P-W-065

Comparing the Cost-effectiveness of aPCC and rFVIIa Prophylaxis Regimen in the Management of Hemophilia Patients with Inhibitors in the US

Oladapo AO[1], Novack A[1], Epstein JD[1]

[1]Baxter Healthcare Corporation, Westlake Village, CA, USA

Introduction

- Three prospective clinical trials has established the benefit of prophylaxis with bypassing agents for hemophilia patients with inhibitors[1-3]
- Prophylaxis with bypassing agents has been shown to:
  - Significantly reduce bleeding frequency[1-3] and prevent the development of new target joints[1]
  - Significantly reduce pain, improve health related quality of life and productivity[1,4-6]
- A recent publication by the Medical and Scientific Advisory Council (MASAC) recommended that patients with inhibitors be considered for prophylaxis treatment with bypassing agents[7]
- Given limited resources, it is important to assess the incremental cost-effectiveness of prophylaxis treatment with the available bypassing agents

Objective

To model and compare the cost-effectiveness of aPCC versus rFVIIa prophylaxis over a one year period

Methods

- A literature-based, cost-effectiveness model was developed
- All clinical inputs were derived from the FEIBA NF and rFVIIa trials[1,3] (Table 1)
- Model assumed 100% compliance to prophylaxis regimen for 1 year
- Model assumed all patients had on-demand annual bleed rate of 28.7 (median bleed rate from the FEIBA NF study)[1] and bleeding was reduced by the percentage reported in the clinical trials
- Cost analysis was from a US payer perspective and was limited to bypassing agent costs only
- The cost of the prophylaxis and cost for breakthrough bleeds were included in the analysis
- Bypassing agent costs was based on the 2013 wholesale acquisition cost (WAC) obtained from the Redbook (Table 1)[8]
- The incremental cost-effectiveness ratio (ICER) was calculated as follows:
  - **ICER** = (Cost of aPCC prophylaxis – Cost of rFVIIa prophylaxis) / (Number of bleeds avoided with aPCC prophylaxis – Number of bleeds avoided with rFVIIa prophylaxis)

Sensitivity Analysis

- One-way sensitivity analyses were performed to determine model robustness by varying key inputs by 25% in the conservative direction
- Threshold sensitivity analyses were also conducted
- Additional sensitivity analysis was conducted using inputs from the Pro-FEIBA study[2]

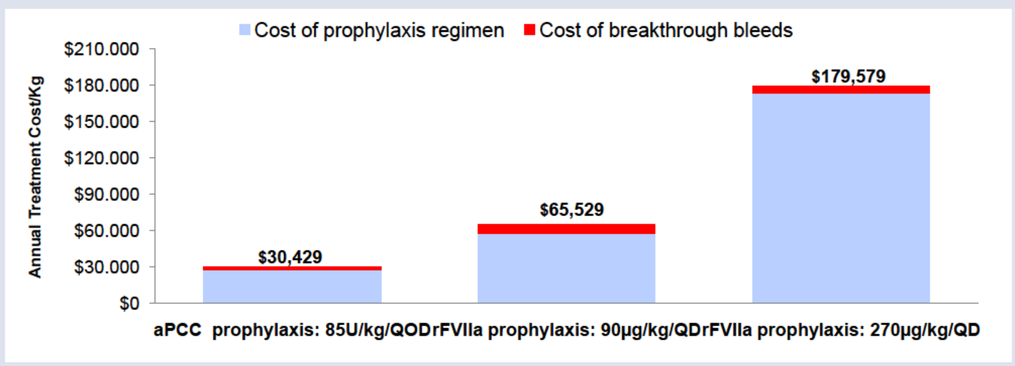
Table 1: Model Input

	aPCC	rFVIIa	
On-demand annual bleed rate‡ [1]	28.7	28.7	28.7
Prophylaxis regimen[1,3]	85 U/kg every other day	90 µg/kg daily	270 µg/kg daily
% bleed reduction on prophylaxis[1,3]	72.5%	45%	59%
Number of breakthrough bleeds** [1,3]	7.9	15.8	11.8
Dose to stop breakthrough bleeds†	85 U/kg x 2	90 µg/kg x 3	90 µg/kg x 3
Cost per unit[8]	$1.81/U	$1.77/µg	$1.77/µg

QOD = Every other day; QD = Every day. ‡Median annual bleed rate from the PROOF study. **Calculated as [(1- % bleed reduction on prophylaxis) x on-demand annual bleed rate]. †The mean [median] number of infusions per bleeding episode reported in the FENOC[9] trial were 1.3[1] and 2.4[2] for aPCC and rFVIIa, respectively. However, we chose to be conservative inputting 2 infusions for aPCC and 3 infusions for rFVIIa

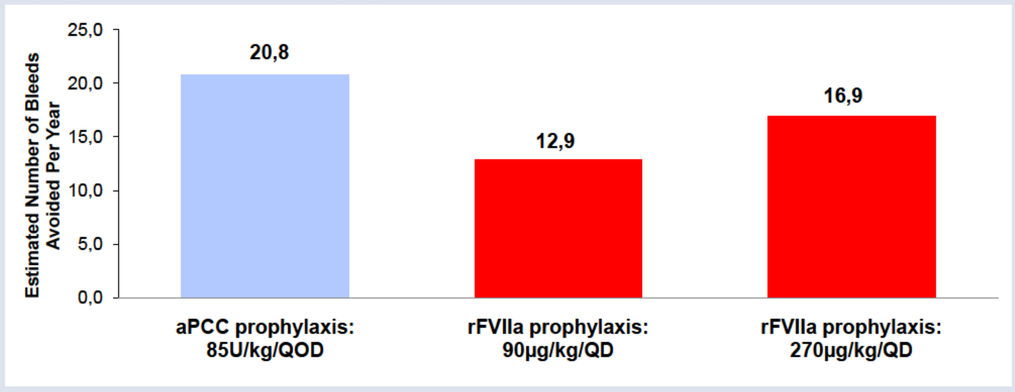
Results

Figure 1: Annual Treatment Cost/kg of aPCC Prophylaxis vs. rFVIIa Prophylaxis



- The estimated annual treatment cost/kg with aPCC prophylaxis was **53.6%** and **83.1%** lower compared to rFVIIa prophylaxis dosed using 90 µg/kg and 270 µg/kg daily, respectively
- For every one patient prescribed 90 or 270ug/kg/day rFVIIa prophylaxis, 2 or 6 patients could be prescribed aPCC prophylaxis for the same cost, respectively

Figure 2: Annual Number of Bleeding Episodes Avoided with aPCC Prophylaxis vs. rFVIIa Prophylaxis



- The estimated number of bleeding episodes avoided per year with aPCC prophylaxis was **38.0%** and **18.8%** higher compared to rFVIIa prophylaxis dosed using 90 µg/kg and 270 µg/kg daily, respectively

ICER: aPCC Prophylaxis Regimen was the Dominant Strategy (less costly and more effective) Compared to rFVIIa Prophylaxis Regimens

- aPCC vs. rFVIIa (90 µg/kg/Day)
  - ICER = $30,429 – $65,529 / (20.8–12.9) = –$4,443/kg/bleed avoided
- aPCC vs. rFVIIa (270 µg/kg/Day)
  - ICER = $30,429 – $179,579 / (20.8 – 16.9) = –$38,244/kg/bleed avoided

Results (Continued)

Sensitivity Analyses

Table 2: One-way Sensitivity Analyses (Cost Comparison Only)

Parameter	Base case value used in the model	Base case value varied by 25%	Overall cost/kg of prophylaxis aPCC vs. rFVIIa 90µg/kg	Overall cost/kg of prophylaxis aPCC vs. rFVIIa 270µg/kg
On-demand bleed rate†	28.7	21.5 35.9	Lower for aPCC	Lower for aPCC
aPCC Price	$1.81/U	$2.26/U	Lower for aPCC	Lower for aPCC
aPCC efficacy	72.5%	54.4%	Lower for aPCC	Lower for aPCC
aPCC dose for breakthrough bleeds	85U/kg x 2	85U/kg x 3**	Lower for aPCC	Lower for aPCC
rFVIIa Price	$1.77/µg	$1.33/µg	Lower for aPCC	Lower for aPCC
rFVIIa efficacy	45% (90 µg/kg) 59% (270 µg/kg)	56% (90 µg/kg) 73.8% (270 µg/kg)	Lower for aPCC	Lower for aPCC
rFVIIa dose for breakthrough bleeds	90 µg/kg x 3	90 µg/kg x 1**	Lower for aPCC	Lower for aPCC

Table 3: One-way Sensitivity Analyses (Cost and Effectiveness Comparison)

Parameter	Base case value used in the model	Base case value varied by 25%	ICER aPCC vs. rFVIIa 90 µg/kg	ICER aPCC vs. rFVIIa 270 µg/kg
On-demand bleed rate†	28.7	21.5 35.9	<0	<0
aPCC Price	$1.81/U	$2.26/U	<0	<0
aPCC efficacy	72.5%	54.4%	<0	$111,764
aPCC dose for breakthrough bleeds	85U/kg x 1	85U/kg x 3**	<0	<0
rFVIIa Price	$1.77/µg	$1.33/µg	<0	<0
rFVIIa efficacy	45% (90 µg/kg) 59% (270 µg/kg)	56% (90 µg/kg) 73.8% (270 µg/kg)	<0	$394,318
rFVIIa dose for breakthrough bleeds	90 µg/kg x 2	90 µg/kg x 1**	<0	<0

ICER < 0 indicates that aPCC is a more effective and less costly alternative. ICER > 0 indicates the annual cost/kg body weight for each additional bleed avoided when rFVIIa is used instead of aPCC
**** In the one-way sensitivity analysis, breakthrough bleeds were assumed to be treated with 3 doses of 85 U/kg of aPCC, while for rFVIIa, a single dose of 90 µg/kg was assumed. Results remained robust when on-demand bleed rate was reduced by ≥50% (i.e. ≤14.4 bleeds per year).**

- aPCC was the dominant strategy in all of the scenarios except for when:
  - We assumed a 25% reduction in the efficacy of aPCC. Here, using rFVIIa 270 µg/kg prophylaxis regimen instead of aPCC would cost $111,764/kg per additional bleed avoided
  - We assumed a 25% increase in the efficacy of rFVIIa 270 µg/kg prophylaxis regimen. Here, using rFVIIa instead of aPCC would cost $394,318/kg per additional bleed avoided
- Results from the threshold analysis indicated that:
  - aPCC prophylaxis remained less expensive even when the efficacy of rFVIIa prophylaxis was increased to 100% for both rFVIIa prophylaxis regimens
  - rFVIIa prophylaxis would only be less expensive if the unit cost of rFVIIa was reduced by greater than 53% and 83% for the 90 µg/kg and 270 µg/kg rFVIIa prophylaxis regimens, respectively
- Results remained robust when FEIBA NF[1] study inputs were replaced with those of Pro-FEIBA[2]

Limitations

- Model inputs were obtained from clinical trials that did not directly compare the bypassing agents compared in the model.
  - Model inputs were varied using sensitivity analysis and study results were robust
- The model only included the direct costs of the bypassing agents in its cost analysis. Additional direct (i.e. hospitalization etc.) and indirect costs were not accounted for.
  - Bypassing agent costs have been reported to account for a significant proportion of the cost of care of inhibitor patients[10]
- Model assumed a 1-year time frame
  - Model did not account for long-term benefits of prophylaxis

Conclusion

- **aPCC prophylaxis regimen of 85 U/kg given every other day was cost effective compared with rFVIIa prophylaxis regimen of 90 µg/kg or 270 µg/kg administered daily**

References

1. Antunes SV, Tangada S, Stasyshyn O, et al. Randomized comparison of prophylaxis and on-demand regimens with FEIBA NF in the treatment of haemophilia A and B with inhibitors. *Haemophilia* 2013. doi: 10.1111/hae.12246. [Epub ahead of print]
2. Leissinger C, Gringeri A, Antmen B et al. Anti-inhibitor coagulant complex prophylaxis in hemophilia with inhibitors. *N Engl J Med* 2011;365:1684-1692.
3. Konkle BA, Ebbesen LS, Erhardtsen E, et al. Pandomized, prospective clinical trial of recombinant factor VIIa for secondary prophylaxis in hemophilia patients with inhibitors. *J Thromb Haemost* 2007;5:1904-1913
4. Gringeri A, Leissinger C, Cortesi PA, et al. Health-related quality of life in patients with haemophilia and inhibitors on prophylaxis with anti-inhibitor complex concentrate: results from the Pro-FEIBA study. *Haemophilia* 2013;19(5):736-743.
5. Hoots WK, Ebbesen LS, Konkle BA, et al. Secondary prophylaxis with recombinant activated factor VII improves health-related quality of life of haemophilia patients with inhibitors. *Haemophilia* 2008;14(3):466-475.
6. Stasyshyn O, Antunes, S, Mamonov V et al. Prophylaxis with anti-inhibitor coagulant complex improves health-related quality of life in haemophilia patients with inhibitors: results from FEIBA NF Prophylaxis Study. *Haemophilia* 2014. doi: 10.1111/hae.12390. [E-pub ahead of print]
7. MASAC Recommendation regarding prophylaxis with bypassing agents in patients with hemophilia and high titer inhibitors. National Hemophilia Foundation. 2013. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac220.pdf. Accessed: Nov. 22, 2013.
8. http://redbook.com/redbook/online. Accessed: October 15, 2013
9. Astermark J, Donfield SM, DiMichele DM, et al. A randomized comparison of bypassing agents in hemophilia complicated by an inhibitor: the FEIBA NovoSeven comparative (FENOC) study. *Blood*, 2007;109(2):546-551.
10. Gringeri A, Mantovani LG, Scalone L, et al. Cost of care and quality of life for patients with hemophilia complicated by inhibitors: the COCIS Study Group. *Blood*, 2003;102(7):2358-2363.

Presented at the WFH 2014 World Congress in Melbourne, Australia • May 11-15, 2014

If you have any additional questions, please feel free to contact Baxter Bioscience Medical Information at medinfo@baxter.com.

Conflicts of interest: All authors are paid employees of Baxter Healthcare

Baxter

WFH2014 65--P-W

Health and Social Economics

Abiola Oladapo

DOI: 10.3252/pso.eu.WFH2014.2014

Poster presented at: WFH 2014 World Congress

PosterSessionOnline.com