Efficacy and Safety of OnabotulinumtoxinA for the Treatment of Pediatric Lower Limb Spasticity: Primary Results

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To view videos of the children at baseline and after onabotulinumtoxinA treatment, please follow the links below:

Girl Baseline: https://vimeo.com/292063912/2e2f236b16
Girl Week 8: https://vimeo.com/292064448/c160a01b48
Boy Baseline: https://vimeo.com/292064627/4df87f9ea7
Boy Week 8: https://vimeo.com/292064795/4ed44475de
**Efficacy Outcomes**

- OnabotulinumtoxinA 8 U/kg and 4 U/kg reduced (improved) average MAS-ankle scores at weeks 4 and 6 compared with baseline.
- Compared with the placebo group, the change in MAS-ankle scores from baseline were significantly improved for both onabotulinumtoxinA treatment groups (Figure 2).
- OnabotulinumtoxinA 8 U/kg and 4 U/kg improved (increased) average CGI scores at weeks 4 and 6.
- The increase with the 8-U/kg dose was statistically significant (Figure 3).
- Both doses of onabotulinumtoxinA demonstrated significant reduction in muscle tone (MAS scores) from baseline throughout the course of the study compared with placebo (Figure 4A).
- A greater treatment response (CGI, as determined by the physician) was observed at weeks 4, 6, and 6 with onabotulinumtoxinA compared with placebo (Figure 4B).

**Safety and Tolerability**

- The incidence of adverse events with onabotulinumtoxinA was similar to that with placebo (Table 3).
- No new safety signals were identified.

**Background**

- Spasticity is a common impairment in children with cerebral palsy, impairing function, worsening quality of life, and creating pain.
- The safety and efficacy of onabotulinumtoxinA treatment have been established in adult patients with muscle spasticity.

**Objective**

To evaluate the safety and efficacy of onabotulinumtoxinA for lower limb spasticity/hypertonia in children with cerebral palsy.

**Study Design**

- Phase 3, randomized, double-blind, placebo-controlled study.
- Double-blind, 12-week trial.
- OnabotulinumtoxinA 4 U/kg and 8 U/kg + physical therapy.
- Standardized physical therapy.
- Assessments: Primary outcome measure - Clinical Global Impression of Change (CGI).
- Secondary outcome measures - Clinical Global Impression of Change (CGI); Change in Modified Tardieu Scale.

**Table 2. Baseline demographics and disease characteristics**

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Mean (SD) Age, y</th>
<th>Sex, n (%)</th>
<th>Race, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onabot 8 U/kg</td>
<td>6.7 (3.6)</td>
<td>74 (58.3)</td>
<td>70 (51.5)</td>
</tr>
<tr>
<td>Onabot 4 U/kg</td>
<td>6.4 (3.6)</td>
<td>53 (41.7)</td>
<td>42 (31.3)</td>
</tr>
<tr>
<td>Placebo</td>
<td>6.7 (3.9)</td>
<td>57 (43.6)</td>
<td>49 (37.4)</td>
</tr>
<tr>
<td>Total</td>
<td>6.6 (3.8)</td>
<td>180 (54.1)</td>
<td>162 (49.4)</td>
</tr>
</tbody>
</table>

**Figure 1. Study design**

- Primary outcome measure: Change from baseline in Modified Ashworth Scale (MAS) ankle score at weeks 4 and 6 (average change from baseline).
- Secondary outcome measures:
  - Clinical Global Impression of Change (CGI).
  - Change in Modified Tardieu Scale.
  - Goal Attainment Score.
  - Edinburg Visual Gait Score.
  - Safety and tolerability were also assessed.

**Figure 2. OnabotulinumtoxinA reduces spasticity over the standard of care, physical therapy**

- With the knee extended, both doses of onabotulinumtoxinA significantly improved the dynamic component of spasticity (Figure 6).
- Both doses of onabotulinumtoxinA improved fast motion angle (R1) and slow motion angle (R2) measures.

**Figure 3. OnabotulinumtoxinA improves CGI over the standard of care, physical therapy**

- In a subset of patients who completed the assessment, similar results were observed when the knee was flexed.

**Figure 4. OnabotulinumtoxinA demonstrates sustained improvement in (A) MAS and (B) CGI**

- The photos in Figure 7 show representative examples of the improvement in gait seen with onabotulinumtoxinA.