Estimating the Potential Cost of a High Dose Immune Tolerance Induction (ITI) Therapy Relative to the Cost 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.
- Currently, immune tolerance induction (ITI) is the only approach to eradicate inhibitors and restore normal clinical responses to FVIII.
- ITI has been reported to achieve a success rate of 60–80% at FVIII doses ranging from 50 IU/kg/TIW to 200 IU/kg/TIW.
- Cost associated with ITI treatment remains a major factor which may influence the choice of ITI regimen.
- The International Immune Tolerance Study (IITT) demonstrated comparable success rate between low (FVIII: 50 IU/kg/TIW) and high dose (FVIII: 200 IU/kg/TIW) regimens.
- However, the high dose ITI regimen resulted in a shorter time-to-treatment success with lower bleeding episodes compared to the low dose regimens.
- Bypassing agent prophylaxis has demonstrated the ability to reduce the frequency of bleeding episodes in addition to other clinical and humanitarian benefits (ie, improvement in patient’s quality of life and productivity).
- The present analysis hypothesized that ITI treatment can be optimized with the addition of prophylaxis with a low dose ITI regimen and this may enable cost constrained countries/countries 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 combination 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 (5-8) (see Table 1 and Table 2).
- Model assumed similar success rate for both the high and low dose ITI regimens based on the IITT study.
- Model assumed 100% compliance to bypassing agent prophylaxis regimen and bleeding was reduced by the percentage in the respective prophylaxis regimen.
- 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).

RESULTS

Sensitivity Analysis
- One-way sensitivity analysis was performed to determine model robustness by varying all model inputs by 25% in the conservative direction.
- Additional sensitivity analyses were done using an aPCC prophylaxis dosing regimen of 85 IU/kg TIV weekly with a 62% efficacy and a rFVIIa prophylaxis dosing regimen of 270 mcg per kg per day with a 59% efficacy.

Table 1. Model Inputs for the ITI Strategies

<table>
<thead>
<tr>
<th>High dose ITI</th>
<th>Low dose ITI</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVIII (high dose) + FEIBA (on-demand)</td>
<td>$37,850</td>
</tr>
<tr>
<td>FVIII (high dose) + rFVIIa (on-demand)</td>
<td>$38,468</td>
</tr>
<tr>
<td>FVIII (low dose) + FEIBA (prophylaxis)</td>
<td>$32,202</td>
</tr>
<tr>
<td>FVIII (low dose) + rFVIIa (prophylaxis)</td>
<td>$32,616</td>
</tr>
</tbody>
</table>

ITI = Immune tolerance induction; BAP = Bypassing agent prophylaxis

DISCUSSIONS
- 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 humanitarian benefits.

REFERENCES

2. Shire, Now part of Shire.