A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

JDD

DRUGS • DEVICES • METHODS

The Importance of Skincare in Eczema: A Novel Over-the-Counter Routine Improves Signs and Symptoms in Patients with Eczema

ISSN: 1545 9616

October 2023 • Volume 22 • Issue 10 (Supplement 2)

This supplement to the *Journal of Drugs in Dermatology* was funded by Galderma Laboratories, L.P.

October 2023 Volume 22 • Issue 10 (Supplement 2)

TABLE OF CONTENTS

Journal of Drugs in Dermatology

The Importance of Skincare in Eczema: A Novel Over-the-Counter Routine Improves Signs and Symptoms in Patients with Eczema

INTRODUCTION

ORIGINAL ARTICLES

Importance of Skin Care in Eczema Patients

Peter Lio MD,[a] Adelaide A. Hebert MD[b]

[a]Medical Dermatology Associates of Chicago, Chicago, IL
[b]UTHealth McGovern Medical School, Houston, TX

In the United States, the National Eczema Association estimates that 1 out of every 10 people have some form of eczema over their lifetime. As any dermatologist can attest, managing patients with eczema and eczema-prone skin can be challenging. For these patients, maintaining good skin hydration and supporting the skin barrier function are two of the most important actions that can be taken. Due to the wide range of over-the-counter (OTC) products available, clinicians benefit by having available data to compare brands and specific products, since not all products are equal.

This supplement includes results from 4 studies of OTC skincare products (Cetaphil®, Galderma Laboratories, Dallas, TX) specifically designed for patients with eczema or eczema-prone skin. These skincare formulations incorporate soothing ingredients, including colloidal oatmeal, proprietary filaggrin breakdown products, and ceramides. Colloidal oatmeal has moisturizing properties that help restore and nourish the skin barrier and is an ingredient recognized by the US Food and Drug Administration for eczema. Filaggrin breakdown products support the skin's acid mantle, helping maintain a normal pH and healthy enzymatic activity. Ceramides help restore the barrier, allowing healing of the skin.

Specifically, the studies compared itch relief products, evaluated a comprehensive skincare regimen and assessed the effect of an eczema cream on signs and symptoms of atopic dermatitis. In an efficacy and tolerability evaluation, Hawash et al compared 2 popular OTC eczema itch relief products – Ich Relief Gel and Itch Relief Moisturizing Cream – and found that the gel provided rapid itch relief and significantly outperformed the moisturizing cream. Hawley and colleagues conducted a multicenter study of a novel 3-step eczema regimen consisting of Itch Relief Gel, Eczema Soothing Moisturizer, and Eczema Flare Relief Cream. This study showed that using the 3-step regimen resulted in statistically significant improvements on several validated assessment tools, including the Eczema Area and Severity Index (EASI), the Patient Oriented Eczema Measure (POEM), and ItchyQuant. Nguyen et al report that 2 OTC moisturizers applied twice daily (Eczema Soothing Moisturizer and Itch Relief Moisturizing Lotion) achieved clinically important improvements in skin hydration, skin barrier, and ceramide levels. In addition, Nguyen and colleagues enrolled a diverse range of patients and were able to show Exzema Smoothing Moisturizer was beneficial across Fitzpatrick skin phototypes. Finally, Hebert et al show that an Eczema Flare Cream had good efficacy in improving atopic dermatitis as shown by significantly reduced scores on the Scoring Atopic Dermatitis (SCORAD) assessment, improvements in signs and symptoms, and quality of life.

We trust that these results will help practicing dermatologists educate their patients and select OTC skincare products with proven benefits.

DISCLOSURES

Dr. Lio reports research grants/funding from AbbVie, AOBiome, National Eczema Association; is on the speaker's bureau for AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, MyOR Diagnostics, ParentMD, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme, Verrica; reports consulting/advisory boards for Alphyn, AbbVie, Almirall, Amyris, Arcutis, ASLAN, Boston Skin Science, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, Dermavant, Eli Lilly, Galderma, Janssen, Johnson & Johnson, Kimberly-Clark, LEO Pharma, Lipidor, L'Oreal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Skinfix, Theraplex, UCB, Unilever, Verrica Yobee Care; stock options with Codex, Concerto Biosciences and Yobee Care. In addition, Dr. Lio has a patent pending for a Theraplex product with royalties paid and is a Board member and Scientific Advisory Committee Member of the National Eczema Association.

Dr Hebert has received research grants paid to medical school from Pfizer, Arcutis, Dermavant, Abbvie;, Leo, Lilly; honoraria from Galderma, Pfizer, Arcutis, Incyte, Beiersdorf, Almirall, Amyrt, Boehringer Ingelheim, Ortho Dermatologics; and as an advisor for Ortho Dermatologics; Sanofi Regeneron, GSK.

AUTHOR CORRESPONDENCE

Adelaide A. Hebert MD
E-mail:..... Adelaide.A.Hebert@uth.tmc.edu

doi:10.36849/JDD.SF388641

ORIGINAL ARTICLE

Journal of Drugs in Dermatology

Efficacy Of Over-The-Counter Cream in Reducing Eczema Signs

Adelaide A. Hebert MD,[a] Mathieu Grivet-Seyve PhD,[b] Sarah Anjuwon MS,[b] Nathalie Piccardi PhD,[c] Nadège Lachmann PhD,[d] Agustin Cruz MD,[e] Christine Emesiani PharmD[e]

[a]UTHealth McGovern Medical School, Houston, TX
[b]Galderma R&D, Dallas, TX
[c]Galderma R&D, Lausanne, Switzerland
[d]Galderma Sensitive Skincare Faculty, Lausanne, Switzerland
[e]Galderma Laboratories, L.P., Dallas, TX

ABSTRACT

Background: Eczema (also called atopic dermatitis) is a chronic, relapsing skin disease characterized by erythema, scaling, and pruritus.
Methods: *Study 1.* A double-blind, uncontrolled study in patients with mild-moderate eczema, ≥2 flares in prior 2 months, and baseline Scoring Atopic Dermatitis (SCORAD) score ≤15. Participants applied Eczema Flare-Up Relief Cream (EFRC) (N=65) BID for 56 days. Efficacy was assessed by SCORAD, patient-oriented SCORAD, skin sensitivity, Dermatology Life Quality Index (DLQI), and digital photography. Standard safety assessments were performed. Study 2. A 21-day open study of EFRC (N=50) to evaluate tolerability as well as its effect on eczema.
Results: *Study 1.* EFRC significantly reduced overall SCORAD scores from baseline to day 56 (11.6 to 4.9, or a 57% reduction). The patient-oriented SCORAD was reduced from 18.6 to 6.8 from baseline to day 56. At day 56, itch and pain improved in 70.4% of children and 62% of adults. DLQI scores were decreased by 75% in adults and 61% in children by day 56. Global skin sensitivity, assessed by the Sensiscale 10-item questionnaire, was 13.1 at baseline and 3.6 at day 56, an improvement of 72%. *Study 2.* EFRC improved eczema-prone skin after 7 and 21 days.
Conclusions: *Study 1* showed that EFRC had good efficacy with significant reductions in overall SCORAD scores and subscores for the extent and intensity of eczema and subjective symptoms. Skin sensitivity also improved along with quality of life. Studies 2-3 also had significantly positive results and good tolerability.

J Drugs Dermatol. 2023;22:10(Suppl 2):s5-9.

INTRODUCTION

Eczema affects approximately 31 million people in the United States and is characterized by dryness, itchiness, scaling, roughness, irritation, or discoloration as well as periodic unpredictable flares.[1] Developing a good skincare regimen, including the use of moisturizing creams targeted to eczema-prone skin can reduce the likelihood of flares.[4] Cetaphil® Eczema Flare-up Relief Cream (EFRC) was specially developed to help repair damaged skin barrier, relieve uncomfortable symptoms, and reduce flare occurrence of those with eczema and eczema-prone skin.

MATERIALS AND METHODS

***Study 1:* Efficacy Clinical Trial**

This was a multi-center (USA, Ukraine, and Georgia), double-blind, uncontrolled comparison study in patients aged 4 to 60 years with mild-to-moderate eczema and sensitive skin, a SCORAD score between 15 and 40 at screening and <15 at baseline visit, and at least 2 flares in the 2 months prior to screening. Patients applied EFRC twice daily on the face and body and were allowed to use hydrocortisone as needed for flare. All patients or parents provided written informed consent, and the study received ethics committee approval and was conducted in accordance with Good Clinical

Practice. Prior to participant enrollment, Institutional Review Board (USA) and local ethics committees in other countries reviewed and approved the study designs.

Efficacy assessments included severity Scoring of Atopic Dermatitis (SCORAD), patient-oriented SCORAD (PO-SCORAD), Sensiscale-10 questionnaire to evaluate skin sensitivity, the Dermatology Life Quality Index (DLQI), and digital photography. SCORAD evaluated the extent of eczema, the intensity of signs/symptoms on a scale of 0=absence to 3=severe, and subjective symptoms (pruritus and sleep) on a 0 to 10 visual analog scale. The 10-item Sensiscale-10 evaluation included inquiries on degree of overall skin irritation during the past 3 days and severity of skin conditions (tingling, burning, sensations of heat, tautness, itching, pain, general discomfort, hot flashes, and redness) during the past 3 days with a worst score of 100 and best score of 0.[5] The 10-item DLQI is a health quality-of-life (QoL) scale specific to dermatologic disorders, with a scale of 0 to 30, and higher scores indicating more severe QoL impairment. Parents of children aged 4 to 14 years completed the PO-SCORAD and a Children's DLQI. Standard safety assessments were performed. Tolerability evaluations included erythema, edema, dryness/scaling, burning, itching, and stinging on scales of 0=none to 3=severe.

Study 2: **Open-label Trial**

This was an open-label, in-use study conducted in Europe (n=50) to evaluate the cutaneous and ocular tolerability, cosmetic acceptability, and performance of EFRC. To be eligible, patients had to be aged 18 to 60 years, could have any ethnic background and skin phototype, had eczema-prone skin with itchy, red, dry scaly skin (mild-to-moderate severity). Twenty participants had active lesions, and 30 had atopic-prone skin. All participants had sensitive skin (as defined by Sensiscale-10). It was conducted according to Good Clinical Practice and all patients completed a written informed consent form. The study was considered non-interventional and, as such, did not require approval by an ethics committee.

Statistical Analysis

For both studies, descriptive statistics were used in the statistical analysis of quantitative data by time point and zone. Categorical data were summarized in frequency and percentage points. T-test, Shapiro-Wilk test (a=0.01), and Wilcoxon signed rank tests were performed. For the subjective evaluation questionnaire, a dichotomic derived variable was used to divide participants into two categories: positive answer (1) or negative answer (0). The proportion of participants with a positive answer was compared to the theoretical value of 50% using a binomial test to assess whether a statistically significant majority of participants had a positive opinion. For all analyses, the type 1 error will be set at a=0.05 in two-tailed approach.

TABLE 1.

Subject Demographic Information, ITT Population	
	N (%)
Gender	
Female	49 (75.4%)
Male	16 (24.6%)
Mean age (range), years	25 (4-60)
Fitzpatrick skin type	
I	5 (7.7%)
II	33 (50.8%)
III	16 (24.6%)
IV	5 (7.7%)
V	6 (9.2%)
VI	0 (0.0%)
Test area	
Body	43 (66.2%)
Face/scalp	10 (15.4%)
Face/scalp and body	12 (18.5%)

FIGURE 1. Reduction in mean SCORAD scores from screening to day 56.

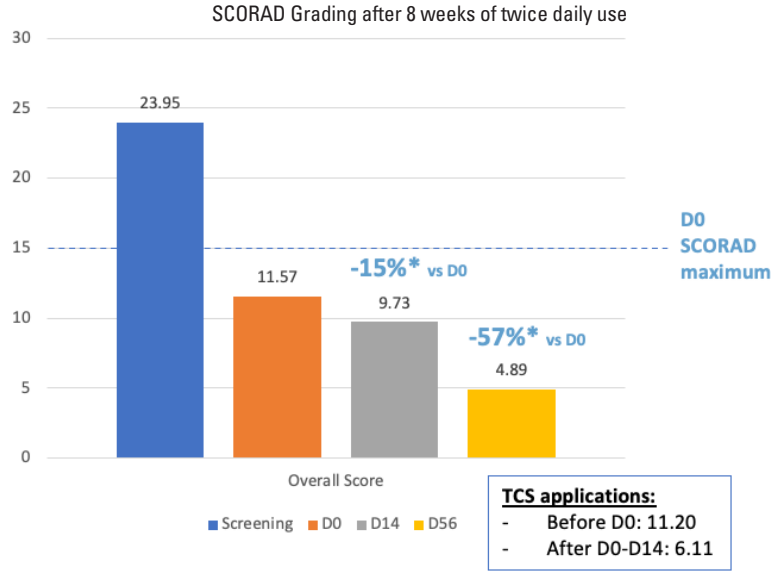


FIGURE 2. Improvement in DLQI scores from baseline to day 56.

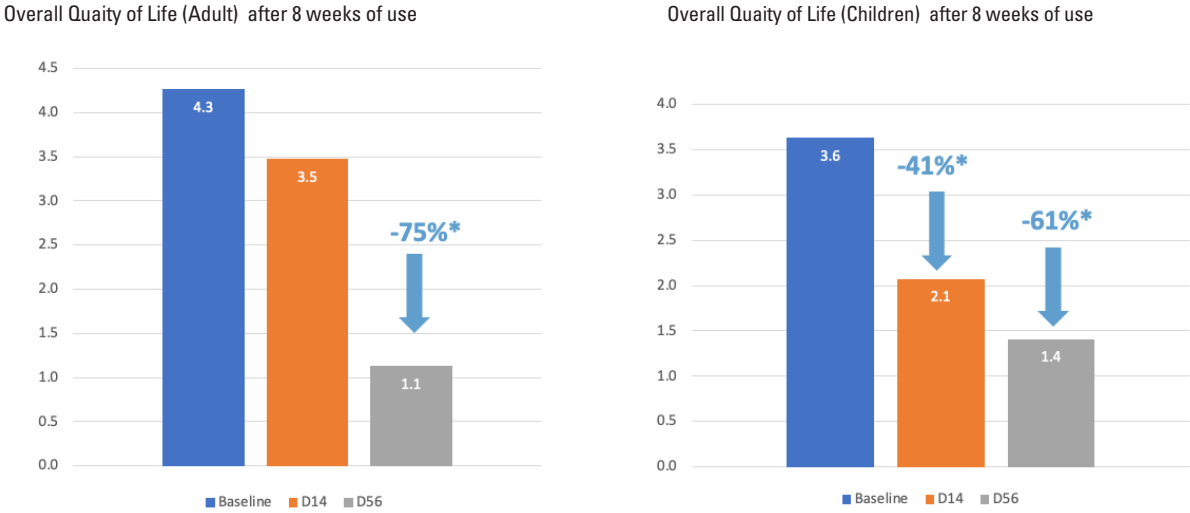
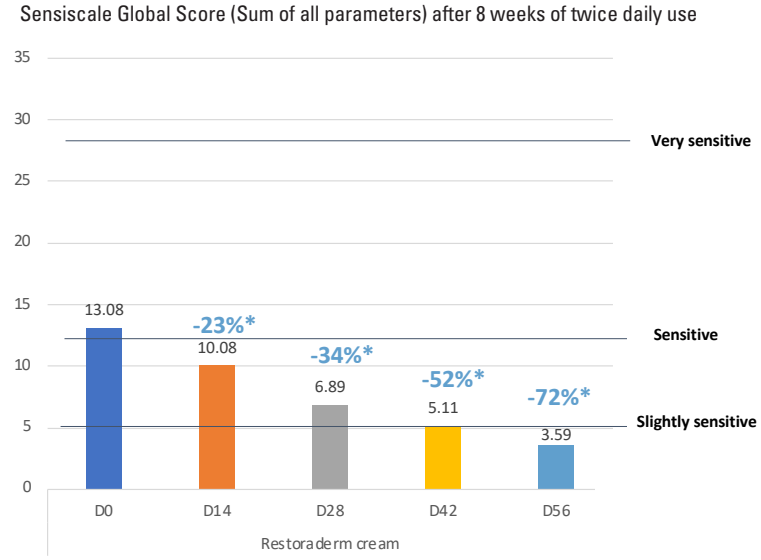


FIGURE 3. Improvement from baseline to day 56 in skin sensitivity as assessed by Sensiscale-10 Global Score (A) and Sensiscale-10 (AD related signs) (B).

(A)



(B)

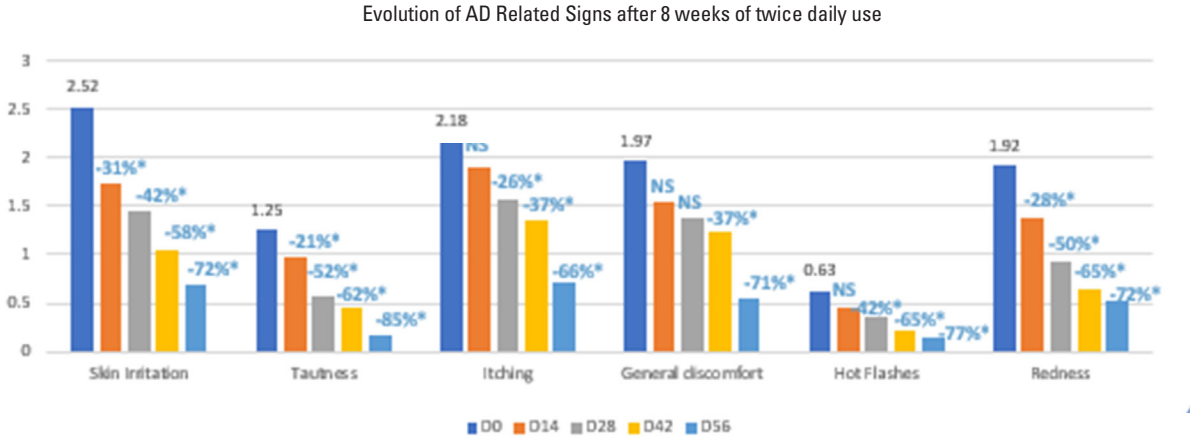
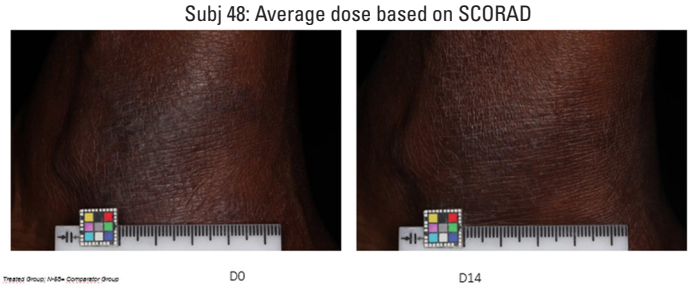


TABLE 2.

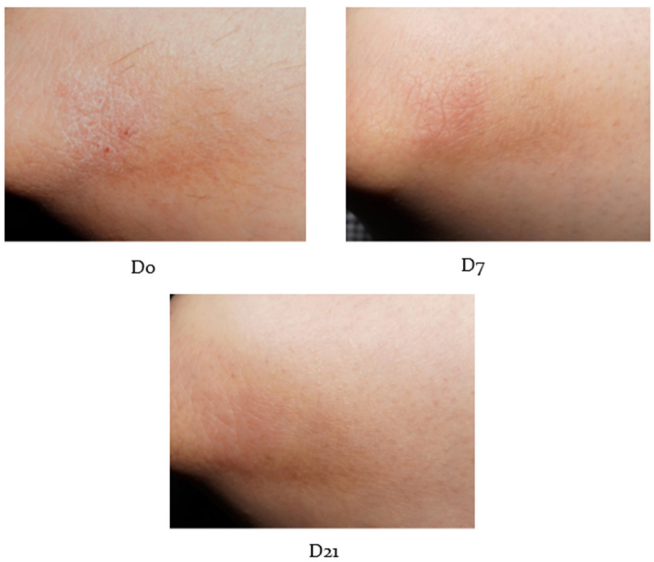
Skin Improvements in Study 2 at Days 7 and 21		
	Day 7	Day 21
Smoothness (tactile)		
Mean change	57%	85%
% patients with improvement	98%	98%
Dryness (visual)		
Mean change	57%	96%
% patients with improvement	88%	98%
Scaling (visual)		
Mean change	67%	98%
% patients with improvement	89%	98%
Skin redness (visual)		
Mean change	38%	80%
% patients with improvement	61%	91%
Itching		
Mean change	75%	98%
% patients with improvement	94%	98%

FIGURE 4. Clinical photo of patient treated with EFRC.



Treated Group; N-50- Comparator Group

FIGURE 5. Clinical photography.



RESULTS

***Study 1:* Efficacy Clinical Trial**

A total of 65 participants were included in the intent-to-treat (ITT) population, and applied EFRC. Table 1 presents patient demographics for Study 1.

The mean SCORAD score was reduced from 11.57 at baseline to 4.89 (-57%, $P<0.001$) at day 56 of twice-daily EFRC use (Figure 1). The mean extent (percentage of area) of involvement was significantly reduced from baseline 7.8 to 2.8 at day 56 (-64.1%, $P<0.001$), and intensity decreased from 2.42 at baseline to 1.05 at day 56 (-56.8%, $P<0.001$). The subjective symptoms of pruritus and sleep loss on dermatologist-assessed SCORAD improved from 1.53 to 0.61 (-60.2%, $P<0.001$) by day 56. The majority of participants maintained a SCORAD score of 15 or below for the 8-week period. The overall PO-SCORAD scores improved from 18.6 at baseline to 6.8 at day 56 (-63%, $P<0.001$). Additionally, there was a statistically significant reduction in itch and sleep disturbance on PO-SCORAD at day 56. In response to the question of how itchy, sore, or painful their skin had been over the last week, 70.4% of pediatric participants and 62.2% of adults reported improvement.

Quality-of-life scores were significantly improved in both children and adults who used twice-daily EFRC by 61% and 75%, respectively (Figure 2). Figure 3 shows the improvements ($P<0.001$) in Sensiscale Global Scores (a measure of skin sensitivity) as well as the evolution of individual eczema-related items ($P<0.001$ for all at day 56). A representative case of eczema improvement in dark skin is shown in Figure 4.

***Study 2:* Open-label Trial**

A total of 36 female and 13 male White patients participated, with a mean age of 41 ± 2 years and phototype I-III skin. All had sensitive skin, and 31 participants reported sensitive eyes. EFRC improved skin smoothness, dryness, scaling, and redness on days 7 and 21 (Table 2). Sensiscale evaluations at day 21 showed significant improvements in all individual aspects of skin sensitivity (irritation, tingling, burning, heat sensation, tautness, itching, pain, general discomfort, hot flashes, and redness) as well as an 86% improvement in mean overall score. As shown in Table 3, participants had favorable impressions of EFRC. Figure 5 shows representative clinical photos.

In Study 1, no adverse events were reported at any study sites. Tolerability evaluations showed a statistically significant decrease (improvement) for erythema and burning on days 14 and 56. Stinging was improved at week 8, and itching decreased after 8 weeks of use compared to baseline. Tolerability was good in Study 2, also.

DISCUSSION

Keeping skin hydrated and moisturized is a key preventative for skin affected by eczema and atopic dermatitis. These studies show that EFRC is effective in providing relief to patients with eczema as reflected by SCORAD, PO-SCORAD, DLQI, and Sensiscale scores. In addition, it is very well tolerated at the cutaneous level without producing any signs of eye irritation. Finally, EFRC improved skin roughness, dryness, scaling, and erythema. Separate studies have provided positive supportive results in both symptoms and skin hydration, also with good safety.

DISCLOSURES

Dr Hebert has received research grants paid to medical school from Pfizer, Arcutis, Dermavant, Abbvie, Leo, Lilly; honoraria from Galderma, Pfizer, Arcutis, Incyte, Beiersdorf, Almirall, Amyrt, Boehringer Ingelheim, Ortho Dermatologics; and as an advisor for Ortho Dermatologics; Sanofi Regeneron, GSK

REFERENCES

1. Silverberg JI. Public health burden and epidemiology of atopic dermatitis. *Dermatol Clin.* 2017;35:283-9.
2. McCleary, KK. The More Than Skin Deep "Voice of the Patient" Report. 2020. Available at: https://www.morethanskindeep-eczema.org/report.html. Accessed May 1, 2023.
3. Wang J, Zhou Y, Zhang H, et al. Pathogenesis of allergic diseases and implications for therapeutic interventions. *Signal Transduct Target Ther.* 2023;8:138.
4. Tollefson MM, Bruckner AL, Section On D. Atopic dermatitis: Skin-directed management. *Pediatrics.* 2014;134:e1735-44.
5. Misery L, Jean-Decoster C, Mery S, et al. A new ten-item questionnaire for assessing sensitive skin: The sensitive scale-10. *Acta Derm Venereol.* 2014;94:635-9.

AUTHOR CORRESPONDENCE

Christine Emesiani PharmD
E-mail:..... Christine.Emesiani@galderma.com

doi:10.36849/JDD.SF388641

October 2023 s10 Volume 22 • Issue 10 (Supplement 2)

ORIGINAL ARTICLE

Journal of Drugs in Dermatology

Evaluation of Efficacy and Tolerability of Two Over-the-Counter Eczema Itch Relief Products

Ahmed Hawash MD PhD,[a] Thu Nguyen PhD,[b] Ana Mantilla DPM,[b] Christine Emesiani PharmD,[b] Matthew Meckfessel PhD[b]

[a]University of Miami, Miller School of Medicine, Miami, FL

[b]Galderma Laboratories, L.P., Dallas, TX

ABSTRACT

Background: Study to compare efficacy, tolerability, and patient perception between an over-the-counter itch relief gel (IRG) and itch relief moisturizing cream (IRMC) after a single application.

Methods: Single-center, randomized, blinded, split-body study comparing IRG vs IRMC in adults with eczema-prone skin and mild-to-moderate itch. Assessments included itch relief duration upon application, itch severity (0=none to 9=severe at baseline [BL], 8, 12, and 24 hours), tolerability (0=none to 3=severe), and self-assessment questionnaire about product attributes and preference.

Results: Thirty-three females and males with a mean age of 49.7 completed the study. Average time to itch relief was 28.5 seconds for IRG vs 41.8 for IRMC ($P<0.05$), with first onset at 5 seconds. In the IRG group, itch severity was reduced from 4.4 at BL to 1.4 at 8 hours; in comparison, itch was reduced from 4.4 at BL to 2.6 at 8 hours in the IRMC group ($P<0.05$). Both products significantly relieved itch vs baseline at all time points. IRG had better tolerability, with burning/stinging going from 1.5 at BL to 0.8 at 24 hours vs 1.5 at BL to 1.2 at 24 hours for IRMC ($P<0.05$). There was a trend in favor of IRG vs IRMC on the patient satisfaction self-assessment questionnaire.

Conclusions: IRG provided rapid itch relief and significantly outperformed IRMC. Both products significantly improved itch severity for up to 24 hours after application, with IRG outperforming IRMC at 8 hours. Additionally, IRG moderated stinging/burning sensations better than IRMC. Further, IRG was preferred by participants over IRMC.

J Drugs Dermatol. 2023;22:10(Suppl 2):s10-15.

INTRODUCTION

Eczema, also called atopic dermatitis, is an inflammatory skin disease characterized by skin barrier damage, which translates to itch, dry skin, rash, scaling, blisters, and skin infections.[1] More than 31 million people – or 10% of the population – in the United States have some form of eczema, including people of all races and ethnicities.[2,3] Itch or pruritus is one of the primary symptoms of eczema, as well as one of the most bothersome for patients.[4,5] Pain may also occur with eczema and is sometimes associated with scratching.[4,6] Eczema pruritus is different from other types of itch, and can be harder to treat.[7,8] Pruritus has a significant impact on quality of life, leading to sleep disturbances, alterations in liver function, and impaired mental health (anxiety, depression, and impaired relationships are common).[5] Indeed, more than two-thirds of children and approximately one-third of adults with atopic dermatitis, a common form of eczema, experience sleep disturbances, often secondary to itching, which impact both the patients' and their parents' ability to function.[5,9-13] In addition, Silverberg et al report that the impact of eczema on mental health is greater than that of heart disease, diabetes, or hypertension.[5] Further, as the severity of eczema increases, so do negative ratings of overall health and day-to-day satisfaction.[5]

As mentioned above, skin barrier damage, itch, and dry skin are highly interrelated.[1] Diseases such as eczema alter skin barrier function, resulting in transepidermal water loss and activation of pruritic nerve fibers.[1] Itch drives the desire to scratch. However, scratching does not always usually relieve itch, rather it worsens it in a phenomenon termed the "itch-scratch cycle."[1,14] It's important to break the itch-scratch cycle, as scratching can exacerbate eczema and damage the skin.[1,8] The itch-scratch cycle, which in eczema is primarily due to activation of non-histaminergic cutaneous nerves, not only worsens skin-barrier damage but also increases release of itch-provoking cytokines in the skin.[8,15] Few medications effectively

manage eczema-associated itch, and reducing the likelihood of itch is a key management strategy.[8] Adherence is also a problem in this setting since more than 50% of adults with eczema express concerns about long-term use of prescription treatments and finding treatment ineffective.[16,17] It has been reported that 44% of patients with eczema discontinue prescription medications. A good daily routine of moisturizing the skin with products designed to reduce itch replenishes the skin barrier and is the first step to managing eczema-associated pruritus.[1,18]

Over-the-counter (OTC) products developed specifically for eczema and itch incorporate ingredients such as colloidal oatmeal to relieve itch and ceramides to support the skin barrier function. We conducted a clinical study to evaluate efficacy, tolerability, and patient perceptions of 2 OTC itch products – Itch Relief Gel (IRG) and Itch Relief Moisturizing Cream (IRMC) – after a single application. IRG contains 0.5% colloidal oatmeal along with a proprietary filaggrin technology that includes filaggrin breakdown products (arginine and sodium PCA) while IRMC includes 1% pramoxine hydrochloride and ceramides; both are free of fragrances and steroids. In addition, the IRG product has a unique roller-ball mechanism of application, which is both soothing and stays cool throughout multiple applications without need for refrigeration.

MATERIALS AND METHODS

This was a single-center, randomized, blinded, split-body (left/right), single application study, conducted in accordance with Good Clinical Practice. Participants administered a single application of Itch Relief Gel (Cetaphil® Eczema Restoraderm Itch Relief Gel, Galderma, Dallas, TX) to one side of the body and Itch Relief Moisturizing Cream (CeraVe® Itch Relief Moisturizing Cream, L'Oreal Active Cosmetics Division, Paris, France) to the other side according to a pre-determined randomization sequence after a 3-day washout period. All participants provided informed consent.

Participant Population

Females and males with atopic dermatitis or eczema-prone skin of all Fitzpatrick skin types were eligible to participate if they had mild-to-moderate itch (defined as a score of 3-6 based on a 10-point scale where 0=none, 1-3=mild, 4-6=moderate, and 7-9=severe) related to atopic dermatitis on each side of the body with no more than 1-point difference between sides. In addition, qualified test areas were required to be symmetrical body parts, eg, left forearm vs right forearm, left hand vs right hand, etc. Participants had to agree to a 3-day washout period for topical corticosteroids and antiseptics and topical/oral antibiotics and discontinue use of current skincare products for duration of the study, be free of dermatologic or systemic diseases that would interfere with results, be able to comprehend an informed consent form, and be willing to comply with protocol requirements. In addition, patients were instructed to refrain from shower or bath from baseline to 24-hour visit and to avoid ultraviolet exposure for the same period. Subjects were excluded if they had participated in a clinical study involving the same test sites within the prior 7 days, or had any of the following: uncontrolled eczema, a history of acute or chronic disease that could interfere with the study, history of cancer or other serious/progressive disease including family history of melanoma, planned hospitalization during study period, pregnant/lactating or planning pregnancy, a medical diagnosis of type 1 diabetes, or known hypersensitivity to any cosmetics, personal care products and/or fragrances. There was a 3-day washout prior to study entry for topical corticosteroids or antiseptics, and a 1-week washout for oral or topical antibiotics and for initiating/changing any systemic treatment for concomitant diseases. Medical treatments or cosmetic products outside of study products that could interfere with the study assessments were prohibited from baseline to the 24-hour visit.

Assessments

To evaluate efficacy, patients rated their itch severity and onset of itch using a 10-point visual analog scale (VAS) at baseline and at 8, 12, and 24 hours after application. Time to itch relief was captured and itch relief duration was calculated. Subjects completed a self-assessment questionnaire for each side of the body for product attributes/skin feel and their preferences between products. Safety was assessed by collection of adverse events and subjective tolerability (burning/stinging based on a 4-point scale with 0=none, 1=mild, 2=moderate, and 3=severe).

Statistical Analysis

Paired T-test was used to determine equality/inequality between sides treated with IRMC vs IRG, using alpha=0.05. Because the tests are two-sided, the *P* values are compared to half of alpha (0.025). For the evaluations over the 24-hour test periods, paired-t tests were used to compare individual scores at each post-baseline time point relative to their respective baseline scores for both efficacy and tolerability scores. Additionally, comparisons between the treatment cells were made using the null hypothesis that the mean change from baseline was equal between the 2 treatment cells at post-baseline time points. For timing until itch relief, data was calculated as average and statistical analysis was performed between the 2 treatment groups. For questionnaires, the onset of itch response frequencies was compared between the 2 treatments. The test null hypothesis was that the proportion of the combined designated favorable responses (Strongly Agree and Agree) was equal between the 2 treatment cells.

RESULTS

A total of 33 patients were enrolled, and all completed the study. Participant demographics are presented in Table 1. As shown, majority of the study patients were females, and the mean age was 49.7 years.

Efficacy

Both IRG and IRMC significantly ($P<0.05$) improved itch from 8 hours until study end (24 hours). Subjects reported that there was a superior reduction in itch on the IRG-treated side compared to the IRMC-treated side at 8 hours (Figure 1, 1.39 vs 2.58, $P<0.025$).

TABLE 1.

Subject Demographics	
	N (%)
Gender	
Female	24 (72.7%)
Male	9 (27.2%)
Mean age (range), years	49.7 (25-69)
Race/Ethnicity	
White/Caucasian	3 (9.1%)
Black/African American	7 (21.2%)
Hispanic/Latin American	8 (24.2%)
Asian/Indian	13 (39.4%)
Other	2 (6.1%)
Fitzpatrick skin type	
I	2 (6.1%)
II	4 (12.1%)
III	5 (15.2%)
IV	7 (21.2%)
V	8 (24.2%)
VI	7 (21.2%)

TABLE 2.

Clinical Assessment for Time to Itch Relief (Time in Seconds), ITT Population		
	IRG	IRMC
Mean ± SD	28.48 ± 16.15	41.84 ± 21.72
Median	30	37
Min, Max	5, 66.56	7, 108
P value	0.0026	

As shown in Table 2, the duration of itch relief and onset of relief were better in the IRG group vs the IRMC group, with a mean of 28.48 seconds for IRG and 41.84 seconds with IRMC (P=0.0026). As shown in Table 2, the maximum time to relief was shorter in the IRG group, as was the time.

Both products significantly improved itch severity; however, IRG reduced itch to a greater degree than IRMC (P=0.0023 at the 8-hour timepoint).

The patient satisfaction questionnaire results showed a favorable perception of both IRG and IRMC among the study participants (Figure 2). Patients gave IRG higher scorings for rapid soothing, cooling sensation, easy to apply, and continuous itch relief. There was also trend toward patients indicating they preferred IRG over IRMC (Figure 3).

Safety

There were no adverse events or unexpected reactions of any kind for any patient during the study period. Both products were well tolerated at 24 hours post-baseline (Figure 4), with IRG statistically significantly superior (0.79 vs 1.18, P<0.05).

DISCUSSION

OTC products that reduce/relieve itch and support skin barrier function are essential in eczema treatment. This study showed that IRG had superior efficacy and tolerability compared to IRMC. IRG achieved itch relief significantly faster and outperformed IRMC in decreasing itch severity at 8 hours post-application. In addition, there was a trend in favor of IRG in the patient self-assessment questions. Participants may have preferred the roller-ball application mechanism with IRG, and its soothing properties may also have contributed to the rapid onset of action observed.

FIGURE 1. Rating of itch severity for IRG and IRMC at baseline and 8, 12, and 24 hours after application.

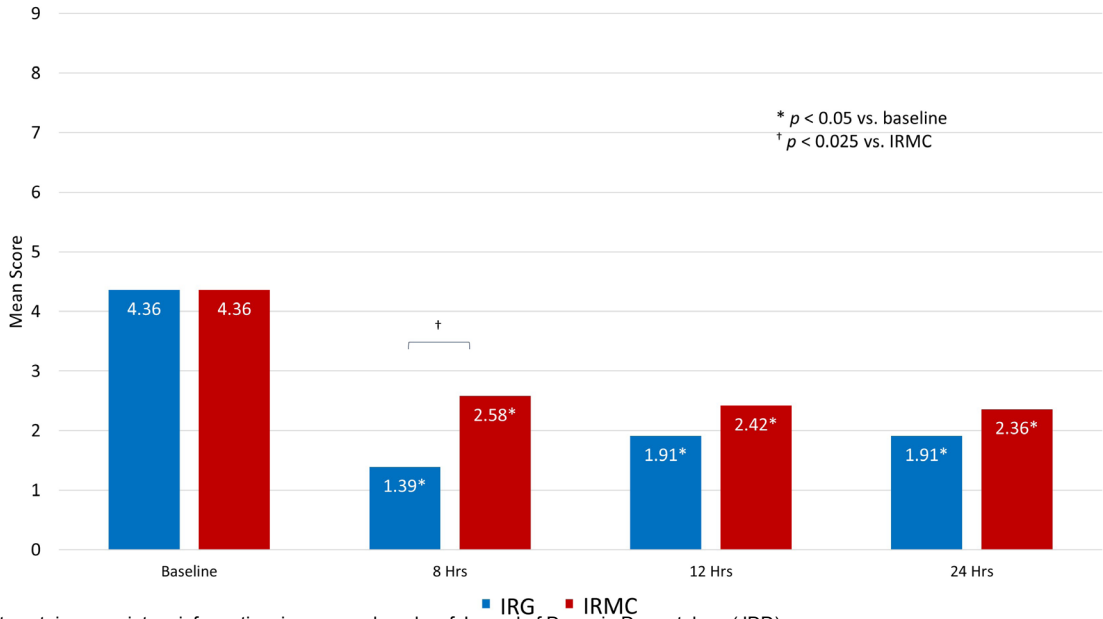
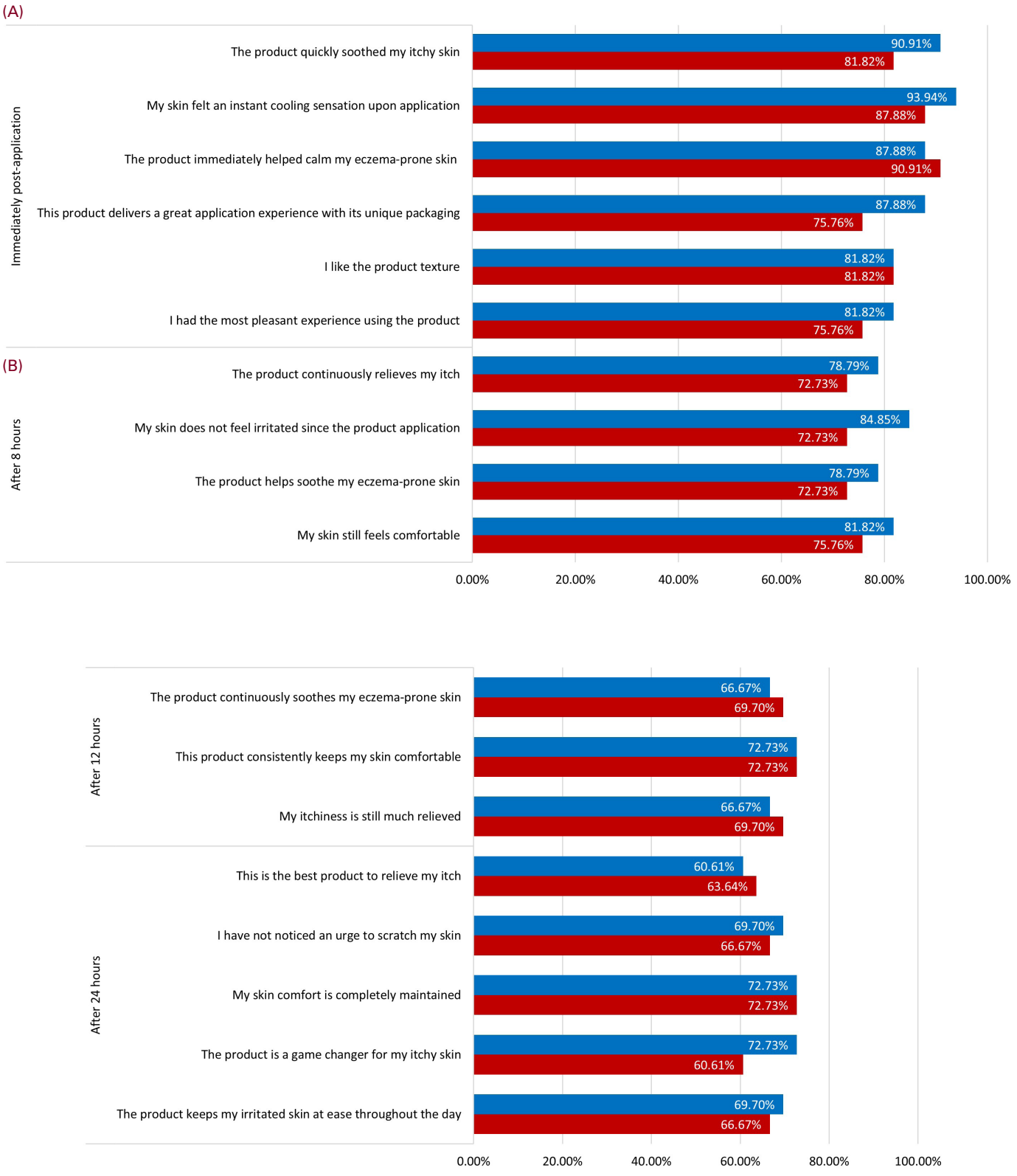
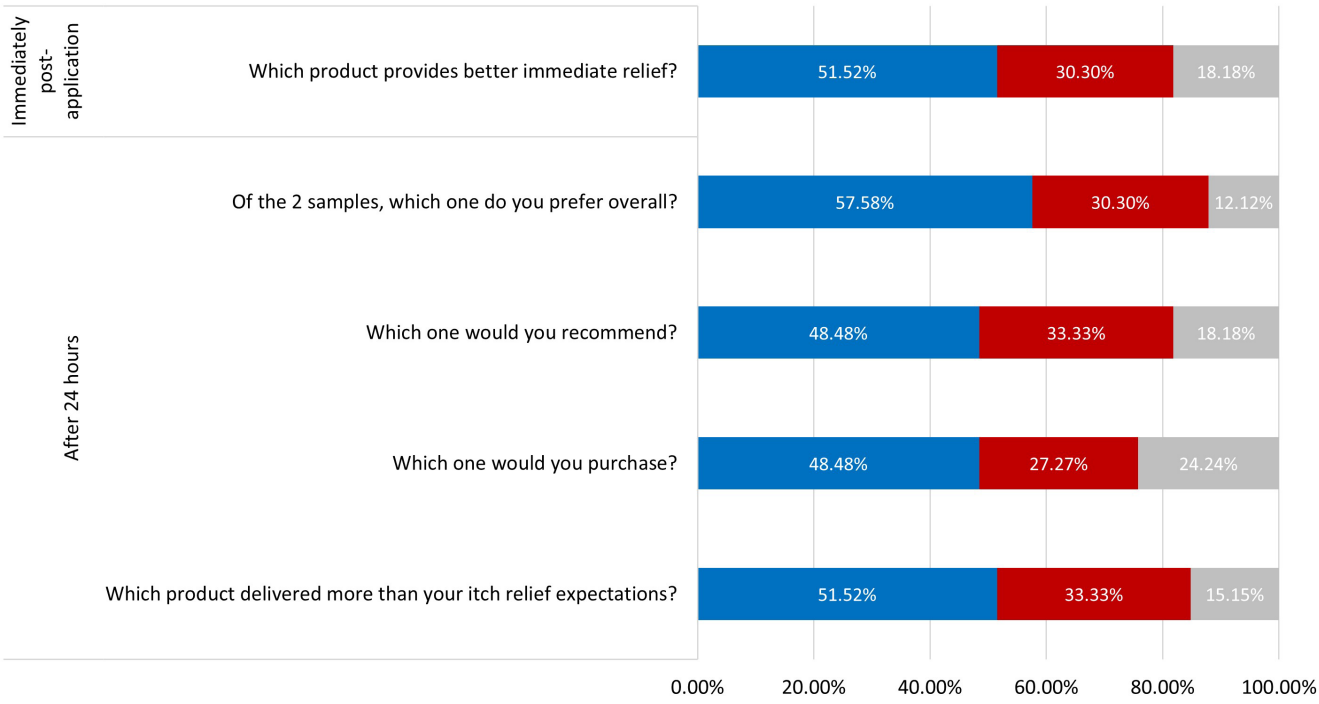


FIGURE 2. Participant satisfaction questionnaire results at each timepoint after application, ITT population.



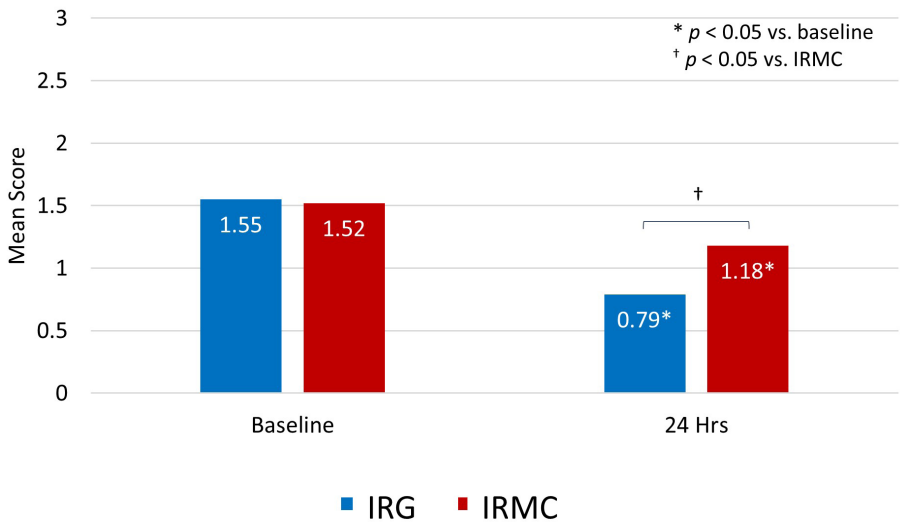
Blue bars = IRG, red bars = IRMC.

FIGURE 3. Patient preferences results.



Blue bars = IRG, red bars = IRMC, grey bars = no preference.

FIGURE 4. Burning/stinging scores, ITT population.



Both products were designed for eczema-prone skin and to protect and hydrate the skin. However, the IRG product includes a cool touch applicator that helps to soothe the skin almost immediately. Additionally, IRG contains 0.5% colloidal oatmeal to help relieve irritated skin and reduce itch. Colloidal oatmeal has long been used to soothe itch and has been shown to significantly improve clinical outcomes in patients with eczema and is consistently well-tolerated.[19] Additional ingredients such as butylene glycol, pentylene glycol, and hydroxyphenyl propamidobenzoic acid help to condition and soothe while tocopherol (Vitamin E), arginine, and sodium PCA help restore the skin barrier and support the cutaneous microbiome. The filaggrin technology attracts hydration and further helps to strengthen the skin barrier. Reduced amounts of cutaneous filaggrin may have a significant role in aggravating impaired epidermal barrier function, particularly in adults.[20] Ceramides constitute an important part of the stratum corneum, accounting for approximately 50% of its lipid composition.[20]

This Itch Relief Gel is effective and well accepted by patients, with itch relief attained in as little as 30 seconds after application that was sustained for 24 hours. This is vital for patients with eczema-prone skin, since this population wants treatments that work fast and provide sustained itch relief.

DISCLOSURES

Dr Hawash has nothing to declare; Dr Nguyen, Dr Mantilla, Dr Emesiani, and Dr Meckfessel are employees of Galderma Laboratories, LP.

REFERENCES

1. Yosipovitch G, Misery L, Proksch E, et al. Skin barrier damage and itch: Review of mechanisms, topical management, and future directions. *Acta Derm Venereol.* 2019;99:1201-9.
2. Abuabara K, Magyari A, McCulloch CE, et al. Prevalence of atopic eczema among patients seen in primary care: Data from The Health Improvement *Network*. *Ann Intern Med.* 2019;170:354-6.
3. Silverberg JI. Public health burden and epidemiology of atopic dermatitis. *Dermatol Clin.* 2017;35:283-9.
4. Maarouf M, Kromenacker B, Capozza KL, et al. Pain and itch are dual burdens in atopic dermatitis. *Dermatitis.* 2018;29:278-81.
5. Silverberg JI, Gelfand JM, Margolis DJ, et al. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. *Ann Allergy Asthma Immunol.* 2018;121:340-7.
6. Silverberg JI, Gelfand JM, Margolis DJ, et al. Pain is a common and burdensome symptom of atopic dermatitis in United States adults. *J Allergy Clin Immunol Pract.* 2019;7:2699-706 e7.
7. National Eczema Association. Managing itch. https://nationaleczema.org/eczema/itchy-skin. Accessed: May 1, 2023.
8. Barbarot S. Targeting the itch-scratch vicious circle in atopic eczema. *Br J Dermatol.* 2022;186:608.
9. Fishbein AB, Cheng BT, Tilley CC, et al. Sleep disturbance in school-aged children with atopic dermatitis: Prevalence and severity in a cross-sectional sample. *J Allergy Clin Immunol Pract.* 2021;9:3120-9 e3.
10. Meltzer LJ, Booster GD. Sleep disturbance in caregivers of children with respiratory and atopic disease. *J Pediatr Psychol.* 2016;41:643-50.
11. Silverberg JI, Garg NK, Paller AS, Fet al. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. *J Invest Dermatol.* 2015;135:56-66.
12. Silverberg JI, Chiesa-Fuxench Z, Margolis D, et al. Epidemiology and burden of sleep disturbances in atopic dermatitis in US adults. Dermatitis. 2022;33:S104-S13.
13. Lee DG, Gui XY, Mukovozov I, et al. Sleep disturbances in children with atopic dermatitis: A scoping review. J Cutan Med Surg. 2023:12034754231159337.
14. Rinaldi G. The itch-scratch cycle: A review of the mechanisms. *Dermatol Pract Concept.* 2019;9:90-7.
15. Rosen JD, Fostini AC, Yosipovitch G. Diagnosis and management of neuropathic itch. *Dermatol Clin.* 2018;36:213-24.
16. Tangthanapalakul A, Chantawarangul K, Wananukul S, et al. Topical corticosteroid phobia in adolescents with eczema and caregivers of children and adolescents with eczema: A cross-sectional survey. *Pediatr Dermatol.* 2023;40:135-8.
17. McCleary, KK. The More Than Skin Deep "Voice of the Patient" Report. 2020. Available at: https://www.morethanskindeep-eczema.org/report.html. Accessed May 1, 2023.
18. Danby SG, Andrew PV, Kay LJ, et al. Enhancement of stratum corneum lipid structure improves skin barrier function and protects against irritation in adults with dry, eczema-prone skin. *Br J Dermatol.* 2022;186:875-86.
19. Fowler JF, Jr. Colloidal oatmeal formulations and the treatment of atopic dermatitis. *J Drugs Dermatol.* 2014;13:1180-1183.
20. Pavel P, Blunder S, Moosbrugger-Martinz V, Eet al. Atopic dermatitis: The fate of the fat. *Int J Mol Sci.* 2022;23.

AUTHOR CORRESPONDENCE

Christine Emesiani PharmD
E-mail:..... Christine.Emesiani@galderma.com

doi:10.36849/JDD.SF388641

October 2023 s16 Volume 22 • Issue 10 (Supplement 2)

ORIGINAL ARTICLE

Journal of Drugs in Dermatology

Over-the-Counter Moisturizers Significantly Improve Skin Hydration in Adults With Eczema/Atopy-Prone Skin

Harrison Nguyen MD MBA MPH,[a] Thu Nguyen PhD,[b] Ana Mantilla DPM,[b] Christine Emesiani PharmD,[b] Matthew Meckfessel PhD[b]

[a]Department of Dermatology, University of Pennsylvania, Philadelphia, PA

[b]Galderma Laboratories, L.P., Dallas, TX

ABSTRACT

Background: Many adults suffer from dry, itchy skin, particularly those with eczema-prone skin. This study evaluated the effects of two over-the-counter (OTC) moisturizing products on skin hydration, transepidermal water loss (TEWL), ceramide levels, and patient experience.

Methods: Single-center, randomized, double-blind, split-body study evaluating the effectiveness of an Eczema Soothing Moisturizer (ESM) versus an Itch Relief Moisturizing Lotion (IRML) applied twice daily for 4 weeks in healthy adults with self-perceived persistent mild-to-moderate eczema-prone skin. Assessments included corneometer for skin hydration, evaporimeter for TEWL, tape stripping to measure ceramide NS and AS levels on the skin of the arm and leg, and a self-assessed participant-reported outcome questionnaire.

Results: A total of 30 adults completed the study. Both products significantly increased hydration, but the effect of ESM was greater than IRML (P=0.001), and both significantly decreased TEWL. At week 4, there were increases in NS and AS ceramides at both the legs and arms for both products (P<0.05 vs BL). Individually, ceramide content was significantly improved for ESM in the leg and for IRML in the arm at week 4 (P<0.05 vs BL). Participant photos show ESM was beneficial across a range of skin phototypes. Both products resulted in favorable perceptions from study participants.

Conclusions: These moisturizers improved skin hydration, skin barrier, ceramide levels in the skin, and were well-perceived by the participants. This suggests that both products are beneficial for patients with eczema and eczema-prone skin. However, the hydrating effect of ESM was significantly greater than IRML.

J Drugs Dermatol. 2023;22:10(Suppl 2):s16-20.

INTRODUCTION

Eczema- or atopy-prone skin frequently has an ineffective skin barrier, which can lead to redness, irritation, and dryness with periods of remission interspersed with flares.[1] When their eczema flares, patients want rapid relief. Over-the-counter (OTC) moisturizers are a cornerstone of eczema therapy and are useful even between itchy periods to soothe the skin and support the skin barrier.[2] Eczema is estimated to affect between 2% and 10% of adults and up to 20% of children.[3,4] In recent years there has been substantial increases in the knowledge-base about abnormalities in skin barrier and immune system function.[5] However, management of eczema and eczema-prone skin continues to pose a clinical challenge. Eczema and associated pruritus may not only have a pronounced negative effect on sleep patterns and quality of life but can also create a substantial economic burden.[6] Existing eczema guidelines highlight the importance of proper cleansing and moisturizing.[4] Patients require education about how to cleanse skin thoroughly yet gently.[4] It is recommended that topical emollients/moisturizers should be applied directly after cleansing. According to Wollenberg et al, proper use of skin care can result in both short- and long-term steroid sparing effects as well as maintenance of stable disease.[4] In a recent systematic review, Maleki-Yazdi and colleagues report patients prefer to start with nonmedical treatments before moving to prescription products.[7]

To be effective in managing eczema symptoms, OTC moisturizing products should support and restore skin barrier function as well as provide itch relief. In addition to OTC product use being recommended in eczema guidelines, Miller et al reported that an OTC moisturizer was as effective as prescription barrier creams, while being less expensive.[8] This study evaluated the effectiveness and patient perception of two moisturizers, Eczema Soothing Moisturizer (ESM) and Itch Relief Moisturizing Lotion (IRML), which contain various beneficial ingredients such as ceramides in formulations designed to be well tolerated by individuals with eczema.

MATERIALS AND METHODS

This was a 4-week, single center, randomized, double-blind, split-body study that consisted of the application of Eczema Soothing Moisturizer (Cetaphil® Eczema Restoraderm Soothing Moisturizer, Galderma, Dallas, TX) versus Itch Relief Moisturizing Lotion (CeraVe® Itch Relief Moisturizing Lotion, L'Oreal Active Cosmetics Group, Paris, France). Participants were randomized to apply ESM to the arm/leg on one side and IRML to the other side twice daily, with test sites at the volar forearms and outer lower legs. The study was conducted according to Good Clinical Practice. All participants provided written informed consent prior to the study start.

Patients were eligible to participate if they were healthy adults and had self-perceived mild-to-moderate eczema-prone skin characterized by dryness, itchiness, and flakiness. In addition, they had dry skin determined by test sites on the forearm and leg with corneometer measurement <30 au (arbitrary unit) at baseline. Patients were excluded if they had active flaring disease, damaged skin at test sites, a recent skin rash, recently treated skin cancer, or were using immunosuppressive therapy and/or undergoing radiation treatments. All participants agreed to discontinue use of current skincare products (cleansers, lotions, sunscreens) for the duration of the study.

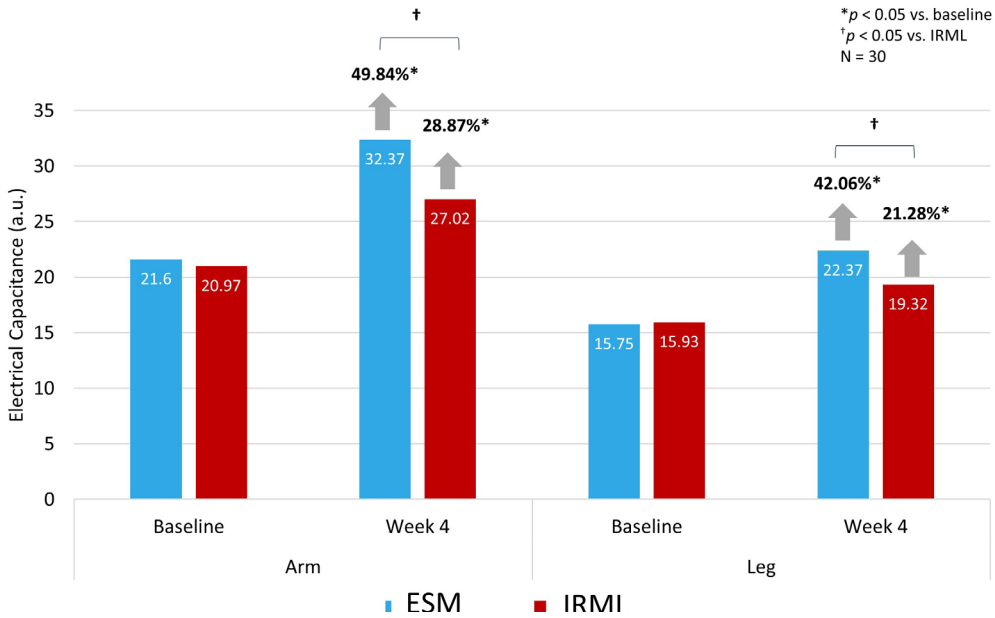
Participants agreed to the following washout periods: 3 days for skincare products; 1-week prior to baseline for anti-inflammatory or antihistamine medications; 2 weeks for acne treatment and topical corticosteroids; 4 weeks for oral corticosteroids, oral antibiotics, and immunosuppressants; and 6 months for oral isotretinoin.

TABLE 1.

Participant Demographics, ITT Population	
Mean age (range), years	54.2 (35-65)
Gender	
Female	25 (83.3%)
Male	5 (16.7%)
Race/Ethnicity	
White/Caucasian	12 (40.0%)
Black/African American	9 (30.0%)
Hispanic/Latin American	7 (23.3%)
Asian/Indian	2 (6.7%)
Fitzpatrick skin type	
I	7 (23.3%)
II	8 (26.7%)
III	3 (10.0%)
IV	4 (13.3%)
V	6 (20.0%)
VI	2 (6.7%)

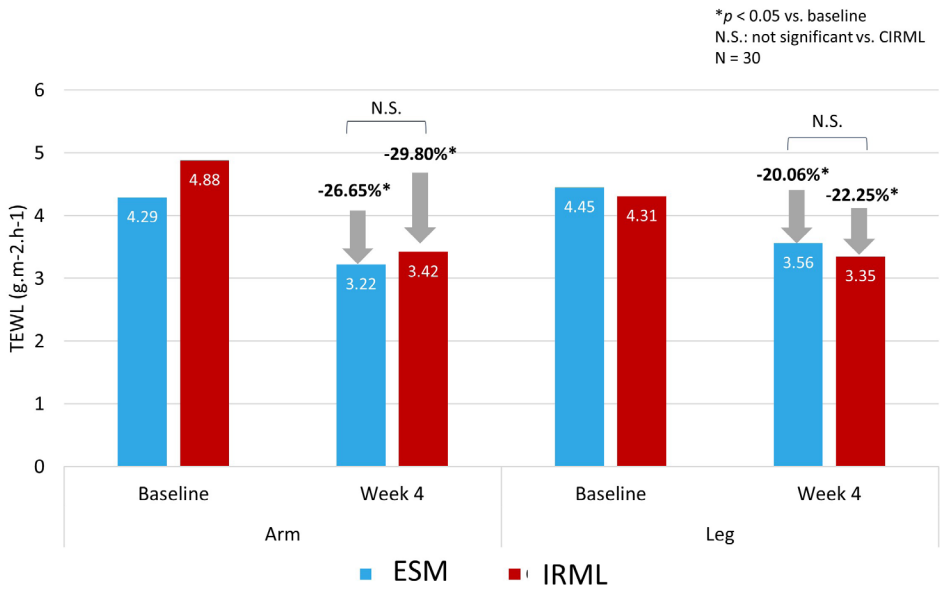
Efficacy assessments included corneometer (Courage and Khazaka, Germany), evaporimeter (Cortex Technology, Hadsund, Denmark), and D-squame® tape stripping (CuDerm®Corporation, Dallas, Texas) at baseline and week 4. Ceramide analysis from the tape strips was analyzed at QIMA Synelvia (Labege, France). In addition, photography was performed on a subgroup of 10 participants. A questionnaire on product attributes, improvements, and overall preference was self-administered at weeks 1 and 4 of treatment. Safety was assessed by collection of adverse events, and evaluation of local skin tolerability.

FIGURE 1. Corneometer measurements.



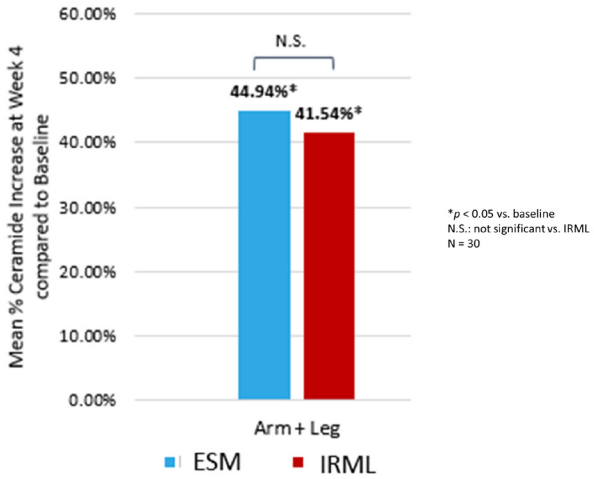
- Both products significantly improved skin hydration at week 4 compared to baseline.
- Restoraderm was significantly more hydrated than CeraVe at week 4 compared to baseline.

FIGURE 2. Impact of moisturizing products on skin barrier function as measured by evaporimeter.



TEWL=transepidermal water loss.

FIGURE 3. Tape stripping analysis of ceramides NS and AS at week 4 compared to baseline.



Statistical methods included descriptive statistics for variables, paired t-test or Wilcoxon signed-rank test if t-test normality fails, and z-test for percentage of participants improved or with favorable responses on the questionnaire.

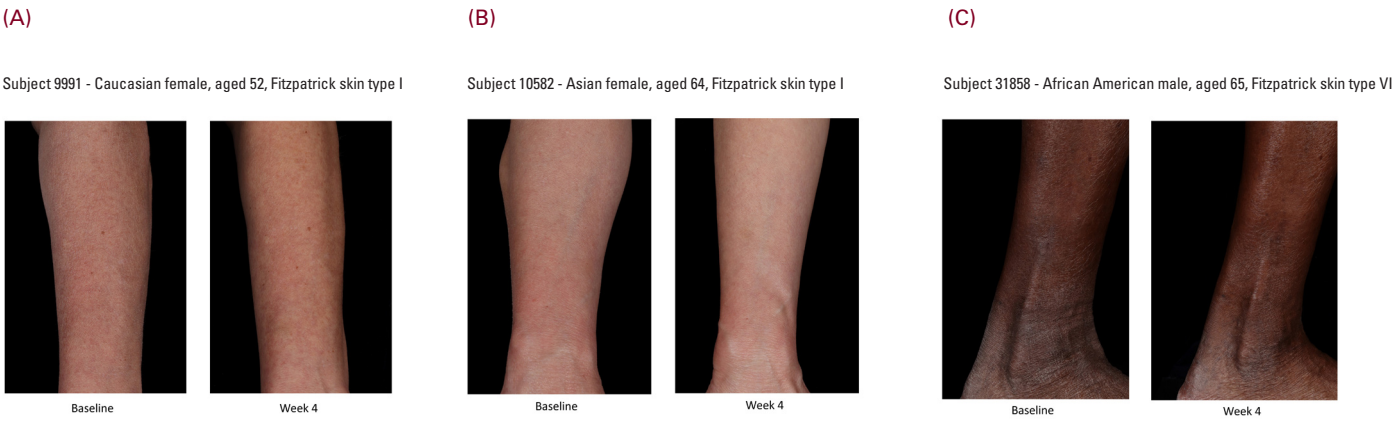
RESULTS

A total of 30 healthy male and female patients participated in the study, with participant demographics shown in Table 1.

Effectiveness

Both products significantly improved skin hydration at week 4 vs baseline as demonstrated by corneometer measurements (Figure 1) with a mean difference from baseline of 10.8 for ESM and 6.0 for IRML ($P \leq 0.001$ for both) at the arm site and 6.6 for ESM and 3.4 for IRML in the leg ($P \leq 0.001$) for both. However, skin hydration was significantly higher in the ESM-treated areas compared to the IRML at week 4 ($P < 0.05$).

FIGURE 4. Photos of representing patients with various Fitzpatrick skin phototypes treated with ESM at baseline and week 4.



Skin barrier function, as indicated by TEWL, also showed significant improvements with both products from baseline to week 4 ($P<0.05$), however, differences between the two products were not statistically significant.

According to the tape stripping results, both products significantly increased ceramide levels for the arm and leg at week 4 compared to baseline (Figure 3). There was no significant difference in ceramide synthesis between the two products at week 4.

As shown in Figure 4, ESM application resulted in an overall skin improvement in a diverse panel (White, Asian, and African American). Eczema and eczema-prone skin present differently in patients with skin of color. Currently, it's variations are not well represented visually. Healthcare professionals need to be able to recognize the differences in order to properly manage a patient's eczema. As can be appreciated in the photos, eczema skin can have a different hue in darker skin types and can also sometimes manifest as an ashen gray appearance.

The participant-perception questionnaire showed that 98.1% of ESM-treated participants and 94.2% of IRML-treated participants felt their skin was softer, with 94.2% of participants in both groups reporting their skin was soothed at week 1. At week 4, participants reported their skin was healthiest (93.3% ESM, 90.0% IRML), their eczema-prone skin had significantly improved (93.3% ESM, 88.3% IRML), and was completely soothed (93.3% ESM, 91.7% IRML). In addition, when asked about their preferences, 50% of participants preferred ESM, 33.3% preferred IRML, and 16.7% had no preference. Further, 46.7% reported ESM provided better soothing benefits compared to 40.0% for IRML.

Safety

Two adverse events occurred during the study and were resolved; however, neither was considered related to the study products.

DISCUSSION

Both ESM and IRML significantly improved skin hydration and barrier function by corneometer and assessment of TEWL after 4 weeks of twice-daily application. ESM had a statistically significantly better effect in hydrating the skin when compared to IRML at week 4. Both products increased skin ceramide content, with no significant differences between them. Participants reported favorable perceptions of both products, but there was a numerical trend in favor of ESM. As shown via clinical photography, ESM was effective and suitable for a range of skin types, which is important in the representation, diagnosis, and treatment of those with eczema and eczema-prone skin across diverse populations.

Supplementation of ceramides through topical products is an important way to support a healthy skin barrier with OTC treatments, and both products tested in this study increased skin ceramide levels. However, moisturizers should not rely on ceramide supplementation alone.[9] ESM has additional beneficial ingredients compared to IRML, such as colloidal oatmeal, a well-established soothing ingredient, and the filaggrin technology including the breakdown products, arginine, and sodium PCA. In eczema, filaggrin abnormalities encourage invasion of foreign substances including antigens and microbes, which in turn trigger allergic reactions.[4,10] Thus, the inclusion of filaggrin technology helps to support skin barrier

function.[11] Together, these ingredients in ESM provide excellent moisturizing, barrier restoring, and soothing effects that contribute to positive clinical results. Both products have been recognized as good for eczema by the National Eczema Association, however, this study shows ESM achieves superior results. In addition, ESM's good cosmetic acceptability could translate to improved adherence and outcomes, which is essential for individuals with eczema- or atopy-prone skin.

DISCLOSURES

Dr. Harrison Nguyen has served on the Advisory Board for Castle Biosciences and has received consulting fees from Apogee and Novant Pharmaceuticals; Dr Nguyen, Dr Mantilla, Dr Emesiani, and Dr Meckfessel are employees of Galderma Laboratories, L.P.

REFERENCES

1. Danby SG, Andrew PV, Taylor RN, et al. Different types of emollient creams exhibit diverse physiological effects on the skin barrier in adults with atopic dermatitis. *Clin Exp Dermatol.* 2022;47:1154-64.
2. Wollenberg A, Werfel T, Ring J, et al. Atopic dermatitis in children and adults-diagnosis and treatment. *Dtsch Arztebl Int.* 2023.
3. Ring J, Zink A, Arents BWM, et al. Atopic eczema: burden of disease and individual suffering - results from a large EU study in adults. *J Eur Acad Dermatol Venereol.* 2019;33:1331-40.
4. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol.* 2018;32:657-82.
5. Wollenberg A, Christen-Zach S, Taieb A, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol.* 2020;34:2717-44.
6. Elias PM. Optimizing emollient therapy for skin barrier repair in atopic dermatitis. A*nn Allergy Asthma Immunol.* 2022;128:505-11.
7. Maleki-Yazdi KA, Heen AF, Zhao IX, et al. Values and preferences of subjects and caregivers regarding treatment of atopic dermatitis (eczema): A systematic review. *JAMA Dermatol.* 2023;159:320-30.
8. Miller DW, Koch SB, Yentzer BA, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment of children with mild-to-moderate atopic dermatitis: a randomized, controlled trial. *J Drugs Dermatol.* 2011;10:531-7.
9. Danby SG, Andrew PV, Kay LJ, et al. Enhancement of stratum corneum lipid structure improves skin barrier function and protects against irritation in adults with dry, eczema-prone skin. *Br J Dermatol.* 2022;186:875-86.
10. Abe T, Koyama Y, Nishimura K, et al. Efficacy and safety of fig (Ficus carica L.) leaf tea in adults with mild atopic dermatitis: A double-blind, randomized, placebo-controlled preliminary trial. *Nutrients.* 2022;14.
11. Basu K, Inglis SK, Bremner SA, et al. Filaggrin gene defects are associated with eczema, wheeze, and nasal disease during infancy: Prospective study. *J Allergy Clin Immunol.* 2020;146:681-2.

AUTHOR CORRESPONDENCE

Christine Emesiani PharmD
E-mail:..... Christine.Emesiani@galderma.com

doi:10.36849/JDD.SF388641

ORIGINAL ARTICLE

Journal of Drugs in Dermatology

A Novel 3-Step Over-the-Counter Eczema Regimen Improves Eczema Severity, Itch, and Life Quality: Randomized Study

Kristi Hawley DO FAAD,[a] Peter Lio MD,[b] Thu Nguyen PhD,[c] Aamir Qureshi MD,[c] Christine Emesiani PharmD,[c] Matthew Meckfessel PhD[c]

[a]The Derm Institute of West Michigan; Associate clinical professor Michigan State University College of Osteopathic Medicine, Petoskey, MI

[b]Medical Dermatology Associates of Chicago, Chicago, IL

[c]Galderma Laboratories, L.P., Dallas, TX

ABSTRACT

Background: Eczema, or atopic dermatitis (AD), is a chronic relapsing skin disease associated with unpredictable flares of erythema, rash, and pruritus. AD arises from a combination of immune system dysregulation and abnormal skin barrier function. Skin barrier support with proper skincare regimens have a central role in management.

Methods: This was a multi-center, 12-week in-use study of a skincare regimen in children and adults with mild-to-moderate eczema (6-16) on the Patient-Oriented Eczema Measure (POEM), and ≥2 flares within 3 months prior to screening. The regimen included Itch Relief Gel, Eczema Soothing Lotion, and Flare Relief Cream. Efficacy assessments included POEM, ItchyQuant, Eczema Area and Severity Index (EASI), Quality of Life and digital photography, along with gathering of adverse events and cutaneous tolerability.

Results: 34 subjects completed the study. In 12 weeks, mean POEM scores improved from 9.7 to 5.3, and EASI scores improved by 17.9% ($P<0.05$ vs baseline). Additionally, mean ItchyQuant scores showed that pruritus was significantly improved from 5.4 at baseline to 2.7 at week 12 ($P<0.05$). The number of flares decreased from 4.2 to 3.2 after 12 weeks of regimen application ($P<0.05$ vs 12 weeks before baseline). Quality-of-life measures also showed improvement in both children and adults from baseline ($P<0.05$). There were no related adverse events, the regimen was well tolerated, and participants had positive perceptions of the regimen.

Conclusions: 12-week use of this OTC skincare regimen resulted in significant improvements in EASI, POEM, and ItchyQuant scores, a reduced number of flares, and improved quality of life.

J Drugs Dermatol. 2023;22:10(Suppl 2):s21-26.

INTRODUCTION

Eczema, or atopic dermatitis (AD), is a common skin condition which is estimated to affect >31 million people in United States, with up to 25% of children and almost 10% of adults diagnosed at least one time with the disease.[1,2] It is characterized by recurrent, unpredictable flares of dryness, itchiness, scaling, roughness, irritation, and/or discoloration.[3] Classic AD is often associated with skin distribution patterns: AD tends to affect flexural areas, but the hands and feet can also be involved, especially in adults.[3] Non-classic forms also exist, which can complicate the picture. Eczema is frequently associated with a negative impact on quality of life (QoL) and sleep loss due to itch.[2,3] Indeed, sleep disruption and fatigue are primarily responsible for poor QoL in eczema, along with restricted activities and depression due to disease and chronic, intractable itch.[3] Further, it has been shown that the effect of eczema on QoL is not limited to the sufferer – rather, oftentimes caregivers and parents also have reduced life quality.[3] The family members report having sleep problems and fatigue, treatment-related costs, and negative feelings surrounding the disease. As an example, Moore et al found that depression is twice as common in mothers of children with eczema compared to mothers of children with asthma.[4] Beyond the humanistic burden, eczema also imposes an economic burden on patients and families.[5] A 2023 study found that pediatric patients with eczema have a mean yearly cost of $3,279, with variations among the countries studied (range: $1,540 to $7,943).[5] Both direct and indirect costs incurred by patients and families increase with eczema severity, with the highest costs associated with biologic treatments.[5]

The pathogenesis of eczema is both complex and multifactorial.[3] However, eczema-prone skin is susceptible to dysbiosis and weakened epidermal barrier function, and exposure to small irritant or allergens can stimulate disease flares.[3,6-8] Because eczema affects the skin barrier, which has a primary function of restricting water loss and preventing the entry of irritants/allergens, supporting skin barrier function is essential.[3]

Utilization of a skincare regimen targeted to eczema-prone skin can be a cost-effective way to minimize symptom flares along with trigger avoidance. This study evaluated a 3-step over-the-counter (OTC) regimen consisting of an itch relief el, flare relief cream, and a soothing moisturizer. The goal of this regimen is to relieve itch and thereby break the itch/scratch cycle of eczema. It was also designed to support and repair skin barrier function while relieving eczema symptoms, as well as to minimize the occurrence of flares in order to improve QoL.

MATERIALS AND METHODS

This was a multicenter, 12-week in-use study of a skincare regimen in patients with eczema and was conducted between March 2, 2022 and February 2, 2023. The test regimen included 3 products: itch relief gel for itchy areas, cream all over face/body, and a moisturizer for eczema-affected areas (Cetaphil® Restoraderm, Galderma Laboratories LP, Dallas, TX). Participants were also allowed to use a neutral cleanser and moisturizer as well as a soothing wash. The study was reviewed and approved by Advarra Institutional Review Board (IRB), followed Good Clinical Practice, and all subjects provided written informed consent.

Patients were eligible to participate if they were aged 12 years and older, inclusive of any Fitzpatrick skin phototypes and any race/ethnicity, and had a score of 6 to 16 on the Patient Oriented Eczema Measure (POEM) questionnaire (mild-to-moderate severity) at screening and baseline. To be eligible, patients also had to have experienced at least 2 flares (defined as a return of eczema symptoms including worsening skin rash) within the 3 months prior to screening with the latest flare occurring within 6 weeks of baseline visit. Participants used a neutral cleanser and moisturizer for 5 to 14 days upon the screening period, then switched to the test regimen at baseline for the remaining study. Participants were also allowed to use 1% hydrocortisone if their eczema flare-up was uncontrolled and/or unbearably itchy.

Efficacy assessments included the Eczema Area and Severity Index (EASI, scores range from 0=no disease anywhere on the body to 72=most severe disease on all body areas) and the Patient-Oriented Eczema Measure (POEM, 0=clear to 28=very severe), both performed at baseline and weeks 4, 8, and 12. Digital photography was also performed. Participants also completed self-assessment questionnaires, including the validated ItchyQuant Assessment (numerical rating scale from 0=none to 10=worst itch imaginable), the Dermatology Life Quality Index (DLQI, 0=no effect at all to 30=extremely large effect), and a satisfaction questionnaire.

TABLE 1.

Baseline Patient Demographics and Characteristics	
Mean age (range), years	32.9 (12-64)
	N (%)
Gender	
Female	33 (84.6%)
Male	6 (15.4%)
Race/background	
White/Caucasian	25 (64.1%)
Black/African American	11 (28.2%)
Asian/Indian	3 (7.7%)
Ethnicity	
Hispanic/Latin American	8 (20.5%)
Not Hispanic/Latin American	31 (79.5%)
Fitzpatrick skin type	
I	3 (7.7%)
II	10 (25.6%)
III	8 (20.5%)
IV	8 (20.5%)
V	9 (23.1%)
VI	1 (2.6%)
Children (12-17 years old)	10 (25.6%)
Test area	
Body	33 (84.6%)
Face	6 (15.4%)

ITT=intent-to-treat; POEM=Patient-Oriented Eczema Measure; DLQI=Dermatology Life Quality Index.

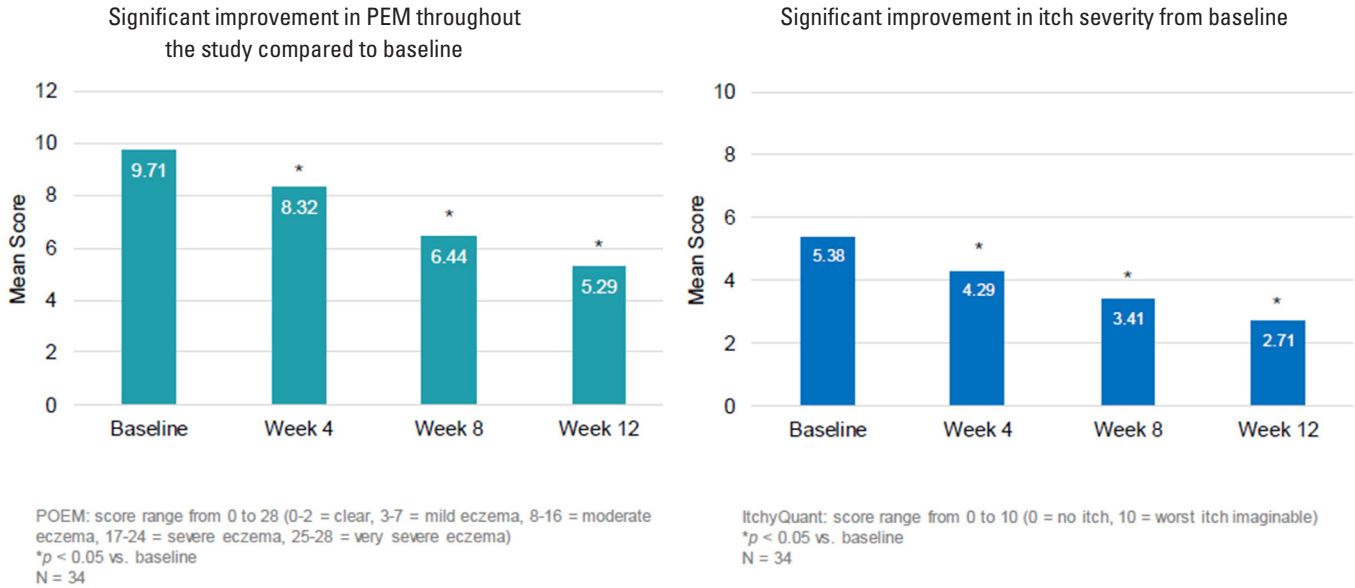
Safety was assessed by tolerability evaluations of burning and stinging (0=none to 3=severe) at baseline and weeks 4, 8, and 12 as well as collection of adverse events for participants who qualified with active lesions and/or dry patches on the face or body.

Statistics included demographic and baseline characteristics, descriptive statistics for continuous variables, and the frequency and percentage per category for categorical variables. Number of flares was summarized for each time point and the total number occurring from baseline to week 12 was compared with the number of flares experienced during the 3 months prior to screening. The Wilcoxon signed-rank test was used to analyze change from baseline and all statistical tests were 2-sided at significance level alpha=0.05. Questionnaire data were tabulated, and the frequency and percentage of all responses were reported.

RESULTS

Forty patients qualified for the study and one discontinued (for a total of 39 participants in the intent to treat [ITT] population); 34 completed all study visits per protocol. Patient demographics and

FIGURE 1. Reduction in mean POEM and ItchyQuant scores from baseline to week 12.



characteristics are shown in Table 1. Approximately two-thirds of subjects were adults (29 aged 18 or older) with the remaining 10 subjects aged 12 to 17.

Efficacy

The skincare regimen achieved a significant improvement in itch throughout the study, as was reflected in the reduction of baseline mean POEM scores from 9.7 to 5.3 at week 12 and mean ItchyQuant score from 5.4 to 2.7 at week 12 (Figure 1, $P<0.05$ for both). The regimen also significantly improved mean EASI scores and reduced flares (Figure 2, $P<0.05$ for both). For the individual EASI parameters, there was a statistically significant improvement in erythema scores on the lower limbs at weeks 8 and 12; improvement of edema, induration, and papulation on the upper limbs at weeks 4, 8, and 12 and on the lower limbs at weeks 4 and 12; improvement of excoriation on upper limbs at all study visits, and less lichenification on upper limbs at week 12 ($P<0.05$ for all vs baseline).

FIGURE 2. Changes in EASI from baseline to week 12 and reduction in flares from 3 months prior to screening to week 12 study visit.

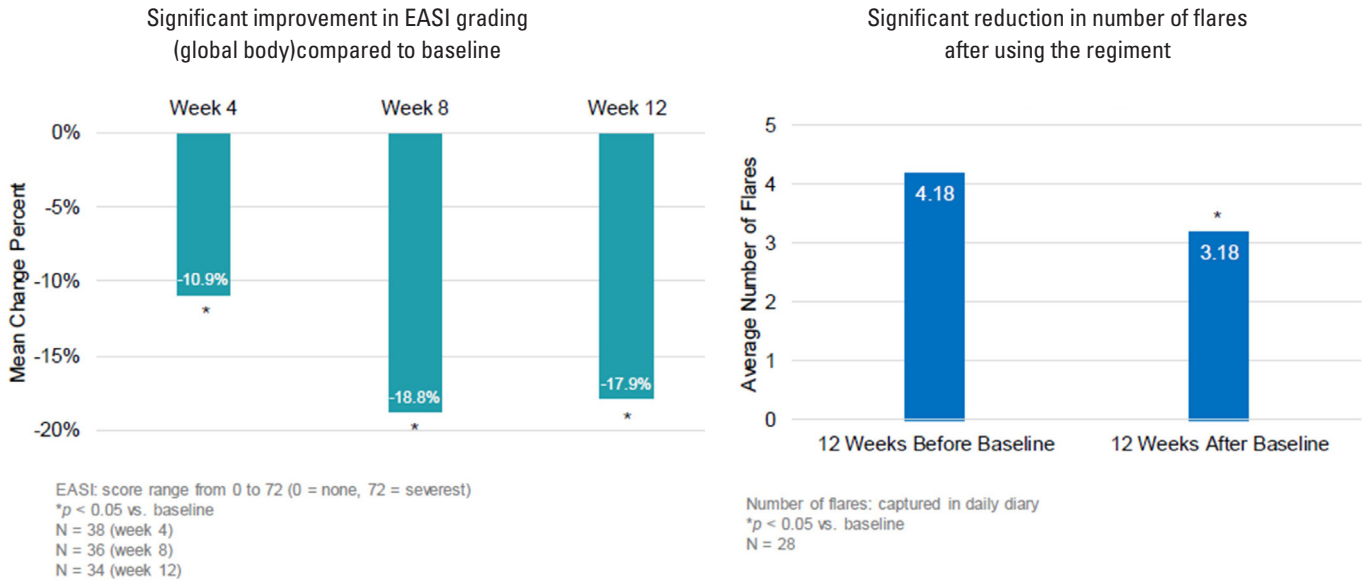


Figure 3 shows skin improvement in patient photos from individuals across a range of ages and a diverse panel. As can be appreciated in the photo of a young African American patient, there is dryness/scaling and an ashen gray look at the initiation of treatment and smoother, more hydrated looking skin at week 12. In the White patient, who was lost to follow up after week 8, a marked improvement in erythema and rash can be seen throughout the study. Similarly, improvements in rash, pigmentation, and overall appearance can be appreciated in the Asian patient.

The skincare regimen was also associated with a positive impact on QoL (P<0.05 for reduction at week 12 vs baseline), with clinically relevant reductions (Figure 4). As shown, this was true for both children and adults.

Analysis of the self-assessment questionnaire showed that a significantly greater proportion of participants selected favorable responses vs those with unfavorable responses on almost all questions at weeks 4 and 12 and to all at week 8. For example, at

FIGURE 3. Patient photos in a variety of ages and skin types.

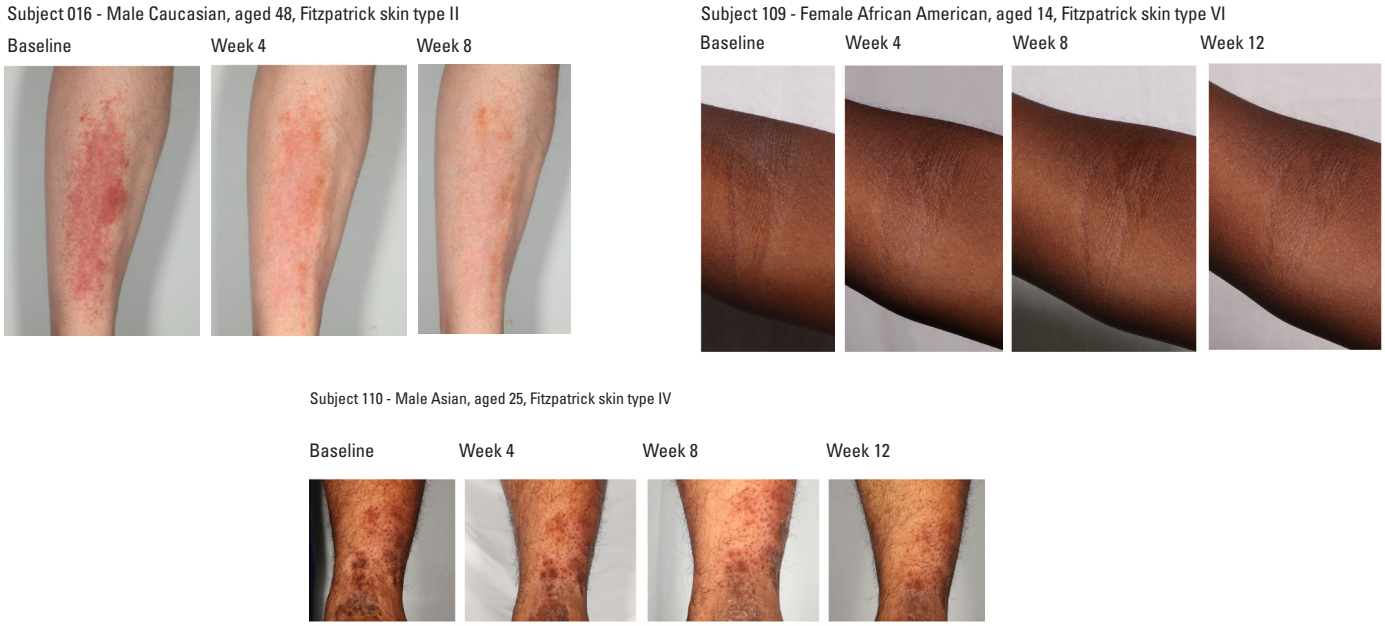
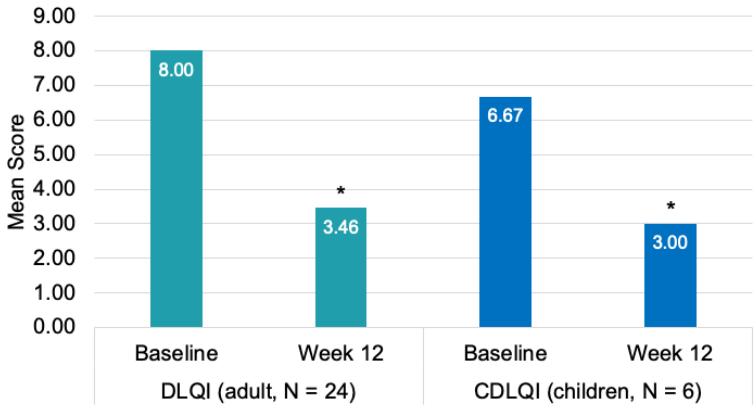
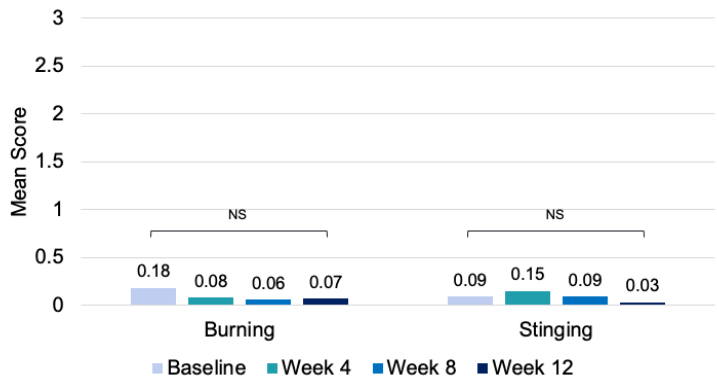


FIGURE 4. Improvement in quality of life from baseline to week 12. Significant improvement in quality of life after using the regimen for 12 weeks



Quality of Life: score range from 0 to 30 (0-1 = no effect, 2-5 = small effect, 6-10 = moderate effect, 11-20 = very large effect, 21-30 = extremely large effect on patient's life)
*p < 0.05 vs. baseline

FIGURE 5. Mean tolerability scores by study visit, safety population. No worsening in subjective tolerability from using the regimen at the test areas for 12 weeks



Tolerability: score range from 0-3 (0 = none, 1 = mild, 2 = moderate, 3 = severe)
NS: non-significant ($p > 0.05$ vs. baseline)
N = 33 (week 4)
N = 32 (week 8)
N = 30 (week 12)

week 4, participants reported improved comfort (82.4%), soothed skin (82.4%), and overall improvement (79.4%). By week 8, patient responses indicated improvements in rough scaly areas (88.2%), eczema symptom relief and less worry (73.5%), visible improvement (76.5%), and healthier looking skin (73.5%). At the last study visit at week 12, participants reported increased confidence (76.5%), better overall comfort (79.4%), and that the regimen had helped their eczema skin (82.4%). In addition, a significantly greater proportion of participants indicated they would recommend/purchase the regimen.

Safety

A total of 4 adverse events were reported, and none were judged by investigators to be related to study treatment (sprained ankle, removal of surgical hardware, seasonal allergy, and COVID-19). All were mild-moderate in severity. The skincare regimen was well-tolerated with no worsening in subjective tolerability at any post-baseline study timepoint (Figure 5). For those with eczema-affected areas of the face, each patient scored burning/stinging on the overall face and periocular area as 0 at all study visits.

DISCUSSION

Twelve-week treatment with the skincare regimen resulted in significant improvements in eczema severity (shown by reductions in EASI and POEM scores) as well as reduced itch severity and number of flares. Consequently, QoL for participants improved to a clinically relevant degree. There was no worsening or significant increase in tolerability grading and no adverse events judged to be related to the regimen. Further, the skincare regimen was well received by study participants.

Maintaining a healthy skin barrier, controlling itch, and managing exposure to triggers are 3 primary components of eczema management, along with good patient and family education.[3] Since good skin care provides the foundation of eczema management, patients and parents should be educated about how to develop good skincare habits and the importance of using skin care daily.[3,9] Frequent moisturizing relieves discomfort associated with dry skin, contributes to skin barrier repair, and reduces the need for pharmacologic interventions.[10,11] Miller et al demonstrated that OTC moisturizers are as effective and less expensive than prescription creams for children with mild-to-moderate eczema.[12] In addition, studies have reported that steroid phobias are not uncommon in both patients and families of children with eczema.[13,14] Regular use of eczema-appropriate moisturizers helps to decrease use of moderate or potent topical corticosteroids while improving eczema symptoms.[9]

The 3-step skincare regimen incorporates a wide range of key active ingredients to address the symptomatology of eczema. These include colloidal oatmeal to protect skin, filaggrin, and ceramides to help strengthen the skin barrier, and moisturizing and emollient ingredients[1] to soothe the skin. The regimen does not have parabens, steroids, propylene glycol, or fragrances, which is ideal for eczema-prone skin.[3] In recent years, it has become accepted that filaggrin has a major role in maintaining the structure and formation of the stratum corneum.[3,8,15] A recent systematic review reported that colloidal oatmeal was associated with statistically significant improvements in skin thickness, dryness, and itching.[16] Colloidal oatmeal is recognized by the US Food and Drug Administration as a monograph OTC skin protectant for the management of eczema skin. In 2022, Larese Filon et al found that regular use of a cream that included ceramides achieved significantly better clinical outcomes in hand eczema compared with creams that did not include ceramides.[17] These data show that the specific ingredients in an eczema regimen can translate to clinical differences.

Our study demonstrated this Eczema skincare regimen was suitable for an inclusive range of ages, genders, skin tones, and races/ethnicities. Epidemiologic studies indicate that eczema is most

common in African American, Asian, Hispanic, and Pacific Islanders patients.[2] Croce et al report that the burden of eczema is higher in these populations, with African American children having an almost double rate of eczema diagnoses compared to White children.[2] African American and Latinx children are prone to more severe eczema and more likely to have persistent eczema.[2] In turn, more severe and persistent eczema is linked to worse overall health.[2,18-20] For these reasons, it is important for healthcare professionals to be aware that the clinical presentation of eczema is often different in light- vs dark-skinned individuals; light-skinned participants tend to have erythema and rash, while darker-skinned participants are more likely to exhibit primarily a purple discoloration and/or an ashy look to the skin.[2]

The results of this study demonstrate that this eczema skincare regimen is safe and effective for all skin types and for both children and adults (note that it has not been studied in infants).

DISCLOSURES

Dr. Kristi Hawley served as a PI for this trial; she reports receiving research grants from Lily, Sanofi, and Leo in the AD field; serves as a consultant and/or speaker for Arcutis, BMS, Dermavant, Incyte, Galderma, Sun Pharma, Amgen, Sanofi, Regeneron, Leo, Novartis, Janssen, Abbvie and UCB pharmaceuticals. Dr. Lio reports research grants/funding from AbbVie, AOBiome, National Eczema Association; is on the speaker's bureau for AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, MyOR Diagnostics, ParentMD, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme, Verrica; reports consulting/advisory boards for Alphyn, AbbVie, Almirall, Amyris, Arcutis, ASLAN, Boston Skin Science, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, Dermavant, Eli Lilly, Galderma, Janssen, Johnson & Johnson, Kimberly-Clark, LEO Pharma, Lipidor, L'Oreal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Skinfix, Theraplex, UCB, Unilever, Verrica Yobee Care; stock options with Codex, Concerto Biosciences and Yobee Care. In addition, Dr. Lio has a patent pending for a Theraplex product with royalties paid and is a Board member and Scientific Advisory Committee Member of the National Eczema Association. Dr Nguyen, Dr Qureshi, Dr Emesiani, and Dr Meckfessel are employees of Galderma Laboratories, LP.

REFERENCES

1. Abuabara K, Magyari A, McCulloch CE, et al. Prevalence of atopic eczema among patients seen in primary care: Data from the health improvement network. ***Ann Intern Med.*** 2019;170:354-6.
2. Croce EA, Levy ML, Adamson AS, et al. Reframing racial and ethnic disparities in atopic dermatitis in black and latinx populations. *J Allergy Clin Immunol.* 2021;148:1104-11.
3. Tollefson MM, Bruckner AL, Section On D. Atopic dermatitis: Skin-directed management. *Pediatrics.* 2014;134:e1735-44.
4. Moore K, David TJ, Murray CS, et al. Effect of childhood eczema and asthma on parental sleep and well-being: A prospective comparative study. *Br J Dermatol.* 2006;154:514-8.
5. Achten R, Van der Rijst L, Piena M, et al. Economic and humanistic burden in paediatric patients with atopic dermatitis. *Acta Derm Venereol.* 2023;103:adv00881.
6. Wang J, Zhou Y, Zhang H, et al. Pathogenesis of allergic diseases and implications for therapeutic interventions. *Signal Transduct Target Ther.* 2023;8:138.
7. O'Regan GM, Irvine AD. The role of filaggrin in the atopic diathesis. *Clin Exp Allergy.* 2010;40:965-72.
8. Drislane C , Irvine AD. The role of filaggrin in atopic dermatitis and allergic disease. *Ann Allergy Asthma Immunol.* 2020;124:36-43.
9. Cork MJ, Britton J, Butler L, et al. Comparison of parent knowledge, therapy utilization and severity of atopic eczema before and after explanation and demonstration of topical therapies by a specialist dermatology nurse. *Br J Dermatol.* 2003;149:582-9.
10. Short RW, Chan JL, Choi JM, et al. Effects of moisturization on epidermal homeostasis and differentiation. *Clin Exp Dermatol.* 2007;32:88-90.
11. Loden M, Andersson AC, Lindberg M. Improvement in skin barrier function in patients with atopic dermatitis after treatment with a moisturizing cream (canoderm). *Br J Dermatol.* 1999;140:264-7.
12. Miller DW, Koch SB, Yentzer BA, et al. An over-the-counter moisturizer is as clinically effective as, and more cost-effective than, prescription barrier creams in the treatment of children with mild-to-moderate atopic dermatitis: A randomized, controlled trial. *J Drugs Dermatol.* 2011;10:531-7.
13. Moret L, Anthoine E, Aubert-Wastiaux H, et al. Topicop(c): A new scale evaluating topical corticosteroid phobia among atopic dermatitis outpatients and their parents. *PLoS One.* 2013;8:e76493.
14. Kojima R, Fujiwara T, Matsuda A, et al. Factors associated with steroid phobia in caregivers of children with atopic dermatitis. *Pediatr Dermatol.* 2013;30:29-35.
15. Palmer CN, Irvine AD, Terron-Kwiatkowski A, et al. Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nat Genet.* 2006;38:441-6.
16. Jones VA, Patel PM, Wilson C, et al. Complementary and alternative medicine treatments for common skin diseases: A systematic review and meta-analysis. *JAAD Int.* 2021;2:76-93.
17. Larese Filon F, Maculan P, Crivellaro MA, et al. Effectiveness of a skin care program with a cream containing ceramide c and a personalized training for secondary prevention of hand contact dermatitis. *Dermatitis.* 2023;34:127-34.
18. Kim Y, Blomberg M, Rifas-Shiman SL, et al. Racial/ethnic differences in incidence and persistence of childhood atopic dermatitis. *J Invest Dermatol.* 2019;139:827-34.
19. Silverberg JI , Simpson EL. Associations of childhood eczema severity: A us population-based study. *Dermatitis.* 2014;25:107-14.
20. Leung DYM. The effect of being african american on atopic dermatitis. *Ann Allergy Asthma Immunol.* 2019;122:1.

AUTHOR CORRESPONDENCE

Christine Emesiani PharmD
E-mail:..... Christine.Emesiani@galderma.com

JOURNAL OF DRUGS IN DERMATOLOGY
JDD
DRUGS • DEVICES • METHODS