

# 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 peptidyl 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 at any of the follow-up evaluations.

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

## Methods

Table 1: Treatments

Treatment Group	N	RT001 Dose (per LCA)	Peptide Dose (per LCA)
<b>Cohort 1</b>			
A	9	1.65 ng	0.5 mcg
B	9	1.65 ng	2.0 mcg
C	10	1.65 ng	4.5 mcg
D (Placebo)	9	0	0
<b>Cohort 2</b>			
E	10	1.65 ng	6.0 mcg
F	10	1.65 ng	7.5 mcg
G	10	1.65 ng	10.5 mcg
H (Placebo)	10	0	0

## Subject Demographics

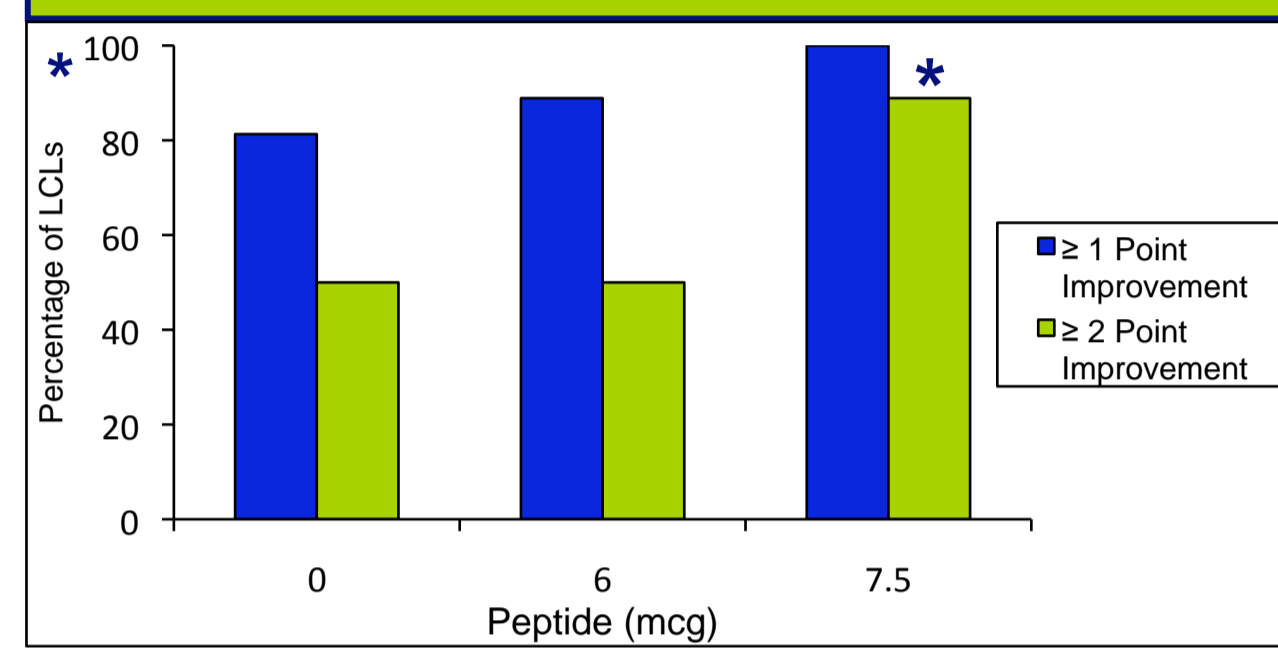
- Mean age 49.2 years ( range 28-65 years)
- 61 females, 16 males
- 50 white, 27 other race
- All Hispanic/Latino

## 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 (Figure 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 at 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.

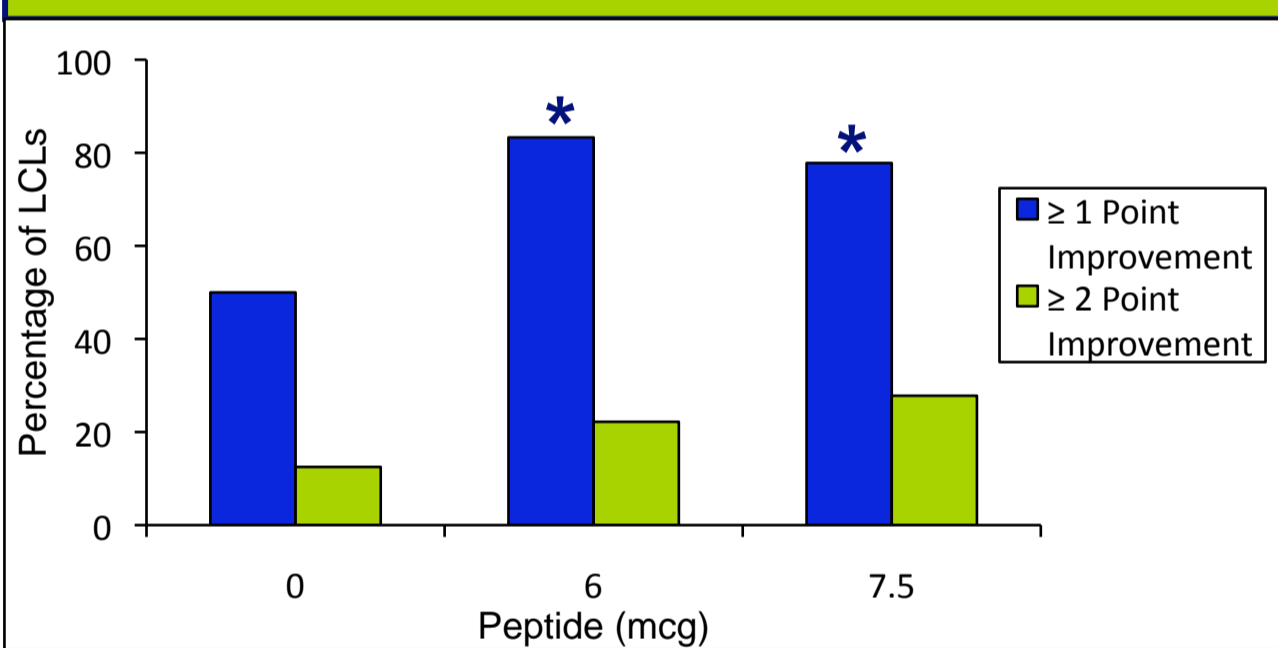
## Results

Figure 1: Day 28 Response At Rest



\* Significant difference vs. placebo, P<0.05

Figure 2: Day 28 Response At Maximum Smile

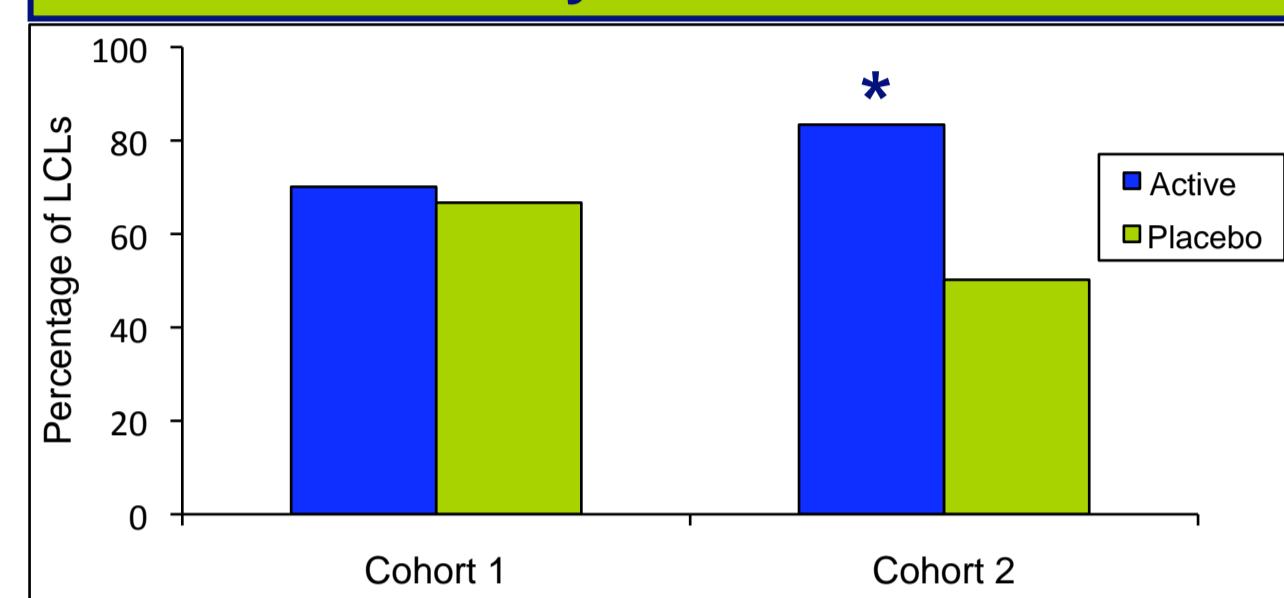


\* Significant difference vs. placebo, P<0.05

Figure 2: LCLs at Baseline and Day 28



Figure 3: Day 28 Response At Smile By Cohort



\* Significant difference vs. placebo, P<0.05

## ADVERSE EVENTS

- 49 subjects (63.6%) had one or more treatment-related AEs.
- The most common AEs were involuntary muscle contraction (29.9%) and application site erythema (23.4%).
- Most related AEs were mild in severity; there were no severe events.
- There were no serious AEs or AEs leading to discontinuation.

## LABORATORY RESULTS

- There were no notable changes from Baseline to Day 28 for mean hemoglobin, hematocrit, RBC count, platelet count, total bilirubin, alkaline phosphatase, ALT, AST, BUN, creatinine, or LDH.
- No clinically significant laboratory results were observed.

## SKIN AND OCULAR IRRITATION

- Skin erythema was observed for 7 subjects in Cohort 1 and 0 subjects in Cohort 2. All events were mild except for 2 subjects with definite erythema (4.5 mcg, placebo) and 1 subject with strong erythema (placebo).
- Other application site events (all Cohort 1): burning or stinging (3 subjects), itching (1 subject), and scaling (1 subject).
- Ocular irritation events (all Cohort 1): erythema (18 subjects), burning sensation (1 subject), dryness (1 subject), stinging sensation (4 subjects), and foreign body sensation (4 subjects). All mild except for moderate erythema (5 subjects).

Table 4: Treatment-Related Adverse Events

Cohort 1	0.5 mcg (n=9)	2.0 mcg (n=9)	4.5 mcg (n=10)	Placebo (n=9)
Eye irritation	1	0	1	1
Eye Pain	0	1	1	1
Foreign body sensation	0	1	2	0
Application site erythema	7	5	2	4
Headache	0	0	0	2
Involuntary muscle contraction	2	0	0	0
Erythema	0	0	0	2
Pain of skin	1	0	0	1
Skin burning sensation	0	1	1	0
Cohort 2	6.0 mcg (n=10)	7.5 mcg (n=10)	10.5 mcg (n=10)	Placebo (n=10)
Involuntary muscle contraction	4	6	7	4

Includes events reported for at least 2 subjects in either cohort

## 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/local 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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