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TRPM8 Agonist (Cryosim-1) Cream for Chronic Prurigo: A Randomized, Vehicle-controlled Trial

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Chronic prurigo (CP) is a distressing dermatological condition lacking effective topical therapies. This randomized, double-blind, vehicle-controlled trial evaluated the efficacy and safety of Cryosim-1, a TRPM8 agonist cream, in 30 adults with CP. Participants were assigned to apply Cryosim-1 0.1%, 0.5%, or vehicle cream 3 times daily for 4 weeks. Both active formulations significantly reduced Prurigo Activity Score (PAS) compared with vehicle, with 0.1% Cryosim-1 showing a mean PAS reduction of −7.3 ($p < 0.001$). Significant improvements were observed in 24-h itch intensity, quality of life (DLQI), transepidermal water loss, and stratum corneum hydration. While both concentrations were effective, the 0.1% formulation showed superior tolerability with fewer reports of stinging and erythema. These findings support the potential of TRPM8-targeted therapy in managing CP through dual mechanisms of itch inhibition and skin barrier restoration.

Key words: chronic prurigo; TRPM8 agonist; topical therapy; antipruritic; skin barrier.

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SIGNIFICANCE

Chronic prurigo is a skin condition that causes severe, long-lasting itching and discomfort. Many patients struggle to find safe and effective relief. This study tested a new cooling cream made from a TRPM8-activating ingredient and found that it significantly reduced itching and improved skin health without serious side effects. The cream was most effective and comfortable at a low concentration. This offers a promising new option for people suffering from chronic itch, especially those looking for non-steroid, daily-use treatments. It may improve quality of life and reduce dependence on stronger medications.

Chronic prurigo represents a challenging dermatological condition characterized by persistent pruritus lasting more than 6 weeks, accompanied by distinctive skin lesions such as excoriated papules, nodules, or plaques resulting from repetitive scratching (1). This debilitating disorder substantially impairs quality of life through sleep disturbance, psychological distress, and interference with daily functioning (2). The pathophysiology involves complex neuroimmunological circuits and histamine-independent mechanisms that distinguish chronic prurigo from acute pruritic conditions (3). Pruritus in chronic prurigo is typically severe, paroxysmal, and accompanied by an uncontrollable urge to scratch, which perpetuates the itch–scratch cycle and drives lesion chronicity. The itch is multifactorial, involving both peripheral neurocutaneous sensitization and central nervous system amplification, which explains its chronic course and resistance to conventional antipruritic therapies. Current therapeutic approaches include topical corticosteroids, calcineurin inhibitors, and various systemic agents, but their efficacy is limited and adverse effects may restrict long-term use (4). The recent FDA approvals of dupilumab and nemolizumab for prurigo nodularis have established systemic biologics as effective options, achieving response rates of 56–60% in phase 3 trials (5, 6). Nevertheless, significant unmet needs remain, including rapid onset of action, cost-effective options, and topical therapies suitable for localized disease or patients who prefer non-systemic treatments. In this study, we acknowledged that topical therapies, including Cryosim-1, provide potential advantages in terms of cost and ease of use. However, in real-world clinical practice, treatment selection is primarily guided by a comprehensive assessment of disease characteristics – including itch severity, extent of skin involvement, and the presence of comorbidities – rather than by cost alone.

For patients with mild or localized pruritus, topical treatments are generally prioritized as a first-line option, whereas systemic therapies and biologics are typically reserved for patients with severe or refractory chronic pruritus. Within this treatment framework, Cryosim-1 cream may serve as a first-line therapy in mild and localized cases and may also function as an adjunctive treatment alongside systemic approaches in patients with more extensive disease. The transient receptor potential melastatin 8 (TRPM8) channel, known as the cold receptor, is a validated therapeutic target for pruritus, as highlighted by the recent FDA approval of acoltremon for dry eye disease (7–10). Cryosim-1 (diisopropylheptylphosphinyl oxide) is a selective TRPM8 agonist that produces cooling sensations without altering tissue temperature, and has demonstrated antipruritic efficacy in both experimental and clinical settings (9). To improve

tolerability for daily long-term use, we developed lower-concentration cream formulations (0.1% and 0.5%) designed as moisturizers rather than acute treatments.

The objective of this study was to evaluate the efficacy, safety, and optimal concentration of low-dose Cryosim-1 cream in adults with chronic prurigo.

MATERIALS AND METHODS

Study design and setting

This randomized, double-blind, vehicle-controlled trial was conducted from June to December 2023 at the outpatient dermatology clinic of Hallym University Kangnam Sacred Heart Hospital, Seoul, Republic of Korea (Fig. S1). The study protocol (Protocol Version 2.0, dated 4 September 2025) was approved by the Institutional Review Board (IRB No. 2023-04-015) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent. The trial was prospectively registered with the Clinical Research Information Service (CRIS; https://cris.nih.go.kr) under the identifier KCT0011008 on 14 June 2023, prior to the enrolment of the first participant, in compliance with the ICMJE requirements. The complete protocol and the statistical analysis plan are available in Table SI. The Week-4 assessment was selected to capture early efficacy and safety signals of topical TRPM8 agonism. Given its mechanism of rapidly modulating pruritus pathways, symptomatic relief can occur within weeks, which justified an early evaluation. Unlike trials of systemic agents such as dupilumab and nemolizumab, which focus on long-term lesion clearance (18–24 weeks), this study was designed as a pilot trial to explore dose-response and short-term safety. The need for longer follow-up to fully assess lesion healing is acknowledged.

Participants

Adult patients aged 20 years or older with a clinical diagnosis of chronic prurigo were eligible for enrolment. Chronic prurigo was defined as persistent pruritus lasting more than 6 weeks with characteristic skin lesions. Key exclusion criteria included active skin infections, use of systemic immunosuppressive medications within 4 weeks, topical corticosteroids or calcineurin inhibitors within 2 weeks, pregnancy or lactation, and known hypersensitivity to study ingredients. Also, we applied the definition of chronic pruritus proposed by the International Forum for the Study of Itch (IFSI) consensus statement (Acta Derm Venereol, 2007) (1), which defines chronic pruritus as pruritus persisting for more than 6 weeks. Only patients who were diagnosed with chronic prurigo by board-certified dermatologists were included. Eligible participants presented with pruritic papules, nodules, or plaques caused by scratching, and individuals with transient or acute pruritus were excluded. Based on these criteria, the study population was clearly restricted to patients with chronic prurigo.

Randomization and blinding

Thirty participants were randomly assigned in a 1:1:1 ratio to receive Cryosim-1 0.1% cream (C1), Cryosim-1 0.5% cream (C5), or vehicle cream (C0) using computer-generated randomization. All study personnel and participants remained blinded to treatment assignment throughout the study period. Study products were supplied by Dongwha Pharm Co, Ltd (Seoul, Korea), and were identical in appearance, texture, and packaging.

Study products

The base formulation for all groups was a commercially available moisturizer (Intrinsic Cream; Dongwa Pharm Co, Ltd) containing no active antipruritic agents. The 0.1% and 0.5% Cryosim-1 creams were identically formulated with only the concentration of active ingredient differing. Cryosim-1 is a recognized cosmetic ingredient listed with the Korean Ministry of Food and Drug Safety. Participants applied the study cream 3 times daily, with patients reporting an approximate usage of ~200 mL/day. Based on weight, this corresponded to ~30 g/day (≈ 60 finger-tip units/day), which is consistent with near-total body application of an emollient. Each 250 g tube was sufficient for the entire 4-week treatment period.

Interventions

Beginning on Day 1, participants applied their assigned study product 3 times daily (morning, evening, and before bedtime) to affected pruritic areas on arms or legs in a symmetrical manner for 4 weeks. Participants were instructed to apply a thin layer to the entire affected area and were provided with standardized application instructions. In this study, a 3-times-daily application schedule was selected based on Cryosim-1's pharmacological properties and supporting pilot data. Although some clinical trials of ruxolitinib cream have also adopted thrice-daily dosing, this was primarily driven by pharmacokinetic considerations. Future studies should directly compare twice- vs three-times-daily application regimens to optimize treatment frequency. Treatment adherence, assessed by tube consumption, showed no significant differences among groups, supporting that PAS improvement was attributable to the study drug rather than differential adherence.

Outcome measures

Primary endpoint. The primary endpoint was change in Prurigo Activity Score (PAS) from baseline to week 4. The PAS is a validated comprehensive scale integrating

subjective pruritus experience with objective lesion assessment and quality of life impact (13). PAS is a clinician-reported outcome (ClinRO) instrument designed to quantify the number and activity of lesions in patients with chronic prurigo (CPG) or prurigo nodularis (PN). The PAS does not include measures of itch intensity or quality of life. Instead, the total score is derived from the physician's assessment of lesion type, estimated lesion counts, distribution and extent of involvement, excoriation marks, and the proportion of healed lesions. In this study, we used the 7-item PAS with a total score range of 1.3–21.3 (Table SI).

Sample size estimation

Sample size estimation was based on an assumed standard deviation (σ) of 2.3 for PAS and a clinically meaningful difference (Δ) of 3.0, derived from previous TRPM8 agonist studies. Using a two-sided $\alpha = 0.05$ and 80% power, the required sample size was calculated to be approximately 9 participants per group. Considering a 10% dropout rate, we targeted 10 participants per group for a total of 30 participants. Sample size calculation was performed post hoc for transparency, as the trial was primarily exploratory.

Secondary endpoints

- Change in 24-h itch intensity (numeric rating scale, 0–10).
- Change in Dermatology Life Quality Index (DLQI).
- Change in 5D Itch Scale (assessing duration, degree, direction, disability, and distribution).
- Change in skin barrier function: TEWL (g/m²/hr) and stratum corneum hydration (SCH, arbitrary units).
- Immediate post-application itch and pain responses (numeric rating scale measured every minute for 10 min).
- Participant satisfaction ratings.
- Safety assessments including adverse event reporting.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp, Armonk, NY, USA). Continuous variables were primarily analysed using repeated-measures ANOVA with Bonferroni post-hoc correction for multiple comparisons. Between-group differences at each visit were assessed using independent *t*-tests, while within-group changes over time were additionally evaluated using paired *t*-tests. The primary analysis included all randomized participants following the intention-to-treat principle. Data are presented as mean ± standard deviation unless otherwise specified. Statistical significance was set at $p < 0.05$.

RESULTS

Participant characteristics

All 30 enrolled participants completed the 4-week study period. The mean age was 47.8 ± 14.0 years, with 12 males and 18 females. Baseline characteristics were well-balanced among the 3 groups, with no significant differences in demographics or clinical parameters (**Table I**).

Participants were randomly assigned to 1 of 3 groups. Simple randomization was performed using a computer-generated random number table, and stratified randomization by age and sex was not applied. Post-hoc analysis confirmed that there were no significant differences in baseline age or sex distribution among the groups ($p > 0.05$).

Primary endpoint: prurigo activity score

Both Cryosim-1 formulations demonstrated significant reductions in PAS scores from baseline to week 4 compared with vehicle. The 0.1% group (C1) showed improvement from 15.3 ± 1.5 to 8.7 ± 1.6 ($p < 0.001$), The 0.5% group (C5) from 15.2 ± 1.4 to 7.2 ± 1.4 ($p < 0.001$), while the vehicle group showed no significant change (15.6 ± 1.5 to 14.8 ± 1.4, $p = 0.8939$). No significant difference was observed between the 2 active treatment groups ($p > 0.05$) (**Fig. 1**A, Table SII).

Secondary endpoints

Itch intensity and quality of life. 24-h itch intensity significantly decreased in both Cryosim-1 groups: 0.1% group from 6.5 ± 1.5 to 4.0 ± 1.5 ($p < 0.001$), 0.5% group from 7.5 ± 1.2 to 3.0 ± 1.4 ($p = 0.002$), with no signifi-

Table I. Baseline participant characteristics

Characteristic	Vehicle ($n = 10$)	0.1% Cryosim-1 ($n = 10$)	0.5% Cryosim-1 ($n = 10$)	*p*-value
Age (years)	48.5 ± 14.2	46.9 ± 13.6	48.0 ± 14.3	0.952
Sex (M/F)	4/6	4/6	4/6	1.000
24-h itch NRS	6.1 ± 1.5	6.2 ± 1.5	5.7 ± 1.6	0.789
TEWL (g/m²/h)	15.5 ± 2.9	14.3 ± 3.1	15.8 ± 3.0	0.701
SCH (AU)	55.7 ± 7.3	58.1 ± 7.0	57.3 ± 7.1	0.854
DLQI	9.1 ± 7.2	7.8 ± 3.2	9.3 ± 4.8	0.723
5D Itch Scale	12.0 ± 2.5	12.2 ± 2.5	13.6 ± 2.7	0.587
PAS	15.5 ± 3.0	15.8 ± 3.2	15.2 ± 3.1	0.812

NRS: Numeric Rating Scale; TEWL: transepidermal water loss; SCH: stratum corneum hydration; AU: arbitrary units; DLQI: Dermatology Life Quality Index; PAS: Prurigo Activity Score.

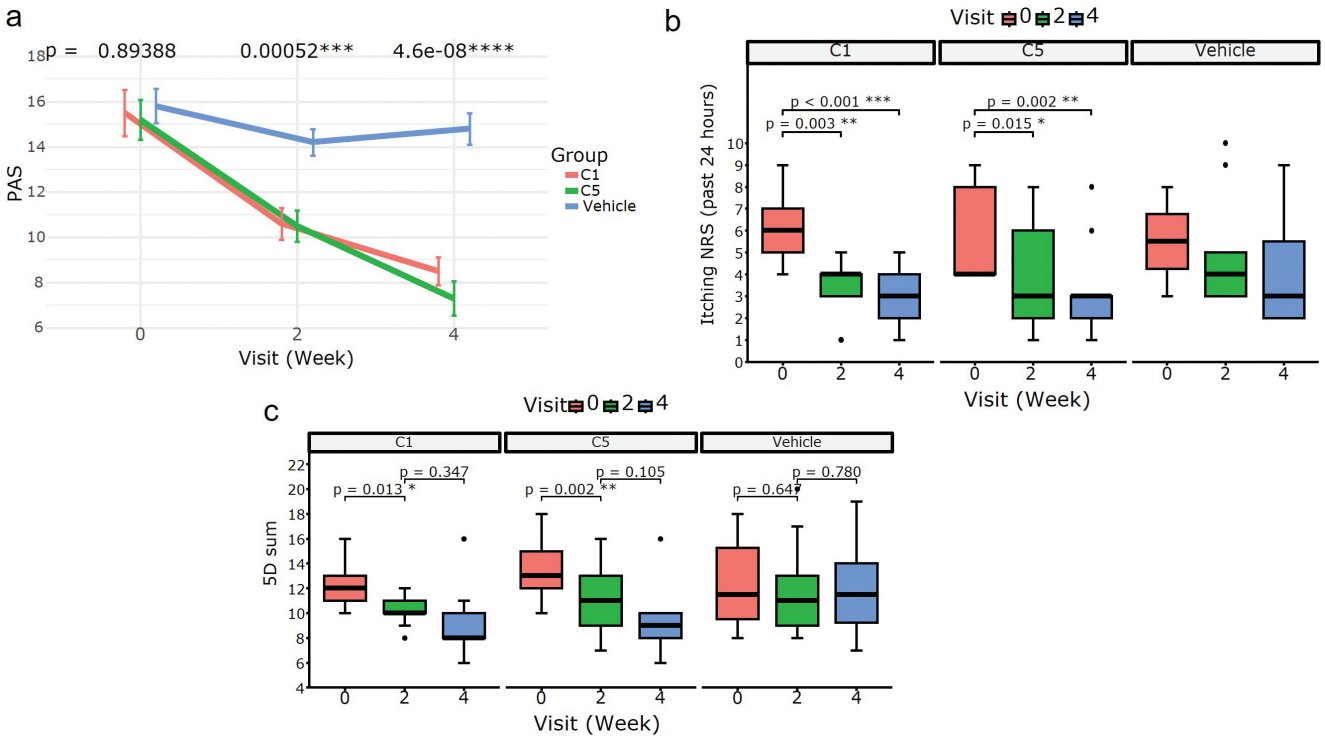

Fig. 1. Improvement in itch severity by Prurigo Activity Score (PAS), 24-h Itch Numeric Rating Scale (NRS), and 5D Itch Scale. (A) Change in PAS from baseline to Week 4 in the C1 (0.1% Cryosim-1), C5 (0.5% Cryosim-1), and vehicle groups. Both active treatment groups showed significant reductions compared with vehicle. (B) 24-h itch intensity measured by NRS at Weeks 0, 2, and 4. Significant within-group reductions were observed in the C1 and C5 groups. (C) 5D Itch Scale total scores across visits, with significant improvement at Week 4 in the C1 group. Box plots indicate median, interquartile range, and outliers; *p*-values calculated using repeated measures ANOVA with post-hoc tests. *$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$.

cant change in the vehicle group (5.5 ± 2.2 to 5.0 ± 2.1, $p>0.05$) (Fig. 1B). 5D Itch Scale scores improved significantly in both Cryosim-1 groups: 0.1% from 12.2 ± 2.5 to 8.9 ± 2.3 ($p<0.013$) and 0.5% from 13.6 ± 2.7 to 9.3 ± 2.5 ($p<0.01$), with no significant change in vehicle (Fig. 1C). DLQI scores improved significantly in both active treatment groups: 0.1% group from 10.5 ± 3.5 to 5.0 ± 2.8 ($p=0.0353$), 0.5% group from 13.0 ± 4.0 to 5.0 ± 2.0 ($p=0.010$), while the vehicle group showed no

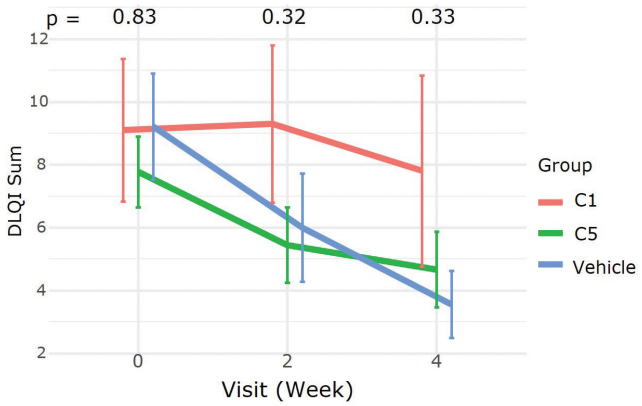

Fig. 2. Effect of Cryosim-1 on 24-h Itch Numerical Rating Scale (NRS) scores. Boxplots showing the distribution of Numeric Rating Scale (NRS) scores for itching (past 24 h) at each visit (Weeks 0, 2, and 4). Significant reductions were observed in both C1 and C5 groups compared with baseline. No significant reduction was observed in the vehicle group. *p*-values represent comparisons with baseline.

significant improvement (6.0 ± 3.5 to 5.0 ± 3.0, $p>0.477$) (**Fig. 2**).

Skin barrier function. Both Cryosim-1 formulations significantly improved skin barrier parameters. TEWL decreased significantly in the 0.1% group (C1, from approximately 14.5 to 8.5 g/m²/h, $p<0.001$) and in the 0.5% group (C5, from 15.5 to 9.0 g/m²/h, $p<0.001$), while the vehicle group showed no significant change (approximately 16.5 to 15.5 g/m²/h, $p>0.05$) (**Fig. 3**A). SCH increased significantly in both active groups: 0.1% (C1) from approximately 60 to 72 arbitrary units ($p=0.004$), 0.5% (C5) from 63 to 75 ($p=0.001$), while the vehicle group showed no statistically significant increase (from 56 to 65, $p>0.05$) (B).

Immediate post-application responses. To evaluate the immediate sensory effects of Cryosim-1, numerical rating scale (NRS) scores for itch and pain were recorded over 10 min following product application at Week 2 (**Fig. 4**A, B). The area under the curve (AUC) for itching NRS revealed a significantly lower cumulative itch burden in both Cryosim-1 groups compared with the vehicle (Fig. 4C, D). The 0.1% Cryosim-1 group (C1) showed an AUC of 15.8 ± 11.8, and the 0.5% group (C5) had an AUC of 16.5 ± 14.2, both significantly lower than the vehicle group (31.8 ± 17.2, $p=0.041$ vs C1; $p=0.067$ vs C5).

In contrast, for pain or stinging sensation, the 0.5% Cryosim-1 group reported a significantly higher AUC

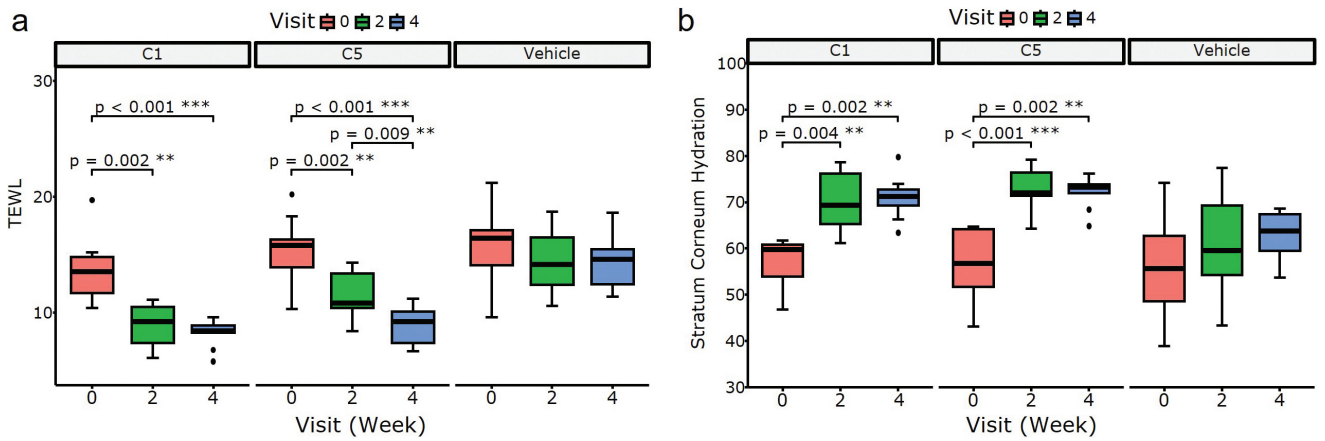

Fig. 3. Improvement in skin barrier function assessed by TEWL and stratum corneum hydration. (A) TEWL (transepidermal water loss) decreased significantly in both C1 and C5 groups from baseline to Week 4, indicating improved barrier integrity. No significant changes were noted in the vehicle group. (B) Stratum Corneum Hydration (SCH) increased significantly in both active treatment groups, while no meaningful changes were observed in the vehicle group. *Error bars indicate variability; **p*-values denote statistical significance.

(12.9 ± 3.8) and peak pain NRS (3.6 ± 1.7) compared with both the vehicle (AUC: 7.1 ± 1.8, peak: 1.1 ± 0.3) and the 0.1% group (AUC: 6.9 ± 1.4, peak: 1.2 ± 0.4), with $p < 0.001$ for all comparisons. There were no significant differences between the vehicle and 0.1% Cryosim-1 groups for either pain AUC or peak scores (Fig. 4E, F). Additionally, peak itching NRS values were not significantly different among the 3 groups, indicating that while

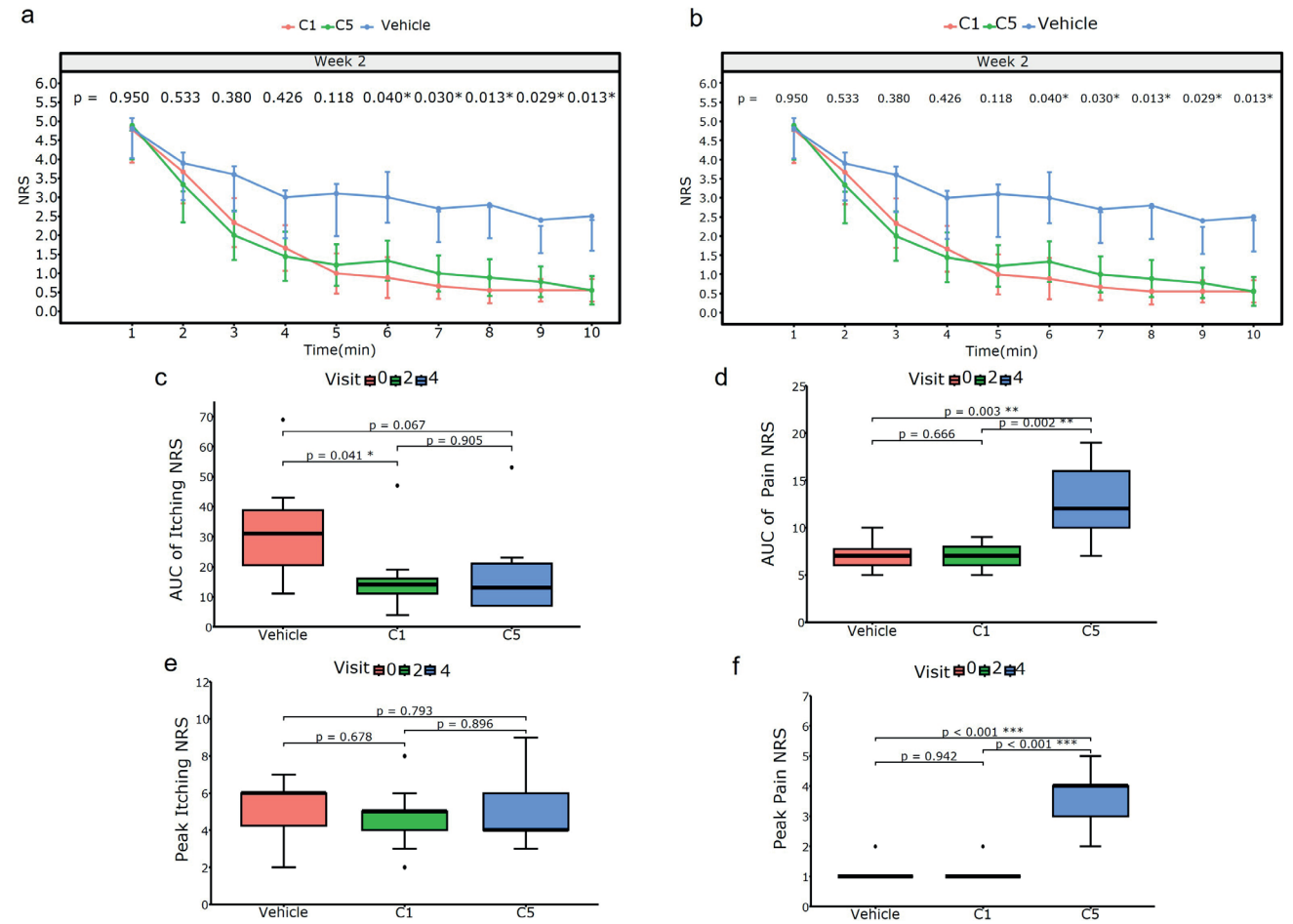

Fig. 4. Immediate sensory response following a single application at Week 2. (A–B) Time-course of itch and pain scores over 10 min. (C–D) Area under the curve (AUC) of itch and pain. (E–F) Peak NRS values. Cryosim-1 significantly reduced itch burden but 0.5% group showed increased stinging sensation.

cumulative itch was lower with Cryosim-1, the maximal immediate itch sensation did not differ significantly across treatments.

Patient satisfaction. For itch relief satisfaction, 60% of participants in the 0.1% group rated their satisfaction as 4 or 5 (satisfied or very satisfied) compared with 40% in vehicle and only 20% in the 0.5% group. Moisturizing effect satisfaction was comparable across all groups (50–60% rating 4 or 5).

Safety and tolerability

Eight adverse events were reported during the study, all classified as mild and transient. No serious adverse events occurred, and no participants discontinued treatment due to adverse events.

The 0.5% concentration showed a higher incidence of transient erythema (40% vs 0% in other groups) and comparable stinging sensation rates (20%) to the 0.1% group. All adverse events resolved spontaneously within 10 min without intervention.

DISCUSSION

The magnitude of PAS reduction (approximately 46% in both active groups vs 4% with vehicle) demonstrates a clinically meaningful improvement in chronic prurigo severity, encompassing itch intensity, lesion characteristics, and quality of life (11, 12) (Table SIII). Recently, Zeidler et al. (12) proposed a simplified PAS scoring system (0–11) based on lesion count, excoriation, and healing status, which may enhance reliability in future Cryosim-1 trials (Table SIV). Furthermore, Cryosim-1's multi-dimensional efficacy and favourable tolerability distinguish it from treatments targeting only inflammation or symptoms, positioning it as a holistic therapeutic approach comparable to dupilumab and nemolizumab in recent phase 3 trials (5, 6).

Improvements in skin barrier function, evidenced by significant reductions in TEWL and increases in stratum corneum hydration, likely contributed to sustained clinical benefit. Barrier restoration may help disrupt the itch–scratch cycle, a key driver of disease chronicity (13). The observed PAS reduction appears to be largely driven by progressive lesion healing rather than absolute lesion count reduction, supported by improved barrier function and reduced scratching behaviour. These findings indicate that Cryosim-1 may help interrupt the itch–scratch cycle by improving both pruritus and barrier dysfunction, complementing its direct TRPM8-mediated antipruritic effect (4, 15).

Interestingly, the higher patient satisfaction rate observed in the vehicle group (40%) compared with the TRPM8 0.5% group may be partly explained by the influence of local adverse sensations reported by some participants, such as cooling sensations or transient irritation. Although PAS improvement was greater in the TRPM8 0.5% group, these findings suggest that subjective satisfaction may be more strongly affected by initial sensory experiences than by objective efficacy. This highlights the need for future studies to evaluate patient satisfaction stratified by the presence or absence of adverse sensory events. The dose-dependent increase in stinging, pain, and erythema with the 0.5% concentration, without proportional efficacy gains, identifies 0.1% Cryosim-1 as the optimal therapeutic concentration. Immediate post-application assessments showed similar itch relief in both groups, but the 0.5% group reported significantly higher pain scores (NRS 3.6 ± 1.7 vs 1.2 ± 0.4) and a 40% incidence of erythema vs 0% in the 0.1% group. Patient satisfaction was also higher with 0.1% (60% vs 20%), highlighting the importance of tolerability in chronic daily application and long-term adherence (9, 11).

Current topical treatments – including corticosteroids, calcineurin inhibitors, and off-label agents – are limited by safety concerns and inconsistent efficacy (4, 16). However, the choice between topical and systemic therapy should be primarily guided by disease extent and severity rather than cost considerations. Systemic biologics are generally recommended for widespread or severe cases, whereas topical treatments such as Cryosim-1 may be particularly relevant for localized or moderate disease. In our cohort, most participants had a limited to moderate number of nodules localized to the extensor surfaces, with prior treatments largely restricted to topical corticosteroids and emollients, supporting the rationale for evaluating a topical TRPM8 agonist in this population. In contrast, Cryosim-1 provides a mechanistically distinct, non-immunosuppressive approach targeting TRPM8-mediated itch modulation, potentially offering a safer and more tolerable long-term therapy validated by recent clinical developments (7–10). TRPM8 channels play a critical role in thermosensation and interact with itch pathways, making them a compelling therapeutic target based on emerging insights into somatosensory processing (7). Activation of TRPM8 produces cooling sensations that modulate peripheral itch signalling through competing neural pathways (3). Additionally, TRPM8 expression in keratinocytes may contribute to improved barrier homeostasis, supporting Cryosim-1's dual benefits on both symptom control and barrier integrity (17).

The immediate post-application assessments demonstrated that Cryosim-1 provided rapid itch relief and sustained improvement over time, as indicated by a significantly lower area under the curve for itch intensity compared with vehicle. These findings highlight Cryosim-1's potential for both acute itch episodes and chronic management, positioning it as a versatile topical therapy that may complement systemic biologics. In the context of the rapidly evolving treatment landscape for

chronic prurigo, where FDA-approved biologics have established high efficacy benchmarks with 56–60% response rates (5), TRPM8 agonists occupy a unique therapeutic niche. While systemic treatments require weeks to months for optimal effect, Cryosim-1 provides rapid onset relief within minutes to hours, making it particularly valuable for breakthrough symptoms or as adjunctive therapy. The cost-effectiveness advantage of topical therapy compared with biologics, which can cost tens of thousands of dollars annually, positions Cryosim-1 as an attractive first-line option or combination treatment. Recent guidelines emphasize the importance of personalized treatment approaches that consider disease severity, patient preferences, and treatment goals (18), and Cryosim-1's favourable risk–benefit profile makes it suitable for a broad range of patients, including those with contraindications to systemic therapies (19, 20).

Limitations

This pilot study's limitations include the relatively small sample size ($n=30$), which limits detection of rare adverse events and may affect generalizability of findings to broader chronic prurigo populations. The 4-week duration, while adequate for initial efficacy assessment and consistent with regulatory guidance for topical antipruritic agents, does not address long-term safety profiles or sustained benefits that would be relevant for chronic management. Although the primary endpoint was assessed at Week 4, we acknowledge that PAS, which captures both lesion count and healing, typically evolves over a longer period. The rationale for selecting Week 4 was to evaluate early safety, adherence, and exploratory efficacy signals of TRPM8 agonism, while recognizing that longer studies are required to fully assess lesion clearance. Future trials with extended follow-up are planned to address this limitation. The single-centre design may introduce selection bias and limit generalizability across different populations and healthcare settings. Additionally, the study population included patients with general chronic pruritus rather than specific prurigo subtypes, which may limit direct applicability to distinct clinical entities like prurigo nodularis, lichen simplex chronicus, or atopic dermatitis with prurigo features (1). Future research should include larger, multi-centre trials with extended follow-up periods to establish long-term safety and durability of response, investigation of Cryosim-1's potential as a combination therapy with existing treatments, and evaluation in specific prurigo populations to optimize clinical applications and identify patient characteristics that predict treatment response. Localized pruritus, with restricted lesion distribution and neurocutaneous changes, may particularly benefit from topical therapies. Cryosim-1 may be particularly effective in localized pruritus, and future studies should include subgroup analyses to confirm this.

The identification of 0.1% Cryosim-1 cream as providing an optimal balance between efficacy and tolerability supports its potential role as a first-line topical therapy for chronic prurigo, particularly in patients seeking alternatives to corticosteroids or calcineurin inhibitors. Its favourable safety profile, dual mechanism targeting both symptoms and barrier dysfunction, and high patient satisfaction indicate broad applicability across diverse patient populations. Furthermore, its non-immunosuppressive mechanism makes it suitable for patients with contraindications to systemic therapies, including those with infections, malignancy history, or immunocompromised states (8, 9). By complementing existing moisturizing strategies and supporting barrier repair, Cryosim-1 may reduce the need for long-term anti-inflammatory therapy and can be integrated into current treatment algorithms as monotherapy for mild-to-moderate disease or adjunctive therapy for severe cases (21).

Conclusion

This randomized controlled trial demonstrates that Cryosim-1 0.1% cream significantly improves chronic prurigo severity across multiple validated outcome measures, achieving an optimal balance between efficacy and tolerability. These findings highlight the therapeutic potential of TRPM8 agonists and position Cryosim-1 0.1% as a promising addition to current treatment options for chronic pruritic conditions.

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IRB approval status: The study protocol was approved by the Institutional Review Board (IRB No. 2023-04-015) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

The authors have no conflicts of interest to declare.

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