Comparison of extended to standard half-life recombinant factor VIII therapy in patients with hemophilia A on prophylactic therapy

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ABSTRACT

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 cascade. The extent of the disease – mild, moderate or severe – depends on the amount of available FVIII in the blood. Patients with severe disease (FVIII levels <1%) experience spontaneous bleeds into the joints or muscles causing pain, inflammation and discomfort. Left untreated, this may lead to long-term complications such as joint damage, chronic pain or joint replacements.

Treatment of hemophilia A involves replacing FVIII through either on-demand or prophylactic infusion of antihemophilic FVIII products. On-demand treatment involves infusing the FVIII product at the time of a bleed to stop the event. Prophylactic therapy is the routine replacement of FVIII to prevent bleeds from occurring. The Medical and Scientific Advisory Council recommends the use of a prophylactic regimen, particularly in patients with severe disease, to maintain FVIII levels above 1%. This has been shown to reduce bleeds and joint damage over on-demand treatment, and may have the potential to improve health outcomes.

Prophylactic treatment with standard half-life (SHL) rFVIII products are typically infused three to four times a week due to an approximate half-life of 8-12 hours. This can have a great impact on patient quality of life, adherence to therapy and treatment outcomes. Improved technology such as PEGylation and fragment-crystallization (Fc) immunoglobulin protein fusion introduced rFVIII products with a half-life of 1.5 to 1.8 times that of standard therapies. These extended half-life (EHL) rFVIII products maintain FVIII levels similar to SHL rFVIII products with an infusion frequency of once to twice weekly. This may present an opportunity for patients to achieve the clinical benefit of prophylactic treatment without the potential limitations and burden of treatment with SHL rFVIII products.

EHL rFVIII products have demonstrated efficacy for prophylactic therapy by reducing bleed rates in patients with hemophilia A, particularly in many clinical trials. However, the benefit of using EHL over SHL rFVIII products for prophylactic therapy has not been universally established, and there is no recommendation for one product over the other. A few studies have indirectly compared EHL and SHL rFVIII products or have looked at patient outcomes and bleed rates after switching from SHL to EHL rFVIII products. Limited studies currently exist that directly compare treatment outcomes between EHL and SHL rFVIII products in a real-world patient population.

Aims: The primary objective of this study was to compare annualized bleed rates (ABRs) of hemophilia A patients on prophylactic therapy prescribed either EHL or SHL antihemophilic rFVIII products. Secondary objectives were to compare quality of life outcomes (pain, missed school or work, use of mobility accessories, and hospitalizations), monthly factor utilization, cost, monthly insurance coverage amounts and monthly patient copays.

Methods: Specialty pharmacy records of patients taking an FDA approved SHL or EHL rFVIII product for the prophylactic treatment of hemophilia A were retrospectively reviewed from 1 January 2017 to 31 December 2018. Data was collected from pharmacy dispensing software, therapy management programs, and chart notes provided from Hemophilia Treatment Centers (HTCs), doctors’ 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), coagulation factor VIIa (recombinant) (NovoSeven™), anti-inhibitor coagulant complex (Feiba®) or emicizumab-kxwh (Hemlibra®). A secondary analysis was also done to compare the individual EHL rFVIII products to the SHL group. Mann–Whitney and independent t-test statistical data analysis was completed utilizing SPSS software®. Study approval was obtained from the Duquesne University Institutional Review Board.
**Results:** Patients prescribed EHL rFVIII products had a statistically significant lower ABR than those prescribed SHL rFVIII products ($p = .005$). No statistically significant difference was found in monthly factor utilization ($p = .824$) or quality of life outcomes between products. EHL rFVIII products were significantly more costly than SHL rFVIII products ($p = .035$). Monthly insurance coverage amounts and patient copays were similar between the groups.

**Conclusion:** Patients prescribed EHL rFVIII products had a statistically significant lower ABR than those prescribed SHL rFVIII products ($p = .005$). No statistically significant difference was found in monthly factor utilization ($p = .824$) or quality of life outcomes between products. EHL rFVIII products were significantly more costly than SHL rFVIII products ($p = .035$). Monthly insurance coverage amounts and patient copays were similar between the groups.

**KEYWORDS**
Hemophilia; extended half-life; recombinant; factor VIII; prophylaxis

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