

# A clinical evaluation of the comparable efficacy of hyaluronic acid-based foam and ceramide-containing emulsion cream in the treatment of mild-to-moderate atopic dermatitis

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## Summary

**Background** A variety of prescription devices have been developed to improve barrier function in persons with atopic dermatitis. These products are based primarily on the use of occlusive agents to decrease transepidermal water loss, creating an environment for optimal healing.

**Aim** A newly developed hyaluronic acid based, pH neutral foam technology formulated to maximize humectancy and normalize transepidermal water loss was evaluated for its ability to optimize barrier function while minimizing unnecessary irritation.

**Methods** This double blind split body study enrolled 20 subjects with mild to moderate symmetrical atopic dermatitis involving body surface area greater than or equal to 10% using the arms or the legs as the target site. Subjects were randomized to apply the hyaluronic acid based emollient foam or the reference ceramide-containing emulsion cream to one side of the body with the other test product applied to the opposite side. Subject and investigator ratings were made for erythema, scaling, lichenification, excoriation, itching, stinging, and burning at baseline, week 2, and week 4.

**Results** Both formulations achieved statistically significant improvement in all clinical signs and symptoms of atopic dermatitis by week 4, however the hyaluronic acid foam achieved statistically significant improvement in overall eczema severity by week 2, whereas the ceramide-containing emulsion cream did not. The subject's preference statistically significantly favored the foam in terms of ability to spread, moisturize, ease of use, and lack of odor. In addition, the foam was preferred for effectiveness and ability to soothe.

**Conclusion** A prescription hyaluronic acid based foam device offers an aesthetic formulation with excellent efficacy in patients requiring an environment for barrier repair with mild to moderate atopic dermatitis.

**Keywords:** ceramides, hyaluronic acid, moisturizer, 510K device

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## Introduction

A major challenge in the management of atopic dermatitis is poor patient compliance with topical treatment

regimens.<sup>1</sup> Atopic patients with multiple treatment failures are familiar to the dermatologist; however, the failure may not be attributed to the ineffectiveness of the medication, but rather problems with medication application. Patients may be reluctant to use topical medications that are difficult to spread or sticky. Thus, an emollient with excellent esthetics may improve compliance and enhance efficacy when applied with topical corticosteroids, standard initial therapy for managing the

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inflammation associated with an atopic dermatitis flare.<sup>2</sup> The combination of topical corticosteroids and therapeutic emollients is considered optimal therapy, because epidermal barrier dysfunction has been identified as a fundamental problem in patients with atopic dermatitis. Further, the extent of barrier abnormality is largely predictive of the severity of the subsequent dermatitis.<sup>3</sup>

The recognition that epidermal barrier dysfunction is an important component of atopic dermatitis has led to the development of a variety of prescription barrier therapies designed to be used as monotherapy or as steroid-sparing adjunctive agents. These prescription barrier therapies are considered medical devices as they have been FDA cleared through the 510K route. One cleared device contains a ceramide-containing mixture of lipids in oil-in-water emulsion cream, while a second contains hyaluronic acid in a lipid-rich emollient foam. This primary research endpoint was the effectiveness of the prescription barrier therapy devices in reducing overall eczema severity when used as monotherapy in the treatment of mild-to-moderate atopic dermatitis. The secondary research endpoint was the different patient preferences and perceptions between the two study products.

## Methods

### Participants

This single-centered, double-blinded, randomized, split body study enrolled 20 female subjects, 18 years or older, with mild-to-moderate atopic dermatitis. Approval to perform this study was granted by Concordia Institutional Review Board. Eligibility requirements included investigator assessed mild-moderate atopic dermatitis, defined by investigator global assessment, with symmetrically distributed target lesions on the arms or legs. Each target lesion required a minimum score of 3, on a 6-point target lesion severity scale (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, 5 = severe), at baseline. Subjects were required to have a minimum total body surface area involvement, including the investigator evaluated target lesions, of 10% to ensure an appropriate level of experience with the esthetics of each product. Additionally, participants agreed to avoid all other topical medications and moisturizers during the study period and for 2 weeks prior to study enrollment.

A two-tailed Mann-Whitney test for nonparametric data was used to analyze the two data sets. Analyses were conducted both intragroup and intergroup. Statistical significance was defined at  $P = 0.05$  or less.

### Treatment

The arms or legs were identified as target sites for dermatologist investigator evaluation. Subjects were randomized based on target site assignment to apply the hyaluronic acid-based emollient foam (Hylatopic; Onset Therapeutics, Cumberland, RI, USA) to one limb and a ceramide-containing emulsion cream (EpiCeram; Promius Pharma, Bridgewater, NJ, USA) to the opposite limb twice daily. In addition, patients were instructed to treat all remaining nontarget sites affected by atopic dermatitis with the randomized barrier therapy, yielding a split body design. However, only target sites on the legs or arms were evaluated by the investigator.

### Evaluation

Blinded investigator ratings, using a standardized target lesion severity rating, were made at baseline, week 2, and week 4 for overall eczema severity, erythema, scaling, lichenification, excoriation, itching, stinging, and burning. The subjects evaluated their skin appearance for redness, peeling, dryness, stinging/burning, and overall skin irritation at the same time points. A standardized six-point ordinal rating scale was used for both investigator and subject assessments (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, 5 = severe). After 4 weeks of treatment with both products, patients completed a survey to report which features of the two study products they favored. Among these features, patients indicated which product attributes they preferred in the following categories: spreadability, moisturization, soothing, skin absorption, and lack of odor. Additionally, subjects were asked to identify the product they believed was more effective, which product they would be more willing to pay for, and which product they preferred.

## Results

Eighteen of 20 subjects successfully completed the study. One subject was discontinued by the investigator because of worsening atopic dermatitis at all sites. A second subject was lost to follow-up. Compliance was determined from subject diaries, and no compliance issues were identified.

The blinded investigator assessment revealed that the hyaluronic acid-based emollient foam and the ceramide-containing emulsion cream both achieved statistically significant improvement ( $P < 0.001$ ) in all clinical signs and symptoms of atopic dermatitis by week 4. However, the hyaluronic acid-based emollient foam achieved

statistically significant improvement in overall eczema severity by week 2 ( $P = 0.016$ ), whereas the ceramide cream did not ( $P = 0.155$ ; Fig. 1). No safety or tolerability issues were present with either formulation.

In all categories (spreads, moisturizers, soothes, ease of use, rubs in, odor, better efficacy), the hyaluronic acid emollient foam was statistically preferred over the ceramide cream by the subjects. Additionally, the subjects stated that they would purchase the hyaluronic acid emollient foam over the ceramide cream, and this finding was statistically significant, as well (Fig. 2). Only in the continued use category was there parity between

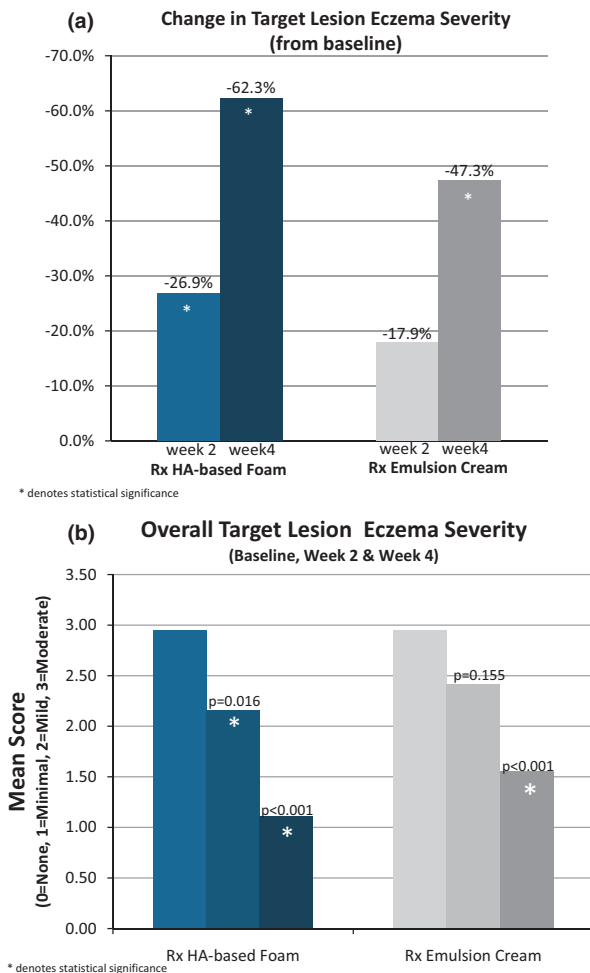


**Figure 1** (a) The hyaluronic acid-based emollient foam and the ceramide-containing emulsion cream both were efficacious in reducing the overall atopic dermatitis severity score; however, the hyaluronic acid-based emollient foam produced a statistically significant reduction in severity at week 2, whereas the ceramide-containing emulsion cream did not. (b) The change in overall severity from baseline was  $-62.3\%$  for the hyaluronic acid-based emollient foam and  $-47.3\%$  for the ceramide-containing emulsion cream at week 4.

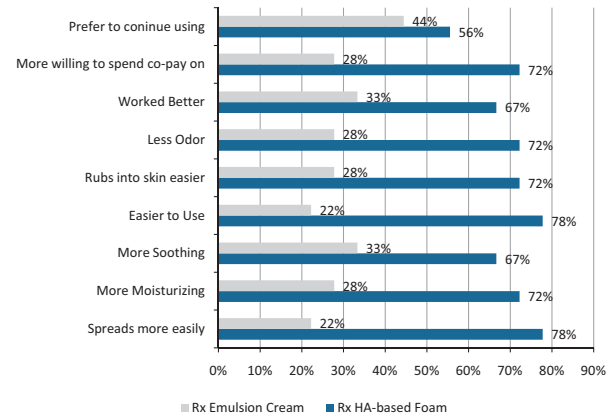


**Figure 2** Subjects statistically significantly preferred the hyaluronic acid-based emollient foam in all esthetic categories evaluated.

the hyaluronic acid emollient foam and the ceramide cream.

## Discussion

Prescription barrier therapies' ability to restore a compromised skin barrier may have a role in the treatment of mild-to-moderate atopic dermatitis. Hyaluronic acid may be pivotal in controlling the natural epidermal responses to injury, including keratinocyte migration and proliferation in wound-healing settings and barrier repair in atopic dermatitis.<sup>4</sup> Previous transepidermal water loss studies have demonstrated the comparable ability of a hyaluronic acid-based emollient foam and a ceramide-containing emulsion cream to recover compromised epidermal barrier function.<sup>5</sup>

The novel foam delivery for the hyaluronic acid-based emollient foam may have accounted for the subject preference. Emollient foams typically spread more easily and leave little residue, making them esthetically pleasing for all body areas, including hair-bearing sites. They do not stain clothing and possess little odor. These factors could improve patient compliance with a treatment regimen. Emollient foams are distinctly different than some of the original ethanol-based foams. They do not contain an astringent vehicle and for this reason do not produce stinging and burning when placed on barrier-compromised skin. Further, emollient foams do not dissolve when released from the aerosolized can. Thus, an emollient hyaluronic acid-based emollient foam may be useful in the treatment phase of mild-to-moderate atopic dermatitis when combined with a topical corticosteroid or in monotherapy to preserve barrier function in the maintenance phase of atopic dermatitis management.

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