Interim results of a Phase IIIb safety and efficacy extension study of a recombinant fusion protein linking coagulation factor IX with albumin (rIX-FP) in patients with hemophilia B

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Introduction

• rIX-FP is a fusion protein genetically linking recombinant human coagulation Factor IX with recombinant human albumin that has an improved pharmacokinetic profile, thus allowing less frequent dosing.

• Two Phase III trials demonstrated the safety and efficacy of rIX-FP in previously treated patients (PTPs) with severe hemophilia B (FIX activity ≤ 2%) in those aged 12–65 years (study 3001, NCT01496274) and in those <12 years (study 3002, NCT01662031).

• To investigate the long-term safety and efficacy of rIX-FP in patients with severe hemophilia B in a Phase IIIb, open-label, multicenter, extension study (NCT02053792).

Methods

• Patients completing studies 3001 or 3002 were included.

• Treatment intervals could be extended to 10–14 days with 50–75 IU/kg of rIX-FP for all patients.

• Adult patients (≥18 years) who were well controlled on a 14-day regimen could switch to a 21-day interval with 100 IU/kg of rIX-FP.

• Primary outcome: number of patients developing inhibitors against FIX.

• Secondary outcomes include clinical efficacy, monthly rIX-FP consumption, and overall adverse events (AEs).

Results

Demographics

• 83 patients from studies 3001 (n=52) and 3002 (n=24) have continued routine prophylaxis in the extension study.

• 7 patients started prophylaxis following major surgery.

Table 1. Baseline patient characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>n (%)</th>
<th>Arm 1 (21 days)</th>
<th>Arm 2 (14 days)</th>
<th>Total (n=83)</th>
<th>Median ED (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3001</td>
<td>52</td>
<td>26</td>
<td>26</td>
<td>52</td>
<td>16 (11–21)</td>
</tr>
<tr>
<td>3002</td>
<td>24</td>
<td>14</td>
<td>10</td>
<td>24</td>
<td>17 (12–21)</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>40</td>
<td>36</td>
<td>76</td>
<td>16 (11–21)</td>
</tr>
</tbody>
</table>

Efficacy

• Low annualized spontaneous bleeding rates (AsBR) in all regimens.

Table 2. AsBR rates in adults

<table>
<thead>
<tr>
<th>AsBR, study (N=27)</th>
<th>Median (IQR)</th>
<th>Estimated mean AsBR (95% CI)</th>
<th>Duration, median (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-day regimen</td>
<td>0 (0, 0.00)</td>
<td>0.65 (0.27–1.13)</td>
<td>240</td>
</tr>
<tr>
<td>14-day regimen</td>
<td>0 (0, 0.00)</td>
<td>0.00 (0, 1.24)</td>
<td>240</td>
</tr>
<tr>
<td>21-day regimen</td>
<td>0 (0, 0.00)</td>
<td>0.00 (0, 1.24)</td>
<td>240</td>
</tr>
</tbody>
</table>

AsBR validated in the extension study.

Low AsBR rates in children for all prophylaxis regimens.

Table 3. AsBR rates in children

<table>
<thead>
<tr>
<th>AsBR, study (N=10)</th>
<th>Median (IQR)</th>
<th>Estimated mean AsBR (95% CI)</th>
<th>Duration, median (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-day regimen</td>
<td>0 (0, 0.00)</td>
<td>0.56 (0.30–1.05)</td>
<td>362</td>
</tr>
<tr>
<td>14-day regimen</td>
<td>0 (0, 0.13)</td>
<td>0.00 (0, 0.05)</td>
<td>362</td>
</tr>
<tr>
<td>21-day regimen</td>
<td>0 (0, 0.13)</td>
<td>0.00 (0, 0.05)</td>
<td>362</td>
</tr>
</tbody>
</table>

Safety

• Median exposure days (EDs) to rIX-FP in the extension study was 67 and was 136 in total across all rIX-FP studies.

• More than 70 (84.3%) subjects have achieved 100 EDs.

Prophylaxis intervals tested

• Over 45 out of 52 (87%) subjects (≥12 years) switched from weekly to 10- or 14-day interval.

• 10 subjects (≥18 years) have switched from 14-day to 21-day interval.

• 11 (46%) children (<12 years) have switched to 10- or 14-day interval.

Conclusion

• Efficacy and safety of routine prophylaxis once every 7-, 10- and 14-days with rIX-FP have been demonstrated in the pivotal Phase III studies and further validated in the extension study.

• Extended treatment intervals of 21 days is possible in adults, with median AsBR of 0.0.

• Extended treatment interval of 10- or 14-day is possible in young children (<12 years), with median AsBR of 0.0 and 1.16, respectively.

Disclosures

EG received honoraria for speaking and/or for consulting from CSL Behring, Bayer, Baxter/Beaulieu, Pfizer, NovoNordisk, Sanofi, FitKan, Kedrion, Octapharma and Grifols and received unrestricted research grants from NovoNordisk and Pfizer; CV, DW, YL, MS, GC, NB and UA are employees of CSL Behring.