Topical Botulinum Toxin Type A for the Treatment of Moderate to Severe Lateral Canthal Lines: Preliminary Safety and Efficacy Results of a Blinded, Randomized, Placebo Controlled Trial

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Background

The topical application of botulinum toxin type A (BoNT-A) to the Lateral Canthal Lines (LCLs) eliminates complications from injections (e.g., bruising, discomfort). An investigational product, RT001 Botulinum Toxin Type A Topical Gel, is being studied for the treatment of moderate to severe LCLs. RT001 contains a proprietary, purified 150 kilodalton (kDa) BoNT-A combined with a novel peptide macromolecule transport system, which facilitates transcutaneous delivery without altering the function of BoNT-A. RT001 may be well suited to offer safe and painless administration of BoNT-A for a variety of indications e.g. hyperhidrosis and hyperpigmentation.

Objective

The objective of this study was to evaluate the safety and efficacy of various concentrations of excipient carrier peptide in RT001.

Methods

A randomized, controlled study was conducted in 77 adult subjects with moderate to severe LCLs. Subjects were enrolled in 2 cohorts and randomized 1:1:1:1 within each cohort to receive placebo or a single dose of BoNT-A with varying levels of the excipient peptide (Table 1). Subjects received a single 30-minute application of 0.5 mL of test article to each lateral canthal area (LCA) at Baseline. Follow-up evaluations were conducted at 7, 14, 21, and 28 days post-treatment. The investigator evaluated LCLs at rest and at smile using a 4-point LCL severity scale (absent, mild, moderate, severe). Responders were defined as those subjects with at least a 1-point improvement from Baseline in LCL severity at rest or smile at any of the follow-up evaluations.

Safety evaluations included adverse events (AEs), skin irritation, eye irritation, cranial nerve examination, and clinical laboratory tests.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>N</th>
<th>RT001 Dose (per LCA)</th>
<th>Peptide Dose (per LCA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>9</td>
<td>1.65 ng</td>
<td>0.5 mcg</td>
</tr>
<tr>
<td>B</td>
<td>9</td>
<td>1.65 ng</td>
<td>2.0 mcg</td>
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<tr>
<td>C</td>
<td>10</td>
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<td>4.5 mcg</td>
</tr>
<tr>
<td>D (Placebo)</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cohort 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>1.65 ng</td>
<td>6.0 mcg</td>
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<tr>
<td>G</td>
<td>10</td>
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<td>10.5 mcg</td>
</tr>
<tr>
<td>H (Placebo)</td>
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<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Results

- RT001 achieved statistically significant improvement of LCL’s versus placebo at both rest and smile (Figures 1 and 2).
- In both cohorts, active treatment groups achieved higher response rates than placebo (Table 3). Cohort 2 which had higher peptide concentration, achieved statistically significant improvement versus placebo.
- There were no significant differences between active doses and placebo in Cohort 1 suggesting that the peptide concentration was not adequate.
- There was significantly higher response for 2-point improvement at rest and 1-point improvement in smile in the 7.5 mcg group and significant improvement for 1-point improvement at smile in the 6.0 mcg group versus placebo.
- There were no serious adverse events; most events were mild, local and transient.
- There was no evidence of any systemic toxicity at any peptide concentration.

Subject Demographics

- Mean age 49.2 years (range 28-65 years)
- 61 females, 16 males
- 50 white, 27 other race
- All Hispanic/Latino

Conclusions

- RT001 significantly improved the appearance of LCLs. There were statistically significant aesthetic gains between RT001 and placebo in the groups with 6.0 and 7.5 mcg peptide.
- Peptide is necessary to achieve efficacy over placebo. An adequate concentration of peptide appears to be required to achieve efficacy in improving LCL’s.
- Based on cranial nerve assessments there was no evidence of diffusion from treatment area.
- RT001 with all peptide concentrations was well tolerated. The majority of AEs were application site reactions that were mild and transient.
- There was no relationship between the peptide concentration and the incidence of AEs, or skin or ocular irritation events.

Commercial Support

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