion therapy. While on-demand treatment is infused at the time of a bleed to stop the event, prophylactic therapy is given on a routine basis as prevention.[1] Prophylactic therapy is utilized in those with severe disease and is recommended by the Medical and Scientific Advisory Council to maintain FVIII levels above 1%, reducing bleeds and joint damage.[2]

FVIII products are either purified concentrates of human plasma (plasma-derived) or genetically engineered using animal or human proteins (recombinant). Standard half-life (SHL) FVIII therapies must be infused three to four times a week, having a great impact on patient quality of life. Improved technology such as PEGylation and fragment-crystallization (Fc) immunoglobulin protein fusion introduced FVIII products with a half-life of 1.5 to 1.8 times that of standard therapies. These extended half-life (EHL) products maintain FVIII levels with an infusion frequency of once to twice weekly.[3]

While indirect comparisons exist between clinical trial data of standard and extended therapies, there is limited real-world patient data directly comparing the outcomes of these products.[4]

OBJECTIVES

To conduct a retrospective analysis comparing the efficacy, safety, cost, and factor utilization, of patients with hemophilia A taking an FDA approved EHL or SHL FVIII product for prophylactic therapy.

METHODS

AllianceRx Walgreens Prime specialty pharmacy records of patients taking an FDA approved SHL or EHL FVIII product for the prophylactic treatment of hemophilia A were retrospectively reviewed from January 1, 2017 to December 31, 2018. Data was collected from pharmacy dispensing software, clinical patient management applications, and chart notes provided from Hemophilia Treatment Centers (HTCs), doctor's offices, and/or home infusion nurses. Data included demographic information, patient reported bleed history, missed work or school, pain, hospitalizations, factor utilization, and cost of treatment. Patients were excluded if they were being treated for an inhibitor with immune tolerance therapy (ITT), emicizumab-kxwh, or recombinant factor VIIa. A secondary analysis was also done to compare the individual EHL products, Eloctate® and Adynovate®, to SHL products. Mann-Whitney and independent t-test statistical data analysis were completed utilizing SPSS®. Study approval was obtained from the Duquesne University Institutional Review Board.

REFERENCES

1. Hemophilia A. National Hemophilia Foundation. https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed November 11, 2018.
2. National Hemophilia Foundation. MASAC Recommendation Concerning Prophylaxis. https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendation-Concerning-Prophylaxis. Published February 28, 2016. Accessed November 11, 2018.
3. Lambert T, Benson G, et al. Practical aspects of extended half-life products for the treatment of hemophilia. Ther Adv Hematol. 2018; 9: 295-308.
4. Iorio A, Krishnan S, et al. Indirect comparisons of efficacy and weekly factor consumption during continuous prophylaxis with recombinant factor VIII Fc fusion protein and convention recombinant factor VIII products. Hemophilia. 2017; 23: 408-416.

All researchers have no conflicts of interest to disclose. For more information, please contact: rich.t.miller@alliancerxwp.com
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RESULTS

Table 1: Patient Demographics

	SHL (%)	EHL (%)
Gender		
Male	59 (100)	50 (100)
Age	24.4	25
Range	1 - 65	3 - 58
≤18	26 (44.1)	16 (32)
>18	33 (55.9)	34 (68)
Severity		
Severe	53 (89.8)	43 (86)
Moderate	4 (6.8)	4 (8)
Unknown	2 (3.4)	3 (6)
Access		
Butterfly	48 (81.4)	44 (88)
Port	11 (18.6)	6 (12)
History of Inhibitors	3 (5.1)	0
Target joints	21 (35.6)	20 (40)

Figure 1: Patient Medications

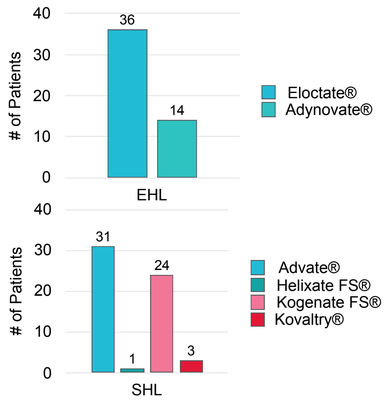


Figure 2: Dosing Regimens

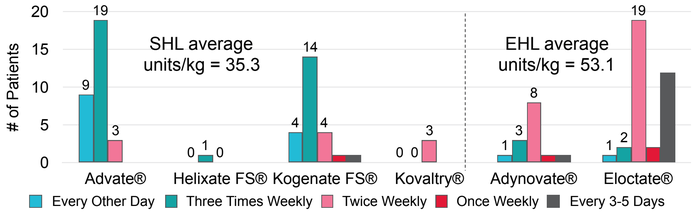


Table 2: Quality of Life Outcomes

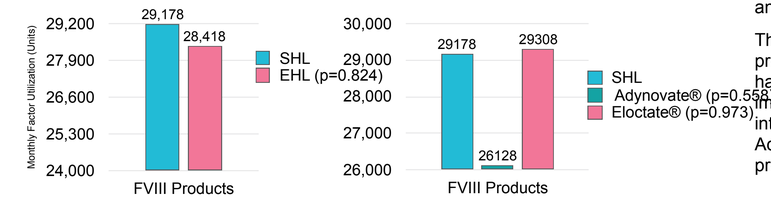
	SHL (%)	EHL (%)	
Pain	22 (37.3)	18 (36)	p=0.890
Missed school/work	10 (17)	8 (16)	p=0.895
Hospitalizations	7 (11.9)	7 (14)	p=0.741
Mobility accessories	8 (13.4)	3 (6)	p=0.194

Table 3: Monthly AWP ($)

	AWP ($)	
SHL	55,183	
EHL	71,191	p=0.035
Adynovate®	63,583	p=0.414
Eloctate®	74,149	p=0.028

*AWP = average wholesale price

Figure 3: Monthly Factor Utilization (Units)



RESULTS CONTINUED

Figure 4: Annualized Bleed Rate (ABR)

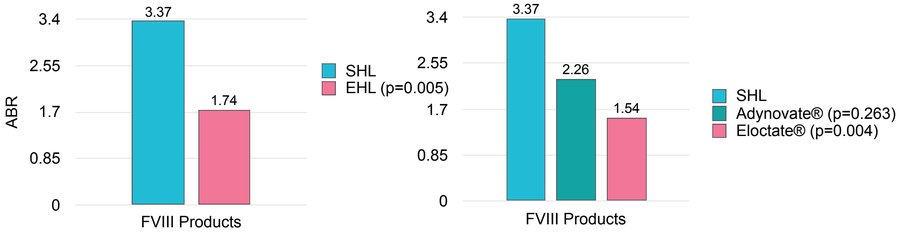


Table 4: Insurance and Copay Data

	# of Patients	Monthly Insurance Copay ($)	Monthly Patient Copay ($)
EHL - Total Patients	50	355.56 (0 - 1,738.67)	27.49 (0 – 519.32)
SHL - Total Patients	59	357.89 (0 - 2,300)	80.13 (0 - 1,225)

*Insurance copay is the patient responsibility prior to secondary coverage (government, manufacturer copay cards, etc.). Patient copay is the final patient cost.

DISCUSSION / CONCLUSIONS

A total of 386 patients taking an SHL or EHL product were identified as eligible. Of the 254 patients taking a SHL product, 56 were excluded due to contractual limitations on including insured members in research, 130 due to a fill count of a less than 6 months, 5 with inhibitors, and 4 on-demand patients. Of the 132 EHL patients, 19 were excluded due to contractual limitations on including insured members in research and 63 due to a fill count of less than 6 months. This resulted in a final patient count of 109 (59 SHL, 50 EHL).

Patient demographics were similar between SHL and EHL regimens including no difference in average age (p=0.831) and a similar number of patients with severe hemophilia, butterfly access, and target joints. More patients taking an SHL product had a history of inhibitors. The dosing regimens for the majority of patients in both groups fell within manufacturer recommendations (SHL - 72.9%, EHL - 78%). (Figure 2)

Patients on an EHL regimen had a statistically significant lower annualized bleed rate (ABR) than those on a SHL regimen (p=0.005). This decrease in ABR was also found when comparing Eloctate® to SHL products (p=0.004), however not when comparing Adynovate® to SHL products (p=0.263). (Figure 4) There was also no statistically significant difference in monthly factor utilization between the two groups, with EHL regimens utilizing slightly less factor than SHL regimens (p=0.824). (Figure 3) Additionally, this study found no difference in quality of life outcomes between the groups. (Table 2)

Financially, EHL products were statistically more costly than SHL products (p=0.035). Interestingly, Adynovate® did not show a statistically significant difference in AWP when compared to SHL products (p=0.414). (Table 3) Due to the high AWP for these medication, a secondary analysis was done to determine the differences in monthly insurance and patient copays. Monthly patient copays after secondary coverage (most common being manufacturer copay cards) were similar between EHL and SHL, with patients paying slightly less for EHL products (p=0.134). (Table 4) While these products are expensive, this analysis shows that patients are only paying a small fraction of the list price.

This study adds valuable information to the treatment of hemophilia. From a patient and payer view, EHL products provide greater control over bleeds, decreasing the number that a patient experiences by almost half. However, this comes at a cost for payers, particularly since quality of life outcomes were not improved. This study was unable to assess the non-drug costs of treatment, allowing for further research into this potential cost savings. While there was no difference in patient-reported outcomes between Adynovate® and Eloctate®, the differences in ABR and AWP when each were compared separately to SHL products emphasize the importance of individualized treatment, patient monitoring, and drug selection.