An Integrated Analysis of Long Term Safety of an Extended Half-Life, Pegylated, Full-length Recombinant Factor VIII (BAX 855) in the Treatment of Hemophilia A in 234 Pediatric, Adolescent and Adult Patients

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INTRODUCTION

- Patients with severe hemophilia A have <1% of normal factor VIII (FVIII) levels and experience frequent bleeding, which can be prevented by regular prophylaxis with FVIII replacement.1
- BAX 855 is built on the full-length recombinant FVIII (rFVIII) of IFAM-ADATE and manufactured via the same plasmid expression-free platform.
- Controlled pegylation with polyethylene glycol was chosen to extend the half-life while maintaining the integrity of the ADATE protein.
- The pivotal PROLONG-ATE trial demonstrated that BAX 855 is safe and effective for prophylactic use and in the treatment of bleeding episodes in patients with hemophilia A and confirmed an extended half-life for BAX 855 compared to ADATE.1

METHODS

Table 1: Data From 5 Studies

To further assess the safety of BAX 855, data from 5 studies were pooled.

Study ID Description Study Status Subjects Treated Doses Administered

20111 NCT01358859 Phase 1, safety Complete 19 None

20121 NCT01705745 Phases 2A, 2B, safety, efficacy, remnantogen Complete 137 FVIII

20122 NCT02525891 Pediatric (Phase 2A), safety, efficacy, remnantogen Complete 68 FVIII

2013A NCT01910885 Phases 3, PN, paclitaxel, safety and efficacy Ongoing 28 patients

2013B NCT01954983 Phase 3, Long-term safety, efficacy, remnantogen Ongoing 174

Figure 1: Subject Disposition

Total number of treated subjects: 234
- No number of subjects (number of unique subjects)

RESULTS

Table 4. Immunogenicity Development of Inhibitors (Neutralizing Antibodies) to FVIII

<table>
<thead>
<tr>
<th>Number of Days</th>
<th>Days Post Dosing</th>
<th>Inhibitor</th>
<th>Proportion Developing Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>25 to 50</td>
<td>15</td>
<td>0</td>
<td>0 (0.020)</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>72</td>
<td>0</td>
<td>0 (0.000)</td>
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</tbody>
</table>

Study (FVIII, PEG): PEG were excluded.

Table 5. Related AEs (or Adverse Drug Reactions) Following Treatment

System Organ Class Prophylaxis Term Number of Events Proportion (%) Number Per 100 Exposures Number Per year Number P=234

None

Nausea

Nausea

Diarrhea

Vomiting

Study: SAEs in 24.10 (2.5%) of 234 patients

- None were considered related to treatment
- No deaths occurred during the conduct of the study*
- “1 death of neuroendocrine tumor occurred 21 days post discontinuation of product and withdrawn from the study, considered not related to BAX 855

Table 2: Demographics

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</tr>
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<td>Complete</td>
<td>137</td>
<td>FVIII</td>
</tr>
<tr>
<td>20122</td>
<td>Complete</td>
<td>68</td>
<td>FVIII</td>
</tr>
<tr>
<td>2013A</td>
<td>Ongoing</td>
<td>28 patients</td>
<td></td>
</tr>
<tr>
<td>2013B</td>
<td>Ongoing</td>
<td>174</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: Race

- White
- Black
- Asian
- Other

Figure 3: Exposure to BAX 855 (Total = 81,762,479)

Figure 4: Exposure Days (Total = 25,517 days)

Table 3: Exposures Days per Treated Patient by Age

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Figure 5: Rate of AEs per Infusion

- 1.7% for moderate AEs
- 2.4% (38/25724) non-serious AEs
- 0.1% (54/25724) serious AEs

Figure 6: Development of Persistent Binding Antibodies to FVIII, PEG-FVIII, PEG, CHO

- None of the 234 treated patients developed a persistent binding antibody response during the studies
- 26 patients had pre-existing binding antibodies, as before BAX 855 exposure: 3 for FVIII, 3 for PEG, 23 for PEG-FVIII
- 12 patients developed transient IgG binding antibodies (i.e., decreasing in severity and then detectable at ≤1 or 2 consecutive visits that were not detectable at subsequent visits or at study completion) 6 for FVIII, 10 for PEG-FVIII
- No conclusion can be drawn yet in 3 subjects who developed binding antibodies shortly before or at the latest data cut-off
- No impact on hemostatic efficacy or safety
- No patients had any binding antibodies to CHO protein

Adverse Events
- Of 234 treated patients, 165 (70.5%) experienced 662 AEs

- 2% (16/25724) non-serious AEs
- 0.1% (54/25724) serious AEs

CONCLUSION

- From this integrated analysis, BAX 855 was safe and well tolerated in 234 pediatric, adolescent and adult PPs with severe hemophilia A. This common adverse events considered related to BAX 855 treatment were consistent with the safety profile of ADATE.

DISCLOSURES

- Authors are employees of Baxalta (1Baxalta Innovations GmbH, 2,3Baxalta US, Inc,), now part of Shire.