Initial results of the impact of valoctocogene roxaparvovec on pain occurrence and interference: Insights from PROBE

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Introduction

• People with severe hemophilia A commonly present with intramuscular bleeding and hemorrhaging, leading to acute and chronic pain with an overall reduction in health-related quality of life
• Chronic pain was identified as an important core outcome in a separate genetic therapy from standard of care1
• The Patient Reported Outcomes, Burdens and Experiences (PROBE) questionnaire was included in the phase 3, open-label, single-arm study (GENEHI-1) as a tertiary endpoint to assess the effects of a single 60 µg/kg dose of valoctocogene roxaparvovec on patient-reported health and life experiences2

Methods

• Here, we report results from the PROBE questionnaire for incidences of acute and chronic pain occurrence and interference at baseline and week 104 post-gen therapy
• PROBE is a validated, hemophilia-specific, patient-reported outcomes questionnaire developed by people with hemophilia for people with hemophilia3
• While further validation to understand the performance of PROBE in this context of use is ongoing, this study summarized pain-related outcomes collected within the PROBE questionnaire

PROBE questionnaire pain-related questions:

1. Any occurrence of acute and chronic pain (recall: 12 months)
   • “Acute pain” is defined as pain that arises in response to an event (like an injury or bleeding episode)
     • “Chronic pain” is defined as pain from a persistent cause: it can vary in frequency and intensity (like back pain, pain from sore joints, or arthropathy).
     • Chronic pain does not include “acute pain”
2. Pain during 8 activities (walking, stair climbing, nighttime restlessness, standing, bearing, playing, after falling/trauma, other)
3. Pain interference in 11 aspects of life (general activity, mood, walking ability, normal work, attending school, relationships with others, sleep, enjoyment of life, playing/participating in sports/exercising, Mfg, other)
4. Use and frequency of pain medication (not reported)
5. Chronic pain in target joints (not reported)

Results

Comparison of participants reporting chronic or acute pain at baseline and week 104

• Data were available for 124 participants at baseline and 129 at week 104
  – Intent-to-treat study population (N = 134; median age, 30.0; range, 18-70)
  – Self-reported acute and chronic pain decreased post-gene therapy (Figure 1)
  – Acute pain decreased from 66.5% to 57.0%

Figure 1. Percent of participants reporting chronic or acute pain at baseline and week 104

Table 1. Intra-patient comparison of pain occurrence

<table>
<thead>
<tr>
<th>Activity</th>
<th>Baseline (n = 124)</th>
<th>Week 104 (n = 129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>% occurrence (%)</td>
<td>% occurrence (%)</td>
</tr>
<tr>
<td>Pain</td>
<td>60.5</td>
<td>57.0</td>
</tr>
<tr>
<td>Acute</td>
<td>61.9</td>
<td>57.0</td>
</tr>
<tr>
<td>Chronic</td>
<td>6.6</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Aggregate instances of pain occurrence

• Aggregate instances of self-reported pain occurrence (% activities including ‘Other’)

Figure 2. Comparison of participants reporting A) chronic and B) acute pain at baseline and week 104

Table 2. Intra-patient comparison of pain interference

<table>
<thead>
<tr>
<th>Activity</th>
<th>Baseline (n = 128)</th>
<th>Week 104 (n = 120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>% difference (%)</td>
<td>% difference (%)</td>
</tr>
<tr>
<td>Pain</td>
<td>-3.1</td>
<td>-1.5</td>
</tr>
<tr>
<td>Acute</td>
<td>26.5, 24.0</td>
<td>26.5, 24.0</td>
</tr>
<tr>
<td>Chronic</td>
<td>-8.1, 9.9</td>
<td>-9.1, 10.3</td>
</tr>
</tbody>
</table>

Figure 3. Aggregate instances of pain interference for A) acute pain, and B) chronic pain at baseline and week 104

Conclusions

• This analysis adds to previous findings from GENEHI-1 of the efficacy of PROBE as a single injection of valoctocogene roxaparvovec relative to FVIII prophylaxis
• Pain is one of the core outcomes of importance to people with hemophilia
• An initial analysis of PROBE data demonstrates that valoctocogene roxaparvovec may be associated with a decrease in self-reported acute and chronic pain occurrence and interference with daily life in this study cohort

The impact of gene therapy on pain, particularly chronic pain as demonstrated from PROBE, a hemophilia-specific tool, has important implications on treatment decision-making and continued disease management

Acknowledgements

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Disclosures

• None

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