

## **Surgery (Cosmetic)**

**P2400**

### **A five patient satisfaction pilot study of calcium hydroxylapatite injection for treatment of the aging hand**

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Background: The process of skin aging is not limited to the face but involves every part of the body-- including the hands. A common manifestation of aging of the hand is the loss of volume, which occurs as the skin loses its subcutaneous fat. Injectable dermal fillers have surfaced as a popular method to address such deficiencies.

Objective: We report the use of calcium hydroxylapatite (CaHA) to address lost volume.

Methods: Five female subjects with soft tissue deficiency of the dorsa of hands were enrolled at Mount Sinai Medical Center. A solution of CaHA with 2% lidocaine was injected interdigitally in amounts of 0.3 to 1.0 mL at each of 3-5 insertion sites; the sites were then massaged and molded up to three times to ensure an optimal cosmetic endpoint. Subjects were seen for a follow up visit after 1, 4, 16, and 24 weeks.

Results: With a single injection, all subjects reached their correction goals without requiring any touch-ups. At the 24-week visit, the subjects still retained the filling effect with no adverse events and high patient satisfaction.

Conclusion: Calcium hydroxylapatite, a new easily injectable and safe dermal filler, has emerged as an excellent option for soft tissue augmentation in aging hands.

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*Commercial Support: None Identified*

## **Surgery (Cosmetic)**

**P2401**

### **A validated hand grading scale**

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**Background:** Following the popularity of facial cosmetic procedures to reverse the signs of aging, cosmetic procedures that rejuvenate the hand are being sought. Aging of the hand is typically characterized by irregular surface pigmentation, prominence of superficial veins and tendons, thinning of the dermis, and loss of subcutaneous fat.

**Objectives:** To develop the Hand Grading Scale for objective quantification of the severity of hand aging and to establish the reliability of this photonumeric scale for clinical research and practice. Material and

**Methods:** The Hand Grading Scale is a 5-point photonumeric rating scale that was developed to objectively quantify the severity of aging of the hand. Nine experts rated photographs of 35 subjects, twice, with regard to the aspect "hand aging" in comparison to morphed images. Inter and intra rater variability was assessed by computing intraclass correlation coefficients

**Results:** The agreement between the experts is considerably high. Bubble plots (bivariate scatter plots) demonstrate linearity in judgment by the experts.

**Conclusion:** The five point photonumeric scale generated spans the severity of the hand aging that most commonly seek correction. The scale is well stratified for consistent rating.

Merz aEsthetic Rejuvenation Zone scale development team:- Derek Jones, MD, Berthold Rzany, MD, PhD, Martina Kerscher, MD, PhD, Timothy Flynn, MD, Corey Maas, MD, Gerhard Sattler, MD Merz team: Alexander Gebauer, MD, Rainer Pooth, MD, Kathleen McClure, RN and Ms. Ulli Simone-Korbel & Mr. Larry Buchner, Canfield Scientific

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*Commercial Support: Merz Pharmaceuticals, LLC*

## **Surgery (Cosmetic)**

**P2402**

### **Safety and efficacy of a novel ribose-crosslinked porcine collagen dermal filler combined with 0.3% lidocaine**

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**RATIONALE AND GOAL:** In current clinical practice, local anesthesia is administered either as a topical treatment or a nerve block to decrease injection pain and increase patient comfort during facial dermal filler placement. Addition of anesthetic directly to calcium hydroxyapatite dermal filler prior to injection has been shown to lessen discomfort in patients receiving hand augmentation. The goal of this study was to assess the efficacy of a lidocaine and GLYMATRIX™-porcine dermal filler mixture to mediate pain relief during implantation while achieving cosmetic correction.

**PATIENTS AND METHODS:** Eligible patients were healthy, ≥18 years of age, and had clinical evidence of bilateral, symmetric aging defects in the nasolabial area with grades 2.0, 2.5, or 3.0, as assessed using a validated wrinkle scale. Exclusion criteria included the use of medications known to affect clotting/bleeding and a history of sensitivity to porcine or bovine-based products. This study used a split-faced design to compare the anesthetic effectiveness of injecting premixed GLYMATRIX™-porcine collagen + lidocaine (0.3% final concentration) with administering treatment a topical anesthetic 30 minutes prior to filler injection in the NLF region. The primary endpoints were the pain score immediately after each procedure assessed using the Visual Analogue Scale (VAS; range: 1 = no pain, 10 = worst pain) and the severity of injection pain assessed by the physician using the Thermometer Pain Scale (TPS). Secondary endpoints include Global Aesthetic Improvement Scale (GAIS) and the change in wrinkle scale immediately after, 12-24 hours after, and 5-7 days after treatment. Adverse events were monitored continuously.

**RESULTS:** Out of the 10 subjects for which data are currently available, compared with topical anesthesia 30 min prior to GLYMATRIX™-porcine collagen injection, 6 patients reported less pain of injection with the premixed GLYMATRIX™-porcine collagen + lidocaine. 4 subjects reported no difference in pain level. Cosmetic improvements were similar for both procedures. Detailed evaluations will be presented.

**CONCLUSIONS:** Admixing lidocaine with GLYMATRIX™-porcine collagen dermal filler during implantation seems to be an effective alternative to the standard procedure.

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## Surgery (Cosmetic)

### P2403

#### **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 area (LCA) 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 lateral canthal lines (LCL). 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 a practical, painless, and safe mode of administration of BoNT-A for a variety of indications.

Goals: This study evaluated the safety and efficacy of various concentrations of excipient peptide in RT001.

Methods: 72 subjects with moderate to severe LCLs were randomized 1:1:1:1 to receive placebo or a single dose of BoNT-A with varying levels of the TransMTS peptide. Subjects received a single 30-minute application of 0.5 mL of test article to each 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 to 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, skin irritation, eye irritation, clinical laboratory tests, and evaluation of cranial nerves II-VII.

Results: Efficacy results were analyzed (N=72) using Fisher's exact test to determine whether the response rates differed among groups. The selected dose demonstrated significant clinical improvement (2-point difference on the 4-point scale) versus placebo for LCLs evaluated at rest. Treatment related adverse events were local and transient and included mild eye and skin events. No systemic abnormalities or trends were observed.

Conclusions: RT001 demonstrated an efficacy response with an acceptable safety profile; indicating that BoNT-A can be delivered effectively by topical administration for the treatment of lateral canthal lines.

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*Commercial Support: Study supported by Revance Therapeutics, Inc.*

## Surgery (Cosmetic)

**P2404**

### **A phase 3, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of bont-a in the treatment of glabellar lines**

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Introduction: Many patients are interested in procedures to correct or reverse the physical effects of advancing age. The growing clinical importance of restoring physical appearance has led to the development of many facial procedures, including surgery (e.g., blepharoplasty, fat injection, face-lifts), dermal resurfacing of various types, and the use of filling agents. Botulinum toxin type A- hemagglutinin complex (BoNT-A) has been under investigation in the USA for the treatment of glabellar lines since 2002. Low doses have been shown to suppress the muscular activity of the glabellar area by temporary paralysis of the procerus and corrugator muscle complex, which, in turn, precludes the expression-related generation of glabellar lines (e.g., at maximal frown).

Objectives: To evaluate the tolerability and clinical effect of a single administration of BoNT-A (50 units), compared to placebo in patients with moderate-to-severe glabellar lines. Investigators' and patients' 30-day post-treatment assessments were co-primary endpoints. The onset and duration of treatment were also assessed. Subgroup analyses evaluated the effect of age, gender, race, severity of glabellar lines at baseline, and study center on efficacy.

Study Design: This was a multicenter, Phase III, randomized, parallel-group, placebo-controlled, double-blind study of 180 days' duration. A total of 158 patients were randomized in a 2:1 ratio to BoNT-A (50 units) or placebo; 145 patients completed the study. Investigator and patient assessments were completed at every visit (Screening/Day 0, 14, 30, 60, 90, 120, 150, 180). There was an additional safety assessment via phone call at Day 7. Patients completed a diary card on Days 1 to 7 to record the onset of treatment effect. Adverse events and concomitant medications were reviewed/updated every visit.

Conclusions: A single treatment with 50 units of BoNT-A reduced the severity of moderate-to-severe glabellar lines significantly better than placebo ( $P < 0.001$ ) at day 30 after injection. The median time to onset of effect was 3 days, based on patient diaries. The median duration of effect was 85 days, with statistically significant efficacy through day 120. BoNT-A was well tolerated and comparable to placebo in type, frequency, severity, and relatedness of AEs, with the exception of ptosis (2.9% vs 0) and injection site reactions (8% vs 0).

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*Commercial Support: Medicis Aesthetics Inc. (Scottsdale, AZ) provided Reloxin and study funding to the authors.*

## Surgery (Cosmetic)

### P2405

#### **A phase 3, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of BoNT-A in the re-treatment of glabellar lines following open-label treatment**

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**INTRODUCTION:** There is a growing demand for procedures to correct or reverse the signs of aging. Clostridium botulinum toxin type A - hemagglutinin complex (BoNT-A) has been evaluated extensively as an agent to reduce or eliminate glabellar lines that contribute to an aged appearance. Low doses of BoNT-A have been shown to induce a temporary paralysis of the glabellar area, helping prevent the formation of glabellar lines due to muscle activity during facial expression.

**OBJECTIVES:** To assess the efficacy of BoNT-A (50 units) after repeat administrations in the treatment of moderate to severe glabellar lines. This objective was evaluated in Cycle C at Day 30 after the double-blind administration of BoNT-A or placebo. The safety of repeat treatment with BoNT-A (50 units) was assessed throughout the study.

**STUDY DESIGN:** The multicenter study took place over 23 months, and 311 patients were enrolled. Patients received 2 to 3 open-label treatments with BONT-A before being randomized 1:1 to treatment with BONT-A or placebo in cycle C. All patients provided informed consent. The study protocol was approved by the appropriate Institutional Review Boards and the US Food and Drug Administration. At baseline, all patients had moderate to severe glabellar lines, defined as a glabellar line severity scale rating of 2 or 3 at maximum frown, by investigator assessment and (independently) patient assessment. Investigator and patient assessments of GLSS at maximum frown were performed at each visit on days 0, 14, 30, then monthly until day 120 of treatment cycles before randomization. Each patient was eligible to receive up to 4 treatments based on the severity of their glabellar lines over the study duration, and there was a minimum of 85 days between each treatment. Ninety-four patients received as many as 2 treatments, and 190 patients received 2 to 3 treatments before randomization. After active treatment cycles, 142 patients were eligible for randomization into cycle C; there were 71 patients in each group (placebo or BONT-A). Patients were treated once during the double-blind portion of the study, assessed at baseline (day 0), day 14, and day 30 for efficacy, and then monthly through day 150 safety evaluation. The main efficacy endpoints were assessed at day 30 of Cycle C.

**CONCLUSIONS:** BoNT-A (50 units) is highly efficacious after repeat administrations for the treatment of moderate-to-severe glabellar lines when compared with placebo as assessed by both investigators and patients. Repeat treatments with BoNT-A are well tolerated. The safety profile was comparable to placebo in terms of type, frequency, and severity, with the exception of ptosis (3.2% vs. 0%).

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*Commercial Support: Medicis Aesthetics Inc. (Scottsdale, AZ) provided Reloxin and study funding to the authors.*

## Surgery (Cosmetic)

### P2406

#### **A phase 3/4, open label, extension study to assess the long-term safety of repeat administrations of clostridium botulinum toxin type A -hemagglutinin complex (BoNT-A in the treatment of glabellar lines: Interim analysis**

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**INTRODUCTION:** Botulinum toxin type A - hemagglutinin complex (BoNT-A) has been shown in low doses to inhibit the formation of moderate to severe glabellar lines by temporarily paralyzing muscle activity during facial expression. The compound is currently approved in at least 17 countries for the treatment of hyperkinetic lines, and has been under investigation in the US.

**OBJECTIVES:** To evaluate the long-term safety of repeat administrations of BoNT-A (50 units) in the treatment of glabellar lines. A subsequent analysis will determine whether, as a result of repeated treatment, there is a substantial change in efficacy and the risk-benefit profile.

**STUDY DESIGN:** This multicenter, open-label, Phase 3/4 extension study will enroll 1,500 patients who have successfully completed one of the 4 Phase 3 trials with BoNT-A. As of the interim analysis data cutoff, 768 patients had enrolled in this study and received at least one treatment with BoNT-A. By extending the protocol to a two-year treatment protocol with a one-year follow-up period, the completed study will provide data on a minimum of 2½ to a maximum of 3½ years of continuous treatment with BoNT-A.

**TREATMENT:** BoNT-A (50 units) was administered at 5 glabellar injection points (0.05mL [10 units] / injection point) (Figure 1). Using a glabellar line severity score, patients with a severity rating of moderate or severe at maximum frown on both Investigator live assessment and patient self-assessment were eligible for retreatment. Since the minimum permissible interval between treatments was 85 days, the completed study will involve a minimum of 1 treatment and a maximum of 8 treatments (depending on duration of efficacy). By the interim analysis data cutoff, no patient had received more than 6 treatments.

**CONCLUSIONS:** Repeat treatment with 50 units of BoNT-A, in equally divided doses, was well tolerated. There were no cumulative safety issues, as the incidence of TEAEs, which were generally mild-to-moderate, decreased with continued therapy. There was no decrease in efficacy with repeated treatments.

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*Commercial Support: Medicis Aesthetics Inc. (Scottsdale, AZ) provided Reloxin and study funding to the authors.*

## Surgery (Cosmetic)

P2407

### **A phase 3, repeat-dose, open-label, safety and efficacy study of botulinum toxin type A - hemagglutinin complex (BoNT-A) with assessment through 13 months**

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**INTRODUCTION:** Patients are particularly interested in minimally invasive techniques, including the use of injectable agents; the most commonly performed cosmetic procedures in the United States. Clostridium botulinum toxin type A - hemagglutinin complex (BoNT-A), prepared from a proprietary Ipsen seed, C. botulinum, has been evaluated extensively in the United States and abroad. Low doses of BoNT-A induce a temporary paralysis of the glabellar area, precluding the formation of glabellar lines due to muscle activity during facial expression.

**OBJECTIVES:** Primary: to evaluate the long-term safety of repeat administrations of BoNT-A (50 units) in the treatment of moderate-to-severe glabellar lines. Secondary: to assess the long-term effectiveness of BoNT-A and evaluate the duration of effect.

**STUDY DESIGN:** This was a multicenter, Phase III, open-label assessment of 1,200 patients who received as many as 5 repeat treatments with BoNT-A (50 units) over 13 months, with at least 85 days between treatments. Investigator and patient assessments took place at each visit (Screening/day 0, 14, 30, and monthly until re-treatment, study completion, or early termination). There was telephone contact 7 days post-injection to check for adverse events and concomitant medications, and patients completed a diary card on days 1 to 7 to record the onset of treatment effect. Adverse events and concomitant medications were reviewed every visit.

**CONCLUSION:** Repeat doses of 50 units of BoNT-A, administered at 10 units/0.05 mL per injection point, were safe and effective in reducing the severity of moderate-to-severe glabellar lines, both during maximum frown and at rest. Efficacy was not diminished with repeat dosing. Adverse events, generally mild-to-moderate, and the incidence of AEs decreased with continued therapy over the 13 months of the study, indicating no cumulative safety issues.

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*Commercial Support: Medicis Aesthetics Inc. (Scottsdale, AZ) provided Reloxin and study funding to the authors.*

## Surgery (Cosmetic)

**P2408**

**A randomized, placebo-controlled, double-blind study of the safety and duration of efficacy of botulinum toxin type A (BoNT-A) in correction of moderate to severe glabellar lines**

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**INTRODUCTION:** A uniquely purified Clostridium botulinum toxin type A - hemagglutinin complex (BoNT-A) has been reported to inhibit the formation of moderate to severe glabellar lines in 50-unit doses. This study was conducted to assess the safety of administering slightly higher doses, which might be clinically useful in patients with large procerus and/or corrugator supercilii muscle mass.

**OBJECTIVES:** To assess the safety, efficacy and duration of the effect of a single variable dose of BoNT-A in ethnically diverse patients with moderate to severe glabellar lines.

**STUDY DESIGN:** In this Phase 3, double-blind, randomized, placebo-controlled, multicenter trial, 816 patients received placebo (n=272) or a single treatment with variably dosed BoNT-A (n= 544). Blinded investigator and patient self-assessments using the validated Glabellar Line Severity Score (GLSS) at maximum frown took place at each visit (baseline/day 0, and days 14, 30, 60, 90, 120, and 150 after injection). Patients recorded onset of effect in a 2-week diary, and received telephone contact at day 7 to check for adverse events and concomitant medications. The co-primary endpoints were investigator and patient live assessments at maximum frown at 30 days post-treatment using the GLSS. Response was defined as a 2-grade reduction from baseline on the GLSS. Duration of effect was recorded in days from patient self-assessment of GLSS 0 or 1 during the diary phase until loss of response (i.e., when a GLSS of 2 or 3 was recorded).

**TREATMENT:** On day 0, BoNT-A or placebo was administered at 5 injection points in the glabellar region (Figure 1). Females received 50, 60, or 70 units and males received 60, 70, or 80 units depending on the mass of the procerus and/or corrugator muscle (larger dose for the larger muscle mass). The dose was divided equally among the 5 injection points.

**CONCLUSION:** A single treatment with BoNT-A, dosed based on gender and muscle mass, is well tolerated, has a good clinical effect on moderate-to-severe glabellar lines.

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