Introduction

Facial wrinkles arise due to diminished production and increased breakdown of dermal matrix components, including collagen and glycosaminoglycans (GAGs), as a result of natural aging and photodamage coupled with repeated facial movement. Injectable neurotoxins arrest facial movement and thus diminish dynamic wrinkles over time, but lack the ability to plump or fill existing depressions. Injectable wrinkle fillers reverse the appearance of deep wrinkles, but are not without risks or discomfort and can be challenging to use on certain areas of the face.

A new topical two-step line plumper has been developed for targeted use on fine and deep lines as an adjuvant or cosmetic alternative to injectable therapies. The Step 1 Activator contains a novel amino acid derivative, N-acetyl tyrosinamide, which has been shown to stimulate collagen production in aged skin cells; increase hyaluronic acid in skin and cartilage cells in vitro; and stimulate pro-collagen and GAGs in vivo via histological assessment of human skin biopsies. The Step 2 Finishing Complex contains complementary dermal matrix building ingredients, triethyl citrate and N-acetyl glucosamine, which increase collagen and hyaluronic acid, respectively. This poster presents a summary of a vehicle-controlled clinical study evaluating the safety and cosmetic effects of the two-step topical line plumper.

Subjects were evaluated at weeks 0, 4, 8, 12, and 16. At each visit, a trained clinician graded glabellar lines, nasolabial folds, under eye wrinkles, and crow’s feet; measured pinch recoil time of one under eye area; and assessed skin irritation. Subjects’ faces were photographed, and subjects completed self-assessment questionnaires.

Seventy women (47 Active group, 23 Vehicle group) completed the study. The topical line plumper was statistically superior (P<0.05) to its vehicle in improving nasolabial folds (10.3% vs. 0.9%), glabellar lines (7.7% vs. 1.3%), crow’s feet (17.8% vs. 7.9%), and under eye wrinkles (20.3% vs. 5.8%), and in reducing pinch recoil time (10.1% vs. 5.7%). Clinical photography and self-assessment scores confirmed improvement to targeted wrinkle areas. Both topical line plumper and its vehicle were tolerated well.

Clinical Photography

Figure 1. Improvement in Under Eye Area Wrinkles in Clinical Photographs and Corresponding Ultrasound Images with Active Treatment
Study Methodology

<table>
<thead>
<tr>
<th>Design</th>
<th>Single center, randomized, double-blind, vehicle-controlled, parallel groups clinical trial</th>
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</thead>
<tbody>
<tr>
<td>Population/Inclusion</td>
<td>Caucasian women, aged 40-65 years, with moderate facial photodamage (scores of 4-6 on a 0-9 grading scale) on at least one of the following areas: glabellar lines, nasolabial folds and/or crow’s feet wrinkles</td>
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<td>Exclusion</td>
<td>Known allergies to skincare products; skin/eye conditions or uncontrolled chronic diseases that could interfere with evaluations; use of medications for skin or eye conditions; routine use of antiaging topical products, including prescription retinoids within 6 months, hydroxyacids, retinol and other antiaging cosmetics within 2 months; and/or cosmetic procedures within 6 months</td>
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<tr>
<td>Duration/Evaluation Time Points</td>
<td>16 weeks with evaluations at weeks 0, 4, 8, 12, and 16</td>
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Evaluation Tools

- **Clinical Measures**
  - Visual grading was conducted by a trained clinician using standardized grading scales
  - Glabellar lines, nasolabial folds, under eye wrinkles, and crow’s feet were graded using a modified Griffiths’ Scale (GS) from 0 (none) to 9 (severe) with 0.5 grade increments. In addition, nasolabial folds were also graded using a modified Wrinkle Severity Rating Scale (WSRS), a validated scale used to grade the effects of injectable fillers, ranging from 1 (absent) to 5 (extreme) with 0.5 grade increments

- **Objective Measures**
  - Timed pinch recoil for firmness/elasticity was measured on the lateral side of one eye area for each subject at each visit
  - Skin density was evaluated via ultrasound imaging of the crown’s feet area at weeks 0 and 16 for half of the subjects in each group as selected by the Investigator

- **Subjective Measures**
  - Self-assessment questionnaires were completed by subjects

- **Photography**
  - Standardized digital photographs of faces were taken at each visit

Statistics

- Clinical improvements were compared within and between groups using t-tests ($P<0.05$)
- Pinch recoil times were compared between groups using the Wilcoxon Rank Sum test ($P<0.05$)

Safety

- Adverse Events were recorded and tabulated

Test Products

<table>
<thead>
<tr>
<th>Product and Usage</th>
<th>Key Benefit Ingredients</th>
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</thead>
<tbody>
<tr>
<td><strong>Active Targeted Treatment Products:</strong></td>
<td>13% total proprietary blend of ingredients including:</td>
</tr>
<tr>
<td>Step 1 Activator</td>
<td>- N-acetyl tyrosinamide</td>
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<tr>
<td></td>
<td>- N-acetyl hydroxyproline</td>
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<td></td>
<td>- Glycolic acid</td>
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<tr>
<td>Step 2 Finishing Cream</td>
<td>- N-acetyl glucosamine</td>
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<td></td>
<td>- Triethyl citrate</td>
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<td></td>
<td><strong>Plus:</strong></td>
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<tr>
<td></td>
<td>- Palmitoyl oligopeptide and palmitoyl tetrapeptide-7</td>
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<tr>
<td><strong>Vehicle Targeted Treatment Products:</strong></td>
<td>No key benefit ingredients.</td>
</tr>
<tr>
<td>Vehicle formulations of Step 1 &amp; Step 2</td>
<td>Base formulations were provided in identical packaging as Active products.</td>
</tr>
<tr>
<td><strong>All-over Facial Moisturizers:</strong></td>
<td>No benefit ingredients</td>
</tr>
<tr>
<td>Day Cream SPF 20</td>
<td></td>
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<tr>
<td>Night Cream</td>
<td></td>
</tr>
<tr>
<td>Applied to entire face by both Active and Vehicle treatment groups after application of Step 1 &amp; 2 targeted treatments</td>
<td></td>
</tr>
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</table>

Results

70 subjects completed the study with 47 in the Active group (mean age 55.2 years) and 23 in the Vehicle group (mean age 58.5 years). Note: the number of subjects in each graded category depended upon meeting the minimum inclusion criteria for the particular graded parameter.

- Under eye wrinkles: N=47 Active, N=23 Vehicle
- Crow’s feet: N=37 Active, N=20 Vehicle
- Glabellar lines: N=30 Active, N=14 Vehicle
- Nasolabial folds: N=44 Active, N=16 Vehicle
- Tolerability was evaluated by assessing the signs and symptoms of objective (erythema, dryness/scaling) and subjective irritation as reported by subjects (burning, stinging, itching, tingling, tightness/dry feeling) globally on each subject’s face at each study visit. One mild product-related adverse event occurred for the Active group which included moderate skin irritation in the crow’s feet area. No product-related adverse events occurred in the Vehicle group.
Clinical Grading Results
The Active group significantly outperformed the Vehicle group on all clinically graded target lines and wrinkles with improvement as early as week 4 and continued improvement through week 16.

- **Under eye lines/wrinkles** improved significantly more with Active (20.3%) versus Vehicle (5.8%) using modified Griffiths’ Scale beginning at week 4, *P*<0.05. (Figures 1, 2 & 4)
- **Crow's feet wrinkles** improved significantly more with Active (17.8%) versus Vehicle (7.9%) using modified Griffiths' Scale beginning at week 8, *P*<0.05. (Figure 4)
- **Glabellar lines** improved significantly more with Active (7.7%) versus Vehicle (1.3%) using modified Griffiths’ Scale at week 16, *P*<0.05. (Figure 4)
- **Nasolabial folds** improved significantly more with Active (10.3%) versus Vehicle (0.9%) using Wrinkle Severity Rating Scale beginning at week 12, *P*<0.05. (Figures 3 & 5)

![Figure 2. Improvement to Under Eye Lines & Wrinkles](image2)
![Figure 3. Improvement to Nasolabial Folds](image3)

Objective Measures
Active group increased dermal density and firmness/elasticity.

- **Pinch recoil times** in the lateral area of the eye decreased significantly more with Active (10.1%) versus Vehicle (5.7%) by Week 16, *P*<0.05.
- **Dermal density** in ultrasound images of crow’s feet areas increased in the Active group. (Figure 1)

Clinical Photography

![Figure 4. Improvement in Glabellar Lines and Under Eye Lines & Wrinkles with Active Treatment](image4)
![Figure 5. Plumping of Nasolabial Folds with Active Treatment](image5)
Self-Assessment

Self-assessment supports clinical grading:

- Study participants agree with clinical grading; lines and wrinkles were less noticeable and appeared to be filling and plumping.
- Study participants agree that skin looks and feels firmer.

Conclusions

- The two-step topical line plumper, containing N-acetyl tyrosinamide, N-acetyl glucosamine, and triethyl citrate, provides measurable and visible skin plumping benefits.
- The Active topical line plumper group exhibited significantly greater improvement to clinician-graded targeted lines and wrinkles than the Vehicle control group, as early as week 4 and continuing through week 16.
- The Active topical line plumper increased skin firmness/elasticity and dermal density.
- The Active topical line plumper can be used to:
  - Supplement or maintain the effects of point-of-entry aesthetic procedures such as peels, microdermabrasion and light treatments as well as injectable anti-wrinkle therapies.
  - Complement the effects of injectable neurotoxins by providing a skin volumizing effect.
  - Treat a younger population (30+) who may not be ready for injectable therapies and needle-shy patients who are seeking an alternative to injections for skin volumizing antiaging benefits.
  - Volumize hard-to-inject treatment sites such as perioral rhytides and under eye lines/wrinkles.

References