

## BACKGROUND

Similar to facial skin aging, visible features of aged lips can be attributed to degradation of structural components of the skin including collagen and elastin fibers. Key features of lip aging include loss of volume, color, and definition as well as increases in lines/wrinkles and uneven skin texture. As a result these factors result in the loss of contrast between lips and surrounding skin and is associated with an older, aged appearance.

## OBJECTIVE

To assess the efficacy and tolerability of a novel, topical two-step lip treatment that contains hyaluronic acid (HA<sup>5</sup> LS).

## STUDY DESIGN

- Open-label, single-center clinical usage study.
- Four week study duration with visits at baseline, week 2 and week 4.

### Subject Inclusion Criteria

- Female subjects aged 22-40 years with Fitzpatrick Skin Types (FST) I to V who have self-perceived and clinically determined average-size lips.
- Must be a non-smoker and have not smoked within the last 5 years.
- Must have mild to moderate dryness on the lips at baseline with a score between 3 and 6 on modified Griffiths' scale.
- Must have mild to severe lip condition (lip texture/visual roughness and lines/wrinkles) with a score of 3 or higher on the modified Griffiths' scale.

### Treatment

Subjects were instructed to apply HA<sup>5</sup> LS (Step 1: Lip Treatment, Step 2: Lip Plumper) at a minimum of three times a day to ensure coverage 8 hours a day for four weeks. Subjects were instructed to apply HA<sup>5</sup> LS at least once prior to each follow-up visit, but not within one hour of the visit.

### Clinical Assessments

To capture the immediate effects of applying HA<sup>5</sup> LS, clinical grading and efficacy parameters were performed post-application at baseline with product on the lips. Long-term efficacy was assessed at week 2 and week 4. The following efficacy parameters were assessed on the lips using a 0-9 scale, where 0=none (best possible condition), 1-3=mild, 4-6=moderate, and 7-9=severe (worst possible condition), with half points allowed as necessary to differentiate degrees of severity:

- Lip Lines/Wrinkles
- Overall Lip Definition/Lip Contour
- Overall Lip Condition
- Lip Texture/Visual Roughness
- Lip Color/Rosiness
- Lip Plumpness

The efficacy parameters of cupping and scaling were assessed on a 0-6 scale, as described below:

- **Cupping:** 0=full, plump, 1=drawing at lip margin, 2=isolated area cupping at margin, 3=few areas cupping along lip margin, 4=cupping all along lip margin, 5=cupping more than lip margin, and 6=entire surface cupping
- **Scaling:** 0=none, 1=dull surface, 2=powdery flakes, 3=few lifting edges, 4=generalized lifting scale-mild, 5=generalized lifting scale-moderate, and 6=generalized lifting scale-severe

Tolerability assessments for erythema, edema, burning, stinging, itching and tightness were conducted on a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe) at all visits.

### Subject Self-Assessment Questionnaires

Subjects completed a self-assessment questionnaire at all visits.

### Instrumentation

Standardized digital photographs were taken using the VISIA-CR Imaging System (Canfield Imaging Systems) at baseline (pre- and post-application), week 2 and week 4 (pre- and post-application). A lip wrinkle image analysis was conducted with a software developed by Stephens & Associates using Image Pro Plus v7 software (Media Cybernetics, Inc., Rockville, Maryland). A digital caliper was used to measure lower lip plumpness, and Corneometer CM 825 (Courage + Khazaka, Germany) was used to measure skin hydration.

## RESULTS

- Thirty-one female subjects, aged 22-40 years with FST II-V who identified as Caucasian, African American, Native Hawaiian or other Pacific Islander and Asian ethnicities, completed the study.
  - Subjects presented with mean scores of 3.11 for lip scaling (dryness) and 4.14 for overall lip condition.
  - Five subjects voluntarily withdrew from the study (not due to adverse events).
- **Immediate effects:** Within 15 minutes of application, statistically significant improvements in mean scores compared to baseline were observed for all parameters (all  $p < 0.001$ ; Wilcoxon signed-rank test;  $n=36$ ).
- **Long-term effects:** Continuing significant improvements at weeks 2 and 4 compared to baseline for all parameters, except for Cupping at Week 2 (all  $p < 0.026$ ; Wilcoxon signed-rank test; Week 2:  $n=32$ ; Week 4:  $n=31$ ).
- HA<sup>5</sup> LS was well-tolerated with no increase in mean tolerability scores at each evaluation time. By Week 4, erythema, burning, stinging, itching, and tightness improved 100% in mean change from baseline.
  - No treatment-related adverse events were reported during the study.
- The lip wrinkle image analysis supported the long-term improvements observed by the investigator, with significant improvements at week 4 post-application in all parameters (all  $p < 0.001$ ; paired t-test;  $n=31$ ).
- Statistically significant improvements in mean scores for corneometer and digital caliper measurements at weeks 2 and 4 indicate an increase in intrinsic hydration and lip thickness, respectively, with continued use.
- HA<sup>5</sup> LS was highly rated by subjects with a statistically significant proportion of favorable responses for instant and long-term self-perceived efficacy and product texture and attributes.
  - At week 4, a significant proportion of subjects felt that HA<sup>5</sup> LS made their lips look and feel more full (90%), made their lips look naturally plump (90%) and added more volume to their lips (87%).

Figure 1: Instant Effects: Investigator Assessments (with product on the lips)

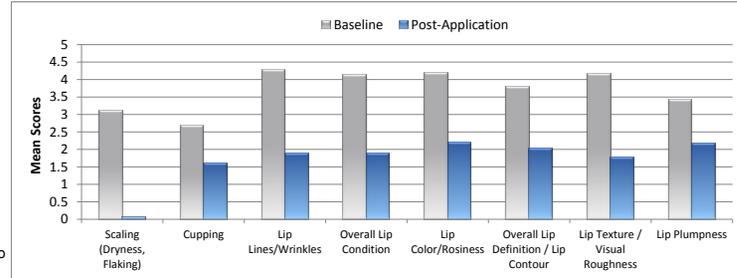


Figure 2: Instant Effects: Baseline vs. Baseline Post-Application (within 15 minutes of application)



Figure 3: Long-Term Effects: Investigator Assessments (no product on the lips)

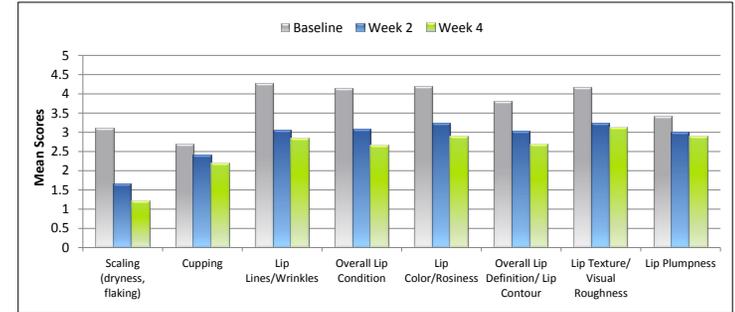


Figure 4: Long-Term Effects (no product on the lips)



Figure 5: Lip Wrinkle Image Analysis on VISIA-CR Standard 2 Photographs

	Total Count	Total Length (mm)	Total Width (mm)	Total Area (mm <sup>2</sup> )	Total Depth (arbitrary units)
Baseline	39.89	63.59	26.50	36.63	298.53
Baseline Post-Application	27.80*	41.24*	17.25*	22.02*	174.34*
Week 4 Post-Application	22.81*	33.86*	13.92*	17.94*	145.48*

\*Statistically significant improvements vs. baseline (all  $p < 0.001$ ; Wilcoxon signed-rank test for Total Count, paired t-test for all other parameters; baseline post-application:  $n=35$ , week 4 post-application:  $n=31$ )

Figure 6: Corneometer and Digital Lip Caliper Measurements

	Corneometer Measurements for Hydration (mean scores)	Digital Lip Caliper Measurements for Thickness in mm (mean scores)
Baseline	23.68	34.33
Week 2	32.67*	34.94 <sup>^</sup>
Week 4	36.26*	36.17 <sup>^</sup>

\*Statistically significant improvements vs. baseline (all  $p < 0.001$ ; paired t-test; week 2:  $n=32$ ; week 4:  $n=31$ )

<sup>^</sup>Statistically significant improvements vs. baseline (all  $p < 0.032$ ; paired t-test; week 2:  $n=32$ ; week 4:  $n=31$ )

## CONCLUSIONS

Results from this study suggest that HA<sup>5</sup> LS addresses the key features of lip aging, providing both instant and long-term benefits.

HA<sup>5</sup> LS may provide an alternative option to patients seeking a non-invasive treatment to rejuvenate and enhance the appearance of their lips with intrinsic benefits beyond cosmetic lipsticks.

## DISCLOSURES

This study was sponsored by Allergan. All authors met the ICMJE authorship criteria. All authors are employees of Allergan.