Estimating the Potential Cost of a High Dose Immune Tolerance Induction (ITI) Therapy Relative to the Cost of a Combined Therapy of a Low Dose ITI Therapy With Bypassing Agent Prophylaxis

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INTRODUCTION

- The development of inhibitory antibodies to clotting FVIII or FIX remains the most serious complications in the management of patients with hemophilia[1]
- Currently, immune tolerance induction (ITI) is the only approach to eradicate inhibitors and restore normal clinical responses to FVIII[2]
- ITI has been reported to achieve a success rate of 60–90% at FVIII doses ranging from 50 IU/kg/thrice-weekly to 200 IU/kg/daily[3–5]
- Cost associated with ITI treatment remains a major factor which may influence the choice of FVIII regimen
- The International Immune Tolerance Study (I-ITI) demonstrated comparable success rate between low (FVIII: 50 IU/kg/thrice-weekly) and high dose (FVIII: 200 IU/kg/daily) regimens[5]
- However, the high dose ITI regimen resulted in a shorter time-to-treatment success with lower bleeding episodes compared to the low dose regimen[5]
- Bypassing agent prophylaxis has demonstrated the ability to reduce the frequency of bleeding episodes in addition to other clinical and humanistic benefits (i.e. improvement in patient's quality of life and productivity) [6-14]
- The present analysis hypothesized that ITI treatment can be optimized with the inclusion of bypassing agent prophylaxis in a low dose ITI regimen and this may enable cost constrained countries/centers to achieve similar outcomes as with a high dose ITI regimen at a lower or comparable treatment cost

OBJECTIVE

- To estimate the cost of a high dose ITI therapy relative to the cost of a combined therapy of a low dose ITI with BAP

METHODS

- A literature-based cost model was developed for a hypothetical patient
- Model inputs (ITI FVIII regimen, time-to-treatment success, number of bleeding episodes, bypassing agent prophylaxis regimen and efficacy, and dose to treat bleeding episodes) were derived from clinical studies[5,9,13] (*see Table 1 and Table 2*)
- Model assumed similar success rate for both the high and low dose ITI regimens based on the I-ITI study[5]
- Model assumed 100% compliance to bypassing agent prophylaxis regimen and bleeding was reduced by the percentage seen in the respective prophylaxis trials[9,13]
- Cost analysis was from a US third party payer perspective and limited to drug costs
- Drug costs were based on the 2016 wholesale acquisition cost obtained from the Redbook® (*see Table 1 and Table 2*)[15]

METHODS continued

Sensitivity Analysis

- One-way sensitivity analysis was performed to determine model robustness by varying all model inputs by ± 20% in the conservative direction
- Additional sensitivity analyses were done using an aPCC prophylaxis dosing regimen of 85 U per kg thrice weekly with a 62% efficacy[10] and a rFVIIa prophylaxis dosing regimen of 270 mcg per kg per day with a 59% efficacy[13]

Table 1. Model Inputs for the ITI Strategies

	High dose ITI[5]	Low dose ITI[5]
FVIII regimen	200 IU/kg/QD	50 IU/kg/TIW
Time to treatment success, months[a]	4.6	9.2
Average number of bleeds before success is achieved[b]	4.2	9.9
FVIII unit cost[c]	$1.41/IU	$1.41/IU

ITI = Immune tolerance induction; QD = Daily; TIW = Thrice weekly.

[a] Defined as median time from initiation of ITI to achievement of negative titer.

[b] Average number of bleeds from initiation of ITI treatment to achievement of negative titer. Calculated as total bleeding episode s divided by total number of patients during the Phase 1 period of the I-ITI study. The Phase 1 period is the time period from initiation of ITI to achievement of negative titer.

[c] Drug cost was based on the 2016 wholesale acquisition cost obtained from the Redbook® (Accessed January 14, 2016). For FVIII, we estimated the average unit price across plasma-derived and recombinant FVIII products in the US. This did not include the extended half-life product given no evidence of their use in ITI was available as at the time of development of this poster.

Table 2. Model Inputs for Prophylaxis Treatment with Bypassing agents

	aPCC[9]	rFVIIa[13]
BAP regimen	85 U/kg/QOD[c]	90 µg/kg/QD[c]
Bleed reduction, percent	72.5%	45%
Dose to stop bleeding episodes[a]	85 U/kg x 2	90 µg/kg x 3
BA unit cost[b]	$2.14/U	$1.91/µg

BA = Bypassing agent; BAP = Bypassing agent prophylaxis; QD = Daily; QOD = Every other day;

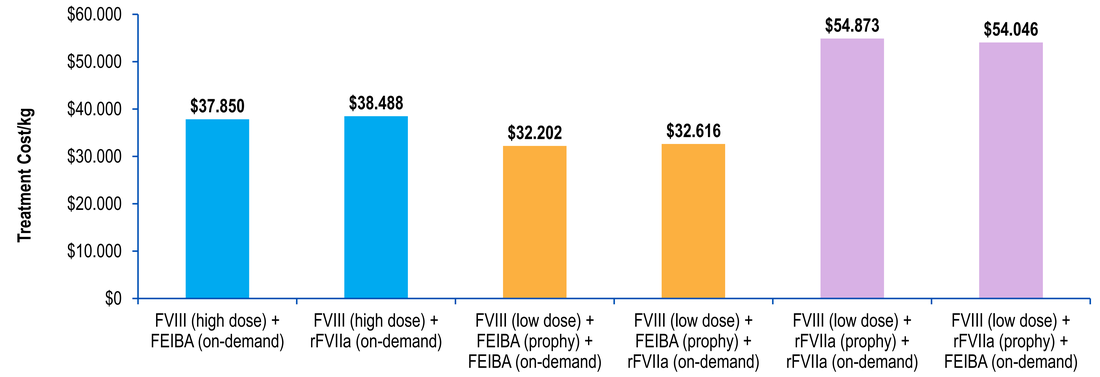
[a] The mean [median] number of infusions reported in the FENOC trial[16] was 1.3[1] and 2.4[2] for aPCC and rFVIIa, respectively. However, we chose to be conservative inputting 2 infusions for aPCC and 3 infusions for rFVIIa. For the sensitivity analysis we increased the number of infusions to 3 for aPCC and reduced the number of infusions to 1 for rFVIIa.

[b] Drug cost was based on the 2016 wholesale acquisition cost obtained from the Redbook®. Accessed Jan.14, 2016.

[c] In the sensitivity analysis, the dosing frequency was also reduced to thrice weekly to match the frequency of administration of the FVIII dosing

RESULTS

Figure 1. Total Treatment Cost/kg of High Dose ITI vs. Low Dose ITI+BAP



ITI = Immune tolerance induction; BAP = Bypassing agent prophylaxis

- **Treatment cost for a low dose ITI regimen with aPCC prophylaxis was 14%–16% lower compared to a high dose ITI regimen.**
- **On the contrary, a low dose ITI regimen with rFVIIa prophylaxis cost 40%–45% higher compared to a high dose ITI regimen**

Sensitivity Analysis

- Results remained robust for all one-way sensitivity analysis except for when the time-to-treatment success was reduced for the high dose ITI or increased for the low dose ITI
- Results also remained robust when using an aPCC prophylaxis dosing regimen of 85 U per kg thrice weekly with a 62% efficacy[10] and a rFVIIa prophylaxis dosing regimen of 270 mcg per kg per day with a 59% efficacy[13]

Limitations

- Model inputs were obtained from clinical trials which may not reflect real world dosing and effectiveness
  - Model inputs were varied conservatively during sensitivity analysis and study results were found to be robust in the majority of the scenarios
- The model only included the cost of hemostatic agents in its cost analysis. Other types of cost (eg, indirect costs) were not accounted for.
- The cost of low dose ITI + bypassing agent prophylaxis may have been overestimated as bypassing agent prophylaxis was assumed to continue until negative titer was achieved. Most guidelines suggest to stop when titers fall below 1-2 BU.[17-18]

CONCLUSION

- A low dose ITI regimen with aPCC prophylaxis may be cost saving compared to a high dose ITI regimen with the potential to reduce morbidity by lowering the risk for bleeding episodes and providing other clinical and humanistic benefits.

DISCLOSURES

* Author formerly an employee of Baxalta US Inc, now part of Shire.

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