Economic Impact of Treating Severe Hemophilia A Patients with Plasma-Derived Factor-VIII/VWF vs. Recombinant Factor-VIII in the United States
Ken O’Day, PhD, MPA1, M. Chris Runken, PharmD2, Kelile Meyer, PharmD, MPH1, Jeffrey Spears, PharmD2
1Xcenda LLC, Palm Harbor, FL, USA; 2Grifols, Research Triangle Park, NC, USA

BACKGROUND/OBJECTIVE
- The development of antibodies (inhibitors) to factor-VIII (FVIII) therapy is a common and the most serious complication of FVIII treatment in patients with hemophilia A.1
- The development of inhibitors in patients with severe hemophilia has resulted in increased morbidity and substantial economic burden associated with immune tolerance induction (ITI) to eradicate inhibitors,2,4
- The frequency of inhibitors in Plasma-Produced Exposed Donors (SPPE) study found higher inhibitor rates in previously untreated patients (PUPs) treated with conventional recombinant FVIII (rFVIII) than those treated with plasma-derived FVIII with von Willebrand factor (pdFVIII/VWF).5
- The objective of this study was to quantify the economic impact of treating PUPs with pdFVIII/VWF versus rFVIII.

METHODS/STUDY DESIGN
- An Excel-based cost-analysis was developed from the perspective of a US healthcare payer over a 3-year time horizon. The analysis utilized a cohort approach to model treatment and outcomes over a monthly cycle to quantify anti-hemophilic agent utilization and costs.
- In the analysis, 1,000 PUPs initiate prophylactic or on-demand treatment with FVIII or pdFVIII/VWF. Patients who develop high-titer inhibitors are treated with immune tolerance induction. Patients who develop low-titer inhibitors, and those who do not develop inhibitors, continue FVIII treatment. Patients who are successfully treated with ITI return to FVIII treatment, while unsuccessfully treated patients receive bypassing agents. (Figure 1)
- Costs captured in the model include pharmacy costs for FVIII treatment and bypassing agents, as well as hospitalization costs for on-demand patients with serious bleeds. It was assumed that patients receiving rFVIII prophylaxis do not have two.
- A one-way sensitivity analysis was conducted to quantify the impact of parameter uncertainty on the total estimated costs (savings) by varying the model inputs by ±25% of the base case value.

Patient Assumptions
- Patients were assumed to be 12 months old at the start of treatment. Annual patient weight was obtained from CDC annual growth charts and monthly weights were interpolated.
- The number of PUPs with severe hemophilia A who would initiate FVIII treatment annually was estimated based on data from the National Center for Health Statistics and National Hemophilia Foundation.2

Factor VIII Treatment Assumptions
- It was assumed that 60% of PUPs were treated with FVIII prophylaxis and 25% received on-demand FVIII.
- Patients treated with FVIII prophylaxis received 3 infusions of 60 IU/kg per week.6
- Patients treated with on-demand FVIII received an annualized bleed rate of 10.0.7 Of those patients, 15% were severe bleeds requiring hospitalization.6
- Patients with severe bleeds received an average of 1.5 infusions of 60 IU/kg and patients with moderate/low bleeds received an average of 1 infusion of 25 IU/kg to stop the bleed.6
- Patients successfully treated with ITI were assumed to receive FVIII prophylaxis consisting of 3 infusions of 40 IU/kg per week.6

Inhibitors, Immune Tolerance Induction, and Bypassing Agents
- Rates of high-titer inhibitor development of 16.5% in pdFVIII/VWF patients and 26.4% in rFVIII patients were based on findings from the SPPE study, a randomized open-label trial comparing the incidence of inhibitors in PUPs with severe hemophilia A.7
- It was assumed in the model that patients’ inhibitors developed over a period of 6 months after initiation of treatment (approximately 50 exposure days) and that patients developing high-titer inhibitors initiated ITI 3 months after inhibitor diagnosis.
- Half of patients received low-dose ITI and half received high-dose ITI.1
- Patients with high-titer inhibitors receiving bypassing agents (FF VIIa or pdPC) prophylactically to prevent bleeds or on-demand to treat bleeds. It was assumed that prior to initiating ITI 50% of patients received prophylactic, during ITI all patients received prophylactic, and after unsuccessful treatment with ITI all patients received prophylactic. (Table 2)
- Costs
- Unit costs for anti-hemophilic agents (FVIII products and bypassing agents) were obtained from 2017 Red Book.13 (Table 3)

Per Results
- Total 3-year costs were $245,000 per pdFVIII/VWF patient and $242,500 per FVIII patient, representing a total savings of $2,625 per patient for an average annual savings of $84,850. (Table 4)

CONCLUSIONS
- Utilizing data from the SIPPET study showing that rates of high-titer inhibitors are higher in patients treated with pdFVIII than patients treated with rFVIII, this analysis found that initiating FVIII treatment in PUPs with severe hemophilia A with pdFVIII/VWF has the potential to result in significant cost savings to US healthcare payers, amounting to a reduction in costs of 25%.
- Further research is warranted to corroborate these findings in real-world analyses, and to quantify the potential indirect health economic benefits of pdFVIII/VWF.

LIMITATIONS
- This analysis is limited to reflect the economic burden from the US healthcare payer perspective. The potentially high indirect costs, such as burden of care and missed school or work, are not included in the model.
- The results of this model are estimates based on a set of treatment strategies for patients with severe hemophilia and are not applicable to patients with other hematologic disorders.
- The model does not include costs associated with surgery (e.g., total joint replacement) and the costs of FVIII for surgical interventions.