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.

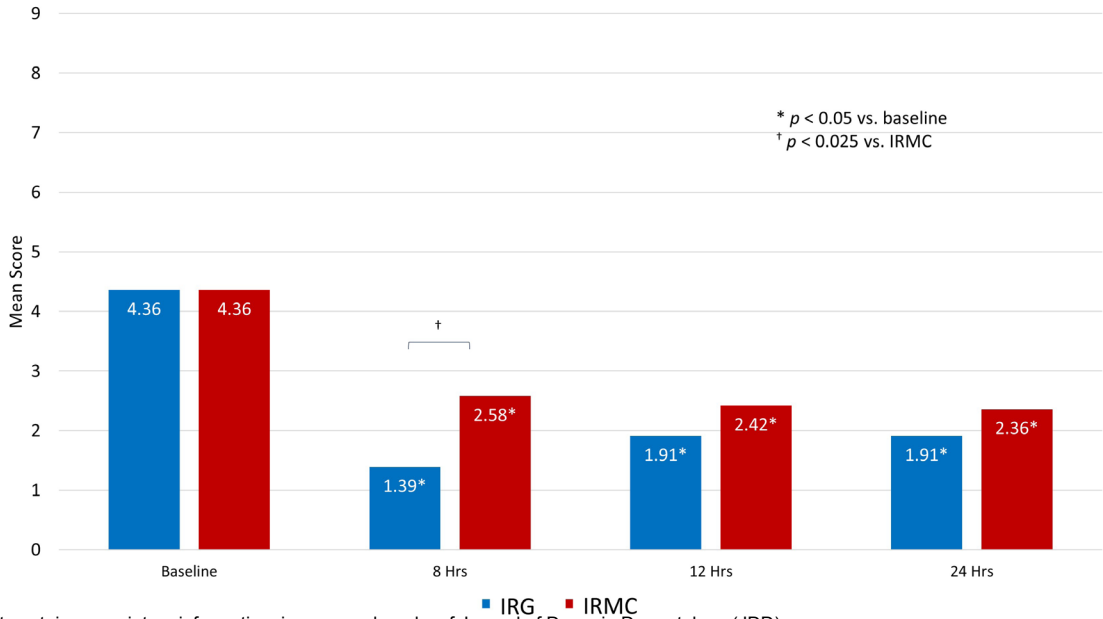
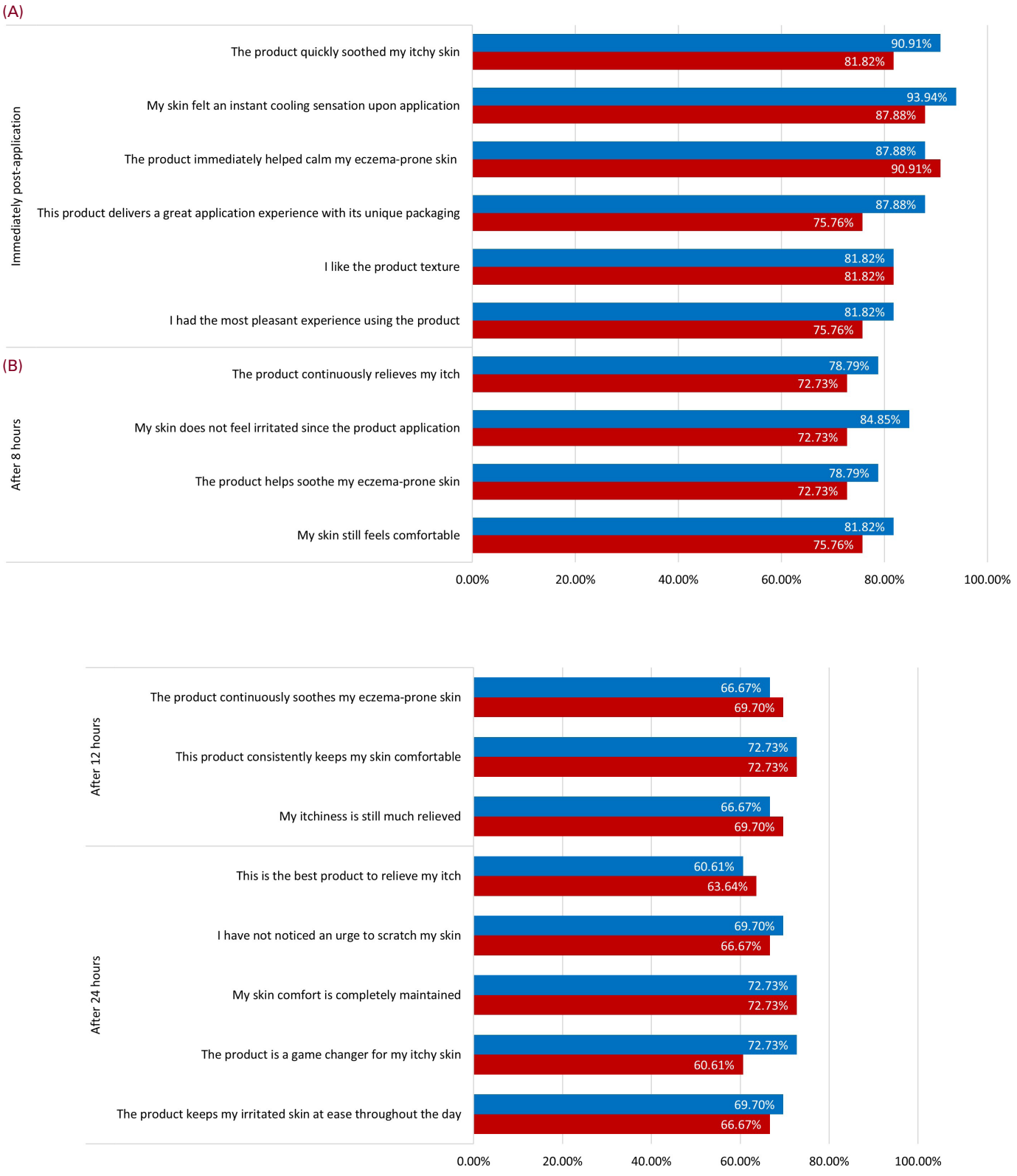
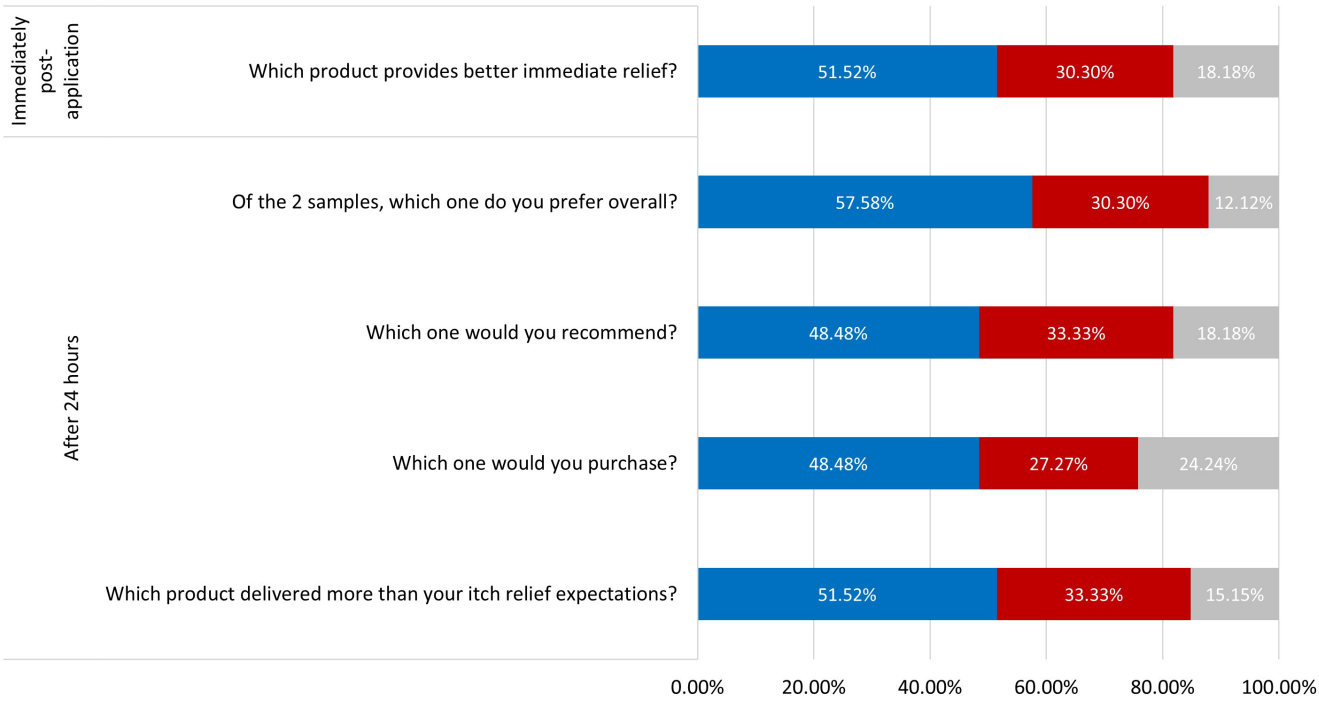


FIGURE 2. Participant satisfaction questionnaire results at each timepoint after application, ITT population.



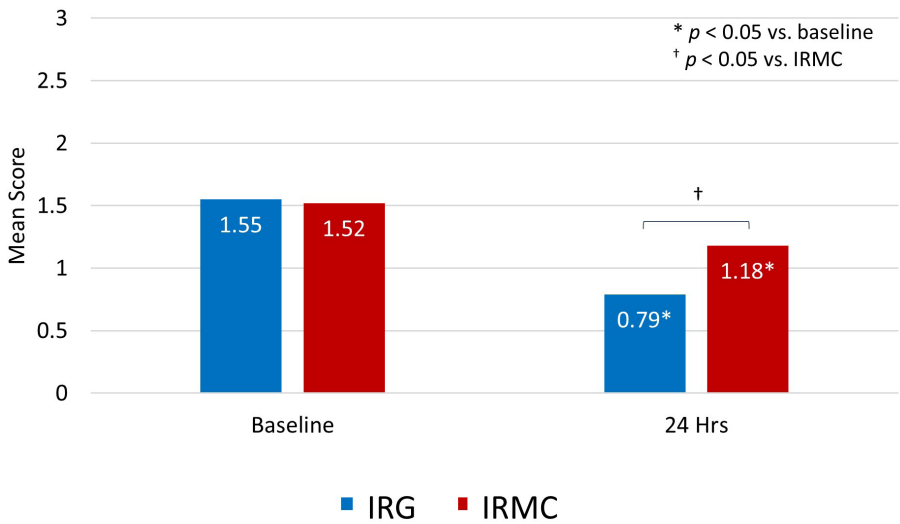
Blue bars = IRG, red bars = IRMC.

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.

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AUTHOR CORRESPONDENCE

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