**Summary**

- While the efficacy and safety of emicizumab prophylaxis in PwHA has been demonstrated during the HAVEN clinical trial program, it is important to continue to assess safety in a broad population for an extended time for a new treatment.

- Results from the second interim analysis of the STASEY trial demonstrate that emicizumab prophylaxis is well tolerated and effective in preventing bleeds in a large cohort of PwHA with factor (F)VIII inhibitors.

**INTRODUCTION**

- Emicizumab, a subcutaneously administered, bi-specific monoclonal antibody, bridges active FIX and FX, replacing the function of missing activated FVIII in PwHA, thereby restoring hemostasis.

- STASEY (NCT0319706) is a Phase IIb, single-arm, open-label, multicentre trial to evaluate the safety and tolerability of emicizumab in PwHA with FVIII inhibitors.

- This report provides results of the second interim analysis from STASEY.

**METHODS**

Participants for the STASEY trial were enrolled globally.

- PwHA aged ≥12 years with FVIII inhibitors were recruited (Figure 1).

  - Following ethics committee approval and informed consent, 193 participants across 24 countries enrolled into the pre-treatment population, 105 of whom received prophylaxis.

Objective for the STASEY trial focused on the safety of emicizumab in a post-marketing setting.

- Primary endpoints evaluated the safety of emicizumab, comprising: incidence and severity of all adverse events (AEs), including non-haemorrhagic adverse events (NAEs), serious AEs (SAEs), AE leading to trial discontinuation or AE leading to treatment withdrawal, AE leading to dose modification or interruption, AE leading to dose discontinuation.

- Secondary endpoints evaluated the safety of emicizumab, comprising: incidence of AEs, incidence of AEs leading to withdrawal of study treatment, incidence of AEs leading to trial discontinuation, incidence of treatment-emergent AEs (TEAEs), incidence of AEs leading to treatment withdrawal, incidence of SAEs, incidence of TEAEs, incidence of AE leading to discontinuation of treatment, incidence of AEs leading to dose modification or interruption.

- Data were collected over 24 weeks prior to trial entry, median (range) 10.4 (5-20) weeks.

- The study was powered to demonstrate the non-inferiority of emicizumab prophylaxis compared with the majority of PwHA having zero treated bleeds during the trial.

- The study was not powered to detect differences in treatment effect or treatment comparison.

- Calculated using a negative binomial regression method.

- The analysis was conducted using a per-protocol population.

- AE leading to trial discontinuation or AE leading to treatment withdrawal, AE leading to dose modification or interruption, AE leading to dose discontinuation.

- All AEs were classified according to MedDRA version 21.1.

- Results presented here are from a second interim analysis of the STASEY trial.

Results presented here are from a second interim analysis of the STASEY trial.

- At trial cut-off (20 May 2019), 193 PwHA (Table 1) had received emicizumab and were evaluable for safety.

- Median (range) treatment duration was 50.3 (11.6-288) weeks.

- No new safety signals were identified for emicizumab in the primary outcomes.

- Emicizumab was well tolerated (Table 2).

- Two AEs were classed as TEIs.

- One achieved mucocutaneous reaction in a 53.5-year-old who had several risk factors, including a history of smoking, hypertension, and family history of coronary heart disease. He did not receive concurrent biopsy agent and continued emicizumab treatment dose adjustment; the treating physician assessed the event as unrelated to emicizumab.

- One hypertensive condition following blood extraction, during which the individual received multiple doses of anti-embolic calibrated with recombinant activated FVIII (Fib); emicizumab-related AEs were reported in 33 (17.1%) PwHA;

- One hobligy was reported (polymyalgia), assessed as unrelated to emicizumab.

- Three PwHA received activated prothrombin complex concentrate and 32 received rFVIIa, with no associated TEA or arrhythmia/ventricular AEs.

- Secondary outcomes as are expected based on the HAVEN clinical trial program.

- Overall, 10/5 (2.5%) participants developed ADEs; in two participants, these were serious.

- No ADEs had neurologic potential (by pharmacokinetic assessment).

- At the end of the trial, 68% of the patients were on the same treatment.

- The study was not powered to detect differences in treatment effect or treatment comparison.

- All ADEs were classified according to MedDRA version 21.1.

- The analysis was conducted using a per-protocol population.

- Results from the second interim analysis of the STASEY trial found no new safety signals, confirming that emicizumab was well tolerated.

- Emicizumab prophylaxis was effective for PwHA with FVIII inhibitors, with the majority of PwHA having no treated bleeds during the trial.

- These findings expand on data supporting the use of emicizumab for prophylaxis as a safe and effective way to prevent bleeding for PwHA.

**CONCLUSIONS**

**REFERENCES**

**ACKNOWLEDGMENTS**

**Table 1.** Demographics and baseline characteristics (safety-evaluable population).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
<th>n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PwHA, n (%)</td>
<td>193</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>12-18</td>
<td>26 (13.5)</td>
</tr>
<tr>
<td></td>
<td>18-24</td>
<td>45 (23.2)</td>
</tr>
<tr>
<td></td>
<td>≥25</td>
<td>120 (62.3)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>163 (84.6)</td>
<td></td>
</tr>
<tr>
<td>Hemophilia severity at baseline, n (%)</td>
<td>40 (20.6)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>2 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>22 (11.4)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>159 (82.6)</td>
<td></td>
</tr>
<tr>
<td>Hemophilia treatment history, n (%)</td>
<td>21 (10.9)</td>
<td></td>
</tr>
<tr>
<td>Prophylactic only</td>
<td>2 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Scheduled when at least 100 patients had received treatment for at least 1 year.</td>
<td>19 (10.2)</td>
<td></td>
</tr>
<tr>
<td>Scheduled when approximately 100 patients had received treatment for at least 24 weeks.</td>
<td>17 (8.9)</td>
<td></td>
</tr>
<tr>
<td>Highest historical inhibitor titer (log10), median (range)</td>
<td>8.11 (5.40-15.3)</td>
<td></td>
</tr>
<tr>
<td>Prior (T) treatment, n (%)</td>
<td>83 (43.1)</td>
<td></td>
</tr>
<tr>
<td>No. bleeds in 24 weeks prior to trial entry, median (range)</td>
<td>6 (0-48)</td>
<td></td>
</tr>
<tr>
<td>Target joints at baseline, n (%)</td>
<td>127 (66.1)</td>
<td></td>
</tr>
</tbody>
</table>

*PwHA, people with hemophilia A; T, treatment.

**Table 2.** Safety summary (safety-evaluable population).

<table>
<thead>
<tr>
<th>Event Category</th>
<th>Number of Events (n)</th>
<th>n (%)</th>
<th>n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>382</td>
<td></td>
<td>198 (101.5)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>19 (10.0)</td>
<td></td>
<td>19 (10.0)</td>
</tr>
<tr>
<td>ADAs†</td>
<td>115 (60.3)</td>
<td></td>
<td>115 (60.3)</td>
</tr>
<tr>
<td>AE leading to trial discontinuation</td>
<td>4 (2.1)</td>
<td></td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>AE leading to treatment withdrawal</td>
<td>11 (5.8)</td>
<td></td>
<td>11 (5.8)</td>
</tr>
<tr>
<td>Fatal AE</td>
<td>1 (0.5)</td>
<td></td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>

†ADAs: antibodies developed to emicizumab.

**Table 3.** Summary of additional bleed endpoints (intent-to-treat population).

<table>
<thead>
<tr>
<th>End Point</th>
<th>Median ABR (IQR)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PwHA with zero bleeds, n (%)</td>
<td>145 (75.1)</td>
<td></td>
</tr>
</tbody>
</table>

Secondary outcomes as expected based on the HAVEN clinical trial program.

- Overall, 10/5 (2.5%) participants developed ADEs; in two participants, these were serious.

- No ADEs had neurologic potential (by pharmacokinetic assessment).

- At the end of the trial, 68% of the patients were on the same treatment.

- All ADEs were classified according to MedDRA version 21.1.

- The analysis was conducted using a per-protocol population.

**REFERENCES**

**ACKNOWLEDGMENTS**

**PUSHED FOR TIME?**

For more information, you can visit the authors’ websites or contact them directly. This is a collaborative effort between multiple institutions and organizations. Please remember to cite the references and authors appropriately in your work.

**Presented at the International Society on Thrombosis and Haemostasis (ISTH) 2020 Virtual Congress | 12-14 July 2020**