

# A Multi-Center, Double-Blind, Randomized, Comparator Controlled Trial Evaluating Topical Formulations for Skin Fragility of the Arms.

Orit Markowitz, MD;<sup>1</sup> Jean Carruthers, MD, FRCSC, FRC (Ophth.);<sup>2</sup> Carolyn Jacob, MD;<sup>3</sup> Tiffany Robison, MS, CCRC;<sup>4</sup> Faiza Shafiq, MBBS, CCRP;<sup>4</sup> and Alan Widgerow, MBBCh, MMed, FCS, FACS<sup>4,5</sup>

<sup>1</sup>Markowitz Medical, Manhattan, NY.

<sup>2</sup>Department of Ophthalmology, University of British Columbia.

<sup>3</sup>Chicago Cosmetic Surgery and Dermatology, SC, Chicago Cosmetic and Dermatologic Research, PLLC, Chicago Skin Science, LLC, Northwestern's Feinberg School of Medicine, Department of Dermatology.

<sup>4</sup>Alastin Skincare, Inc., a Galderma company.

<sup>5</sup>Center for Tissue Engineering, University of California, Irvine.

## Introduction

Dermatoporosis was the term coined by Kaya and Saurat in 2007 to describe fragile aging skin. The condition varies from simple skin thinning, beginning in most individuals from around 40 years, to marked atrophy with purpuric lesions in older individuals<sup>2</sup> (also known as senile purpura). It is the equivalent of the skin to osteoporosis, occurring as a result of an alteration in supportive dermal structures, including collagen, elastin and the ground substance of the extracellular matrix (ECM)<sup>2-5</sup>. Blood vessels are supported by the ECM in healthy young patients, and as the ECM regresses, the vessels become more vulnerable to damage, resulting in the unsightly bruising that is commonly reported by these patients<sup>5-7</sup>.

It was thus logical to approach this problem using a topical formulation that has demonstrated efficacy in re-establishing the ECM, diminishing bruising, and increasing skin tone. ReFORM & RePAIR COMPLEX with TriHex Technology® - R&R (Alastin Skincare, Inc. Carlsbad, CA) contains actives that aid in these regenerative and reparative functions<sup>1,8</sup>. In addition to ECM replenishment, the formulation contains peptides that stimulate macrophage absorption of red blood cells, and previous studies have corroborated efficient resolution of bruising<sup>9</sup>. Thus, this product is well suited for addressing acute episodic purpura, resolving bruising, decreasing inflammation, and recycling the ECM<sup>1</sup>.

## Objectives

This study was designed to evaluate the efficacy of R&R compared to a ceramide moisturizer for reducing acute episodic purpura events and improving atrophic skin associated with dermatoporosis over a 24-week period in subjects with varying degrees of the disease process.

## Materials and Methods

- Multicenter, randomized, comparator study. Eligible Subjects were men and women, ages 58-90 years presenting with a history of skin fragility (dermatoporosis) of at least two years, with or without active purpura at baseline.
- Eligible participants were randomized to receive R&R COMPLEX with TriHex Technology® to apply on one arm and a ceramide moisturizer (CeraVe) on the other arm. Subjects were instructed to apply the blinded designated product, twice daily, to both the extensor and volar aspect of the assigned treatment arm, and from shoulder to wrist, for the duration of the study. Each Subject was also dispensed a cleanser and sunscreen to use throughout the study.
- Subjects were evaluated at screening/baseline and follow-up visits at weeks 4, 8, 12, 16 and 24.
- Study diaries were completed by study participants to record new skin events (bruising/skin discoloration and skin tears) that occurred during study participation.
- Photographs of both arms were taken at every visit.

• Ultrasound measurements were collected using An EPISCAN-i-2000 system utilizing a 35MHz ultrasound probe (Longport Inc., Chadds Ford, PA) to measure skin dermal and epidermal thickness in millimeters. Measurements averages from each respective time point were then used to determine the impact of treatment with R&R compared to the ceramide moisturizer, where impact is the difference in epidermal thickness and represents the increased presence and integrity of the rete pegs/DEJ undulation changes between the two treatment arms for each patient.

• Line-field Confocal Optical Coherence Tomography (LC-OCT) imaging of the skin was performed on both the Alastin R&R and ceramide moisturizer arms, and in approximately the same area for each time point using pre-marked transparencies.

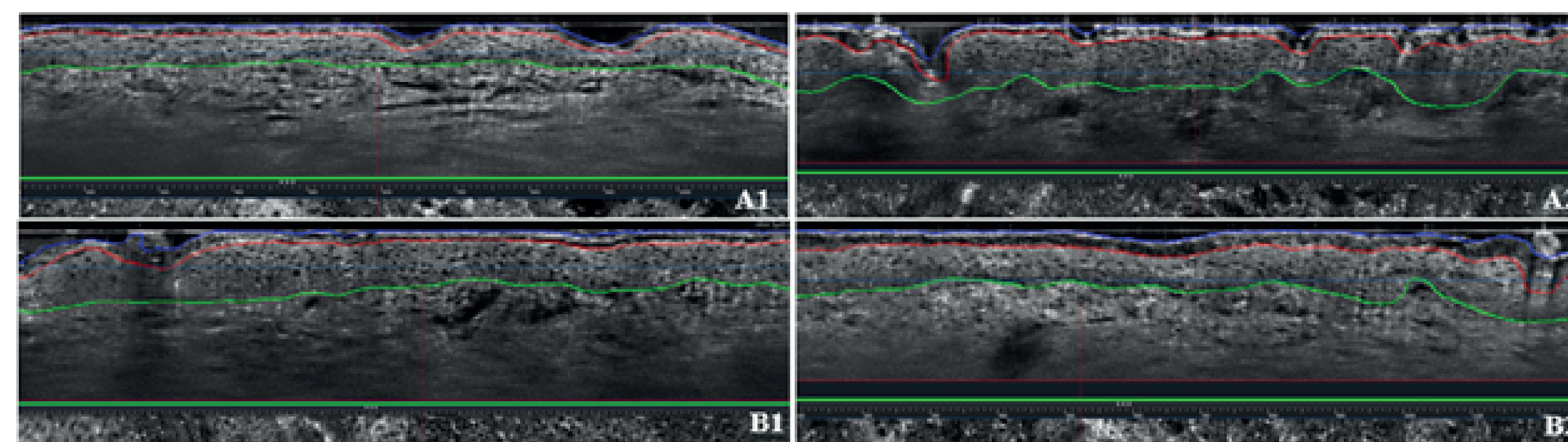
• Five participants underwent 3mm punch biopsies collected on the forearm of both arms prior to the use of the randomized topical products at baseline, 12 weeks post use of topical products (1 participant), and at 24 weeks post product use (4 participants). All biopsies underwent H&E (Hematoxylin and Eosin), Herovici and Movat staining, and were evaluated for histological changes by an independent blinded dermatopathologist.

• Measurements of skin barrier function and hydration were performed via TEWL measurements. Investigator Assessments were completed at baseline and week 24 to evaluate texture, crepiness, tone/color/evenness. Subject's global Aesthetic Improvement of Arm Skin Quality was also measured at every visit.

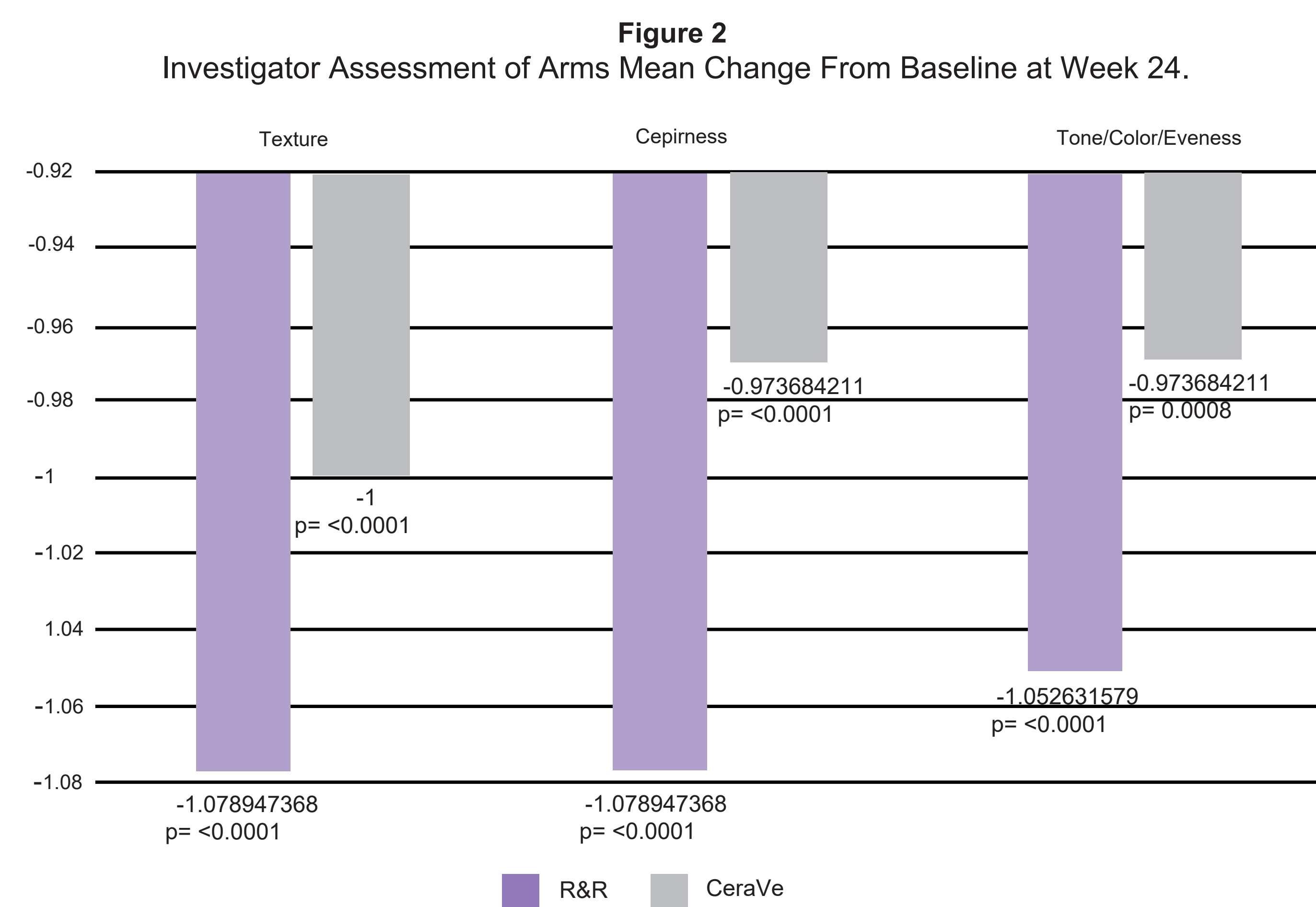
## Results

The primary measurement for evaluable LC-OCT study data demonstrated statistically significant changes from baseline to the week 12 midpoint in the dermo-epidermal junction (DEJ), where a mean difference of 3.05 (P= 0.058) was achieved between the Alastin R&R and ceramide moisturizer treated arms, which trended through week 24. Increased DEJ undulation was noted for the R&R treated arms (P= 0.317) compared to the ceramide moisturizer, which was demonstrated visually on imaging, where an increase in size and dilation of DEJ undulation was observed. (Figure 1).

**Figure 1**  
LC-OCT 2D vertically sliced imaging showing increased DEJ undulation on the R&R treated arm (A2) compared to baseline (A1) (top images) and compared to the ceramide moisturizer treated arm at the same time point (B2) vs baseline (B1) (bottom images).

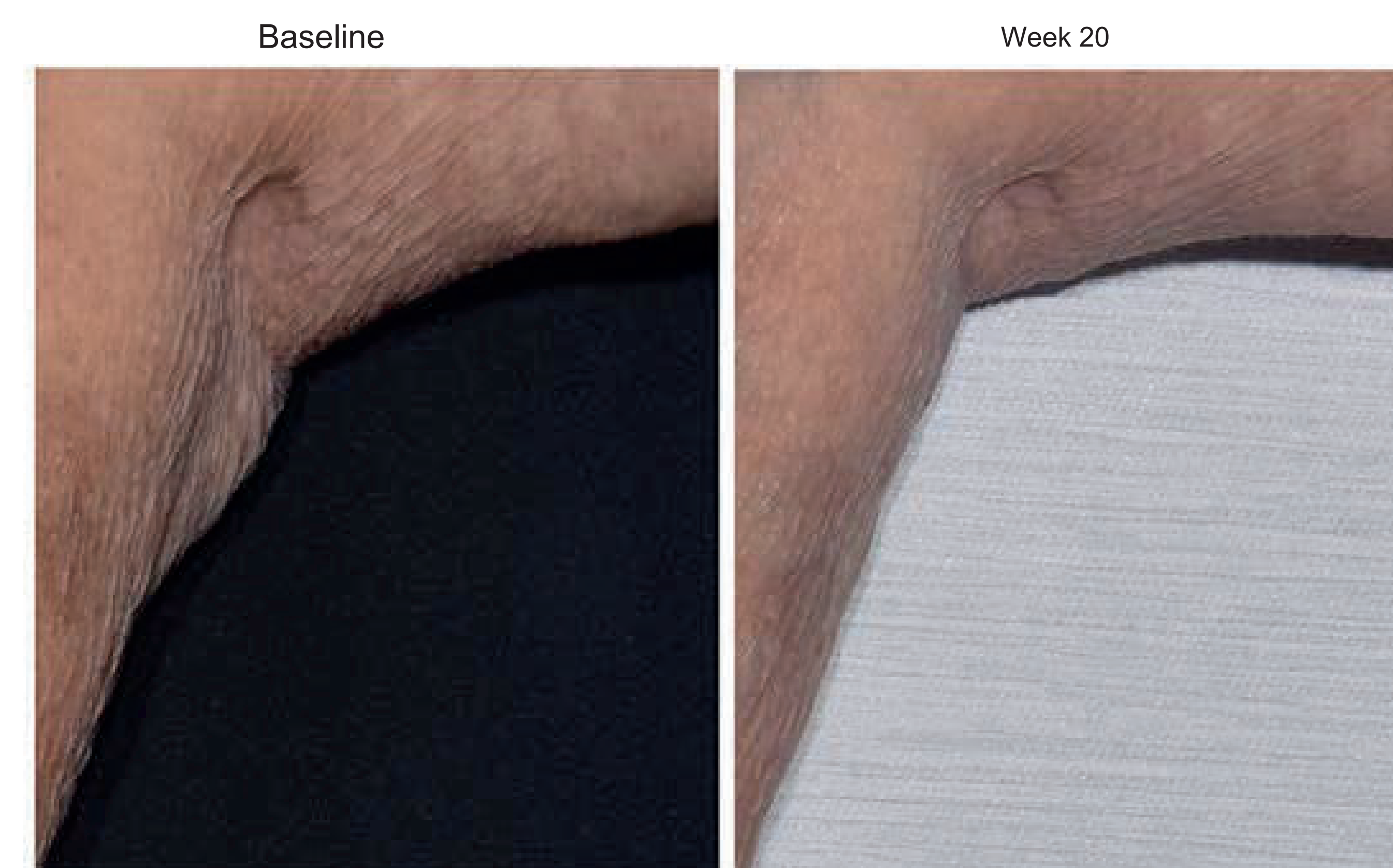


Statistically significant improvements were demonstrated across all assessed arm skin parameters at week 24 from baseline. The R&R treated arms achieved greater mean improvements compared to the ceramide moisturizer at week 24, where arm skin texture improvement was 16% greater than the ceramide moisturizer treated arm, arm skin crepiness improved 15% more, and arm skin tone/color/evenness improved 10% more compared to the ceramide moisturizer treated arm. (Figure 2).



Standard imaging of arms revealed improvements congruent with the statistically significant blinded investigator assessment of arms findings, across all evaluated arm skin parameters for the R&R treated arms. (Figure 3).

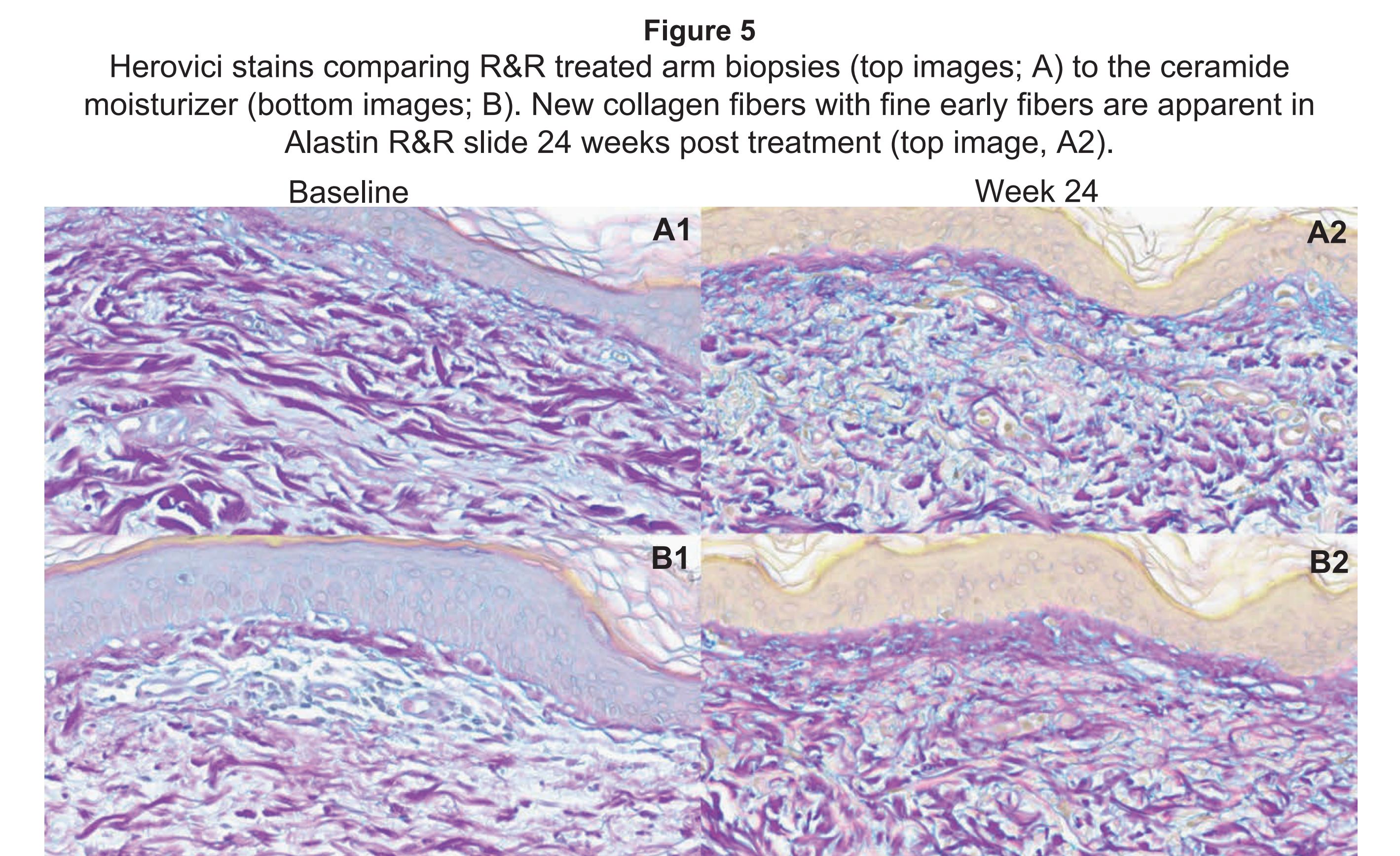
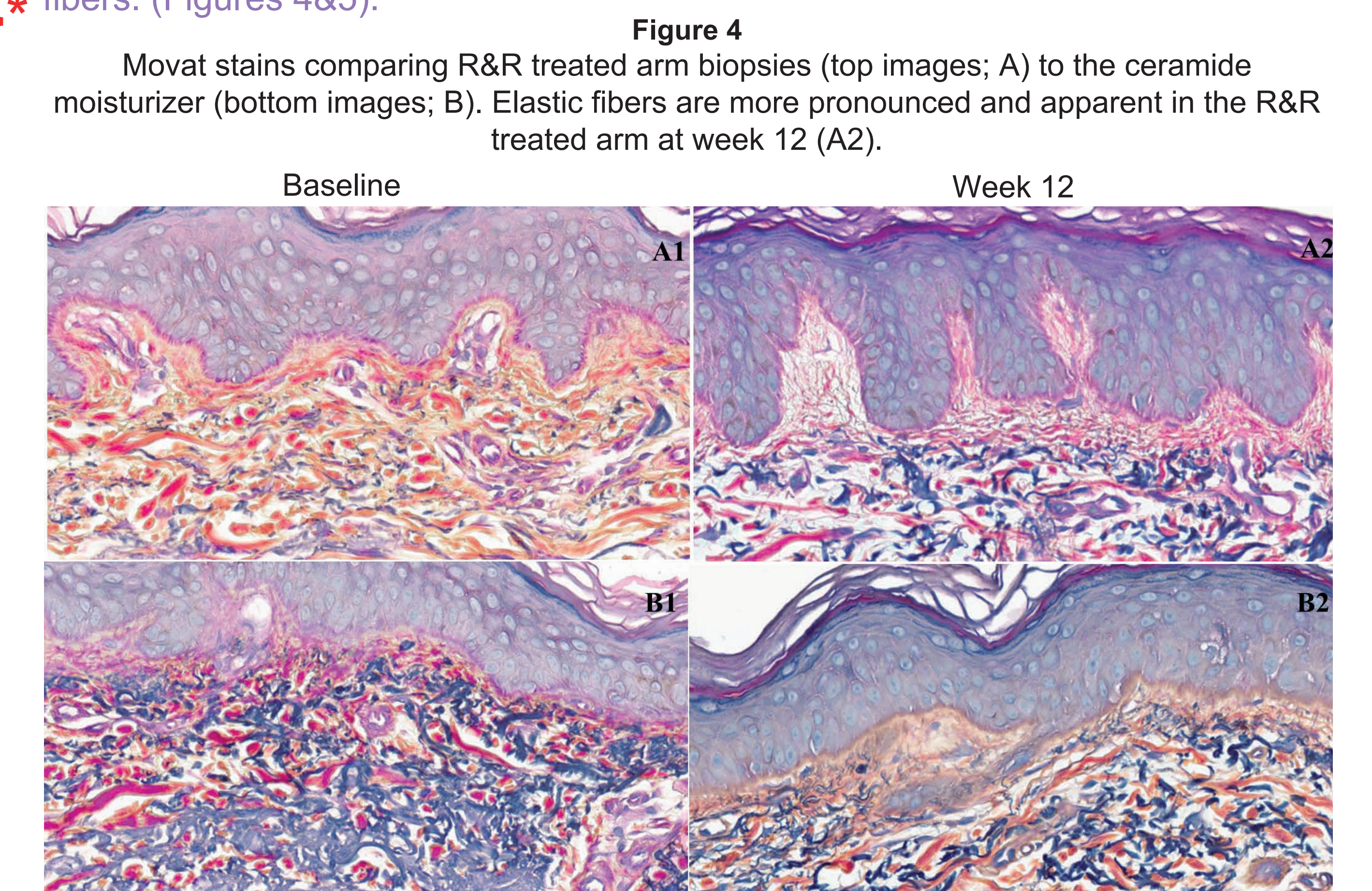
**Figure 3**  
Right arm (extensor side) demonstrating improvements in all parameters, texture (50%), tone/color/evenness (57%), crepiness (50%), post 20 weeks of treatment with R&R, which trended through week 24.



Skin barrier function and hydration measurements revealed overall greater improvements in the R&R treated arms over the 24-week treatment period, compared to ceramide moisturizer treatment. Both sides of the R&R treated arm demonstrated less TEWL (mean change extensor (-0.624) and volar (-0.556)) when compared to the ceramide moisturizer treated extensor (0.327) and volar (0.794) from baseline at week 24.

Ultrasound image analysis revealed an improvement in rete pegs and DEJ undulation for the R&R treated arm in 5 out of 6 study participants (83%), compared to the ceramide moisturizer treated arm (17%).

In 4 of the 5 biopsy specimens, Movat and Herovici stains displayed a marked greater increase in the Alastin R&R subject biopsies in new collagen and elastin fibers. (Figures 4&5).



## Conclusion

Dermatoporosis is a condition that is not widely recognized but is pervasive and ubiquitous in most populations starting around 40 years of age. The gradual thinning of the skin and loss of structural support manifests as crepiness, dryness, fragility, and bruising. This study has revealed that the condition can be managed using the Alastin ReFORM & RePAIR COMPLEX with TriHex Technology® formulation with notable early subjective changes noted in general skin health and diminished episodes of skin fragility. Importantly from an objective perspective, early improvements in DEJ status and ECM changes appear to herald encouraging potential long-term improvements in the condition.

## References

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