e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(3); 1920-1926

Original Research Article

# Randomized Clinical Study of Topical Pimecrolimus Versus Clobetasone in Seborrheic Eczematous Otitis Externa

**Bhawesh Rajak[1], Sanjay Kumar[2], Anwar Kabir[3]**

[1]Senior Resident, Department of Skin and VD, GMCH, Purnia, Bihar, India
[2]Associate Professor, Department of Physiology, GMCH, Purnia, Bihar, India
[3]Senior Resident, Department of ENT, GMCH, Purnia, Bihar, India

**Received: 05-12-2025 / Revised: 06-01-2026 / Accepted: 07-02-2026**
**Corresponding Author: Dr. Anwar Kabir**
**Conflict of interest: Nil**

**Abstract:**

**Background:** Seborrheic dermatitis is a chronic inflammatory dermatosis that frequently extends to involve the external auditory canal, manifesting as chronic eczematous otitis externa. The condition is characterised by persistent pruritus, greasy scaling, erythema, and a relapsing clinical course. While topical corticosteroids constitute the cornerstone of therapy and afford rapid symptomatic relief, their prolonged use in this anatomically sensitive region carries the risk of cutaneous atrophy, rebound inflammation, and disease chronicity. Calcineurin inhibitors represent an emerging steroid-sparing class that may overcome these limitations.

**Objective:** To compare the efficacy and safety of topical pimecrolimus 1% cream with clobetasone butyrate 0.05% cream in patients with chronic seborrheic eczematous otitis externa over a six-month period.

**Methods:** A randomised, prospective, comparative clinical study was conducted among patients attending dermatology and ENT outpatient departments with a diagnosis of seborrheic eczematous otitis externa. Eligible participants were randomised into two groups: Group A received topical pimecrolimus 1% cream twice daily, and Group B received topical clobetasone butyrate 0.05% cream twice daily. Clinical outcomes — including pruritus score, erythema, scaling, canal oedema, and patient satisfaction — were assessed at baseline, 1 month, 3 months, and 6 months.

**Results:** Both groups demonstrated statistically significant improvement in symptom scores during follow-up. Patients in Group B (clobetasone) showed earlier symptomatic relief at the one-month assessment. However, patients in Group A (pimecrolimus) exhibited superior long-term disease control, lower recurrence rates at three and six months, and a more favourable safety profile. Mild transient burning was the principal adverse effect noted in the pimecrolimus arm, whereas prolonged clobetasone use was associated with local dryness, irritation, and a higher propensity for symptom recurrence on discontinuation.

**Conclusion:** Topical pimecrolimus 1% cream is an effective and safe alternative to topical corticosteroids for the management of chronic seborrheic eczematous otitis externa, particularly in patients who require prolonged or repeated treatment courses. Its steroid-sparing properties and sustained disease control render it a clinically meaningful therapeutic option.

**Keywords:** Seborrheic Dermatitis; Otitis Externa; Pimecrolimus; Clobetasone Butyrate; Calcineurin Inhibitors; Ear Eczema.

**DOI:** 10.25258/ijcpr.18.3.316



## Introduction

Otitis externa refers to a heterogeneous group of inflammatory conditions affecting the external auditory canal (EAC) and the auricle. Among its diverse aetiologies, seborrheic dermatitis — a chronic, relapsing, papulosquamous condition driven by host immune responses to commensal Malassezia species — represents one of the most prevalent dermatological causes of chronic eczematous otitis externa. [2,4] The EAC shares histological characteristics with sebaceous gland-rich skin and is therefore particularly susceptible to seborrheic involvement, which may occur in isolation or as part of a more generalised craniofacial distribution.

Clinically, patients present with pruritus, greasy or fine scaling within the canal, mild erythema, and a sense of canal fullness or discomfort. The condition tends to follow a waxing-and-waning course, with exacerbations precipitated by environmental humidity, excessive cerumen production, use of hearing aids, and psychosocial stress. [5,6] In a subset of patients, secondary bacterial or fungal

colonisation may complicate the clinical picture and necessitate adjunct antimicrobial therapy.

The conventional management of seborrheic eczematous otitis externa relies on topical corticosteroids, either alone or in combination with antifungal agents. [8,9] Topical corticosteroids exert their anti-inflammatory effects by suppressing the production of pro-inflammatory cytokines and attenuating cellular immune responses. In clinical practice, low- to mid-potency preparations such as clobetasone butyrate 0.05% are preferred for use within the EAC, balancing therapeutic efficacy against the risk of local adverse effects. However, the anatomical confinement of the EAC, combined with the need for prolonged treatment in chronic and relapsing cases, heightens the potential for steroid-related cutaneous atrophy, rebound inflammation, secondary infection, and long-term patient non-compliance. [22,23]

In recent years, topical calcineurin inhibitors (TCIs) have emerged as a class of non-steroidal anti-inflammatory agents with substantial clinical relevance in the management of eczematous dermatoses affecting sensitive or occluded skin regions. [20,21] Pimecrolimus, a member of the ascomycin macrolactam family, exerts selective inhibition of the calcineurin-dependent activation of T-lymphocytes, thereby reducing the transcription and release of pro-inflammatory cytokines including interleukin-2 (IL-2), tumour necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ). [21] Crucially, unlike topical corticosteroids, pimecrolimus does not impair collagen synthesis and does not carry the risk of inducing cutaneous atrophy, rendering it particularly suitable for chronic application in sensitive anatomical sites. [20]

Despite the theoretical basis for the efficacy of pimecrolimus in seborrheic eczematous otitis externa, comparative clinical evidence evaluating its performance against established topical steroid regimens in the EAC setting is limited. The present study was therefore undertaken to evaluate and compare the therapeutic efficacy and safety of topical pimecrolimus 1% cream versus clobetasone butyrate 0.05% cream in patients with chronic seborrheic eczematous otitis externa over a six-month follow-up period.

## Materials and Methods

**Study Design:** This was a randomised, prospective, open-label, comparative clinical study conducted over a period of 12 months (six months of active treatment and follow-up per enrolled patient) at the Departments of Dermatology and Ear, Nose, and Throat (ENT) of [Institution, City, Country]. The study was conducted in accordance with the principles of the Declaration of Helsinki and received approval from the Institutional Ethics Committee (IEC Reference No.: [Information Required]). All participants provided written informed consent prior to enrolment.

**Study Population:** Consecutive patients presenting to the dermatology and ENT outpatient departments with clinical features of seborrheic eczematous otitis externa were assessed for eligibility. A total of 128 patients were screened, of whom 100 met the inclusion criteria and were enrolled.

### Eligibility Criteria

### Inclusion Criteria

- Age above 18 years
- Clinical diagnosis of seborrheic dermatitis involving the external auditory canal, established by a consultant dermatologist and/or ENT surgeon
- History of chronic or recurrent pruritus and/or scaling of the EAC of at least 3 months' duration
- Willingness to attend scheduled follow-up visits at 1, 3, and 6 months
- Ability to provide written informed consent

### Exclusion Criteria

- Acute bacterial otitis externa requiring systemic antimicrobial therapy
- Otomycosis or clinically confirmed fungal otitis externa
- Tympanic membrane perforation, confirmed on otoscopy
- Immunocompromised status, including patients with HIV infection, active malignancy, or those receiving immunosuppressive pharmacotherapy
- Systemic corticosteroid uses within four weeks prior to enrolment
- Pregnancy or lactation
- Known hypersensitivity to pimecrolimus, clobetasone, or any constituent of the study preparations
- Active infection of the EAC requiring antimicrobial treatment at the time of enrolment

**Randomisation and Treatment Allocation:** Eligible participants were randomised in a 1:1 ratio into one of two treatment groups using a computer-generated random number sequence. Allocation concealment was maintained using sequentially numbered, sealed, opaque envelopes.

Group A (Pimecrolimus): Patients applied topical pimecrolimus 1% cream to the affected EAC twice daily using a clean fingertip or cotton applicator.

Group B (Clobetasone): Patients applied topical clobetasone butyrate 0.05% cream to the affected EAC twice daily using a similar technique.

Both groups were advised to avoid the use of any other topical or systemic anti-inflammatory agents

for the duration of the study. Topical antifungal agents and otic antiseptic drops were not permitted unless clinically necessitated by secondary infection, in which case the patient was considered a protocol deviation and managed accordingly.

**Clinical Assessment:** All patients were assessed at baseline and at scheduled follow-up visits at 1 month, 3 months, and 6 months. Clinical assessments were performed by trained physicians blinded to the treatment allocation where feasible. The following parameters were evaluated using standardised scoring systems:

Pruritus was scored on a four-point scale: 0 = none; 1 = mild (occasional, not interfering with daily activities); 2 = moderate (frequent, partially interfering); 3 = severe (constant, significantly interfering).

Erythema, scaling, and canal oedema were each scored on a four-point scale: 0 = absent; 1 = mild; 2 = moderate; 3 = severe.

Patient satisfaction was recorded at each follow-up visit on a visual analogue scale (VAS) ranging from 0 (completely unsatisfied) to 10 (completely satisfied). Adverse effects — including burning, stinging, local dryness, secondary infection, and any other untoward events — were recorded at every visit.

**Outcome Measures:** The primary outcome measure was the change in total composite symptom score (sum of pruritus, erythema, scaling, and canal oedema scores) from baseline to six months. Secondary outcome measures included: (i) within-group and between-group symptom score changes at 1 and 3 months; (ii) disease recurrence rate at six months; (iii) patient satisfaction scores; and (iv) adverse effect profile.

**Statistical Analysis:** Statistical analyses were performed using [Statistical Software, Version; e.g., SPSS version 26.0, IBM Corp., Armonk, NY]. Continuous data are expressed as mean ± standard deviation (SD). Within-group comparisons across time points were performed using the Wilcoxon signed-rank test for non-parametric data or the paired t-test for parametric data, as appropriate. Between-group comparisons at each time point were performed using the Mann–Whitney U test or independent samples t-test. Categorical data are presented as frequencies and percentages, and between-group comparisons were made using the chi-square test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant for all analyses.

## Results

**Participant Enrolment and Baseline Characteristics:** A total of 100 patients were enrolled and randomised: 50 to Group A (pimecrolimus) and 50 to Group B (clobetasone). Ninety-four patients (47 in each group) completed all four assessment visits and were included in the final per-protocol analysis; six patients were lost to follow-up (three per group) for reasons unrelated to study treatment. The two groups were comparable at baseline with respect to age, sex distribution, duration of symptoms, laterality of canal involvement, and prior treatment history (Table 1). No statistically significant inter-group differences in baseline clinical scores were identified ($p > 0.05$ for all parameters).

**Table 1: Baseline Demographic and Clinical Characteristics of the Study Population**

| Characteristic | Group A – Pimecrolimus (n = 50) | Group B – Clobetasone (n = 50) |
|---|---|---|
| Age, years – mean ± SD | 34.6 ± 9.2 | 35.1 ± 8.7 |
| Sex – Male / Female | 28 / 22 | 26 / 24 |
| Duration of symptoms, months | 7.8 ± 3.4 | 8.2 ± 3.6 |
| Prior topical steroid use, n (%) | 31 (62.0) | 29 (58.0) |
| Bilateral canal involvement, n (%) | 18 (36.0) | 20 (40.0) |

SD, standard deviation. Values are mean ± SD or n (%) as indicated.

**Primary Outcome: Change in Composite Symptom Score:** Both treatment groups demonstrated statistically significant reductions in the total composite symptom score across all follow-up time points compared with baseline ($p < 0.05$ for all within-group comparisons). At the one-month assessment, patients in Group B (clobetasone) exhibited a numerically greater reduction in composite score compared with Group A (pimecrolimus), suggesting a faster onset of anti-inflammatory action associated with topical corticosteroid therapy.

However, at the three-month and six-month assessments, Group A demonstrated superior overall maintenance of clinical improvement, with lower recurrence rates and more stable symptom scores. Between-group differences in composite symptom scores at three and six months were statistically significant in favour of pimecrolimus (mean composite score 2.4 versus 4.2 at six months; $p < 0.01$).

**Secondary Outcomes Pruritus and Erythema:** Pruritus scores declined significantly in both groups at one month. At three and six months, Group A maintained lower mean pruritus scores compared with Group B, consistent with the better sustained

disease control noted in the pimecrolimus arm. Erythema resolution followed a similar pattern, with clobetasone-treated patients exhibiting faster early improvement but higher rates of relapse upon treatment discontinuation (Table 2).

**Table 2: Mean Clinical Symptom Scores at Baseline, 1 Month, and 3 Months by Treatment Group**

| Parameter | Baseline Group A | Baseline Group B | 1 Month Group A | 1 Month Group B | 3 Months Group A | 3 Months Group B |
|---|---|---|---|---|---|---|
| Pruritus score (0–3) | 2.6 | 2.5 | 1.4 | 0.9 | 0.8 | 1.3 |
| Erythema score (0–3) | 2.3 | 2.2 | 1.2 | 0.7 | 0.6 | 1.1 |
| Scaling score (0–3) | 2.4 | 2.3 | 1.3 | 0.8 | 0.7 | 1.2 |
| Canal edema score (0–3) | 1.6 | 1.5 | 0.7 | 0.4 | 0.3 | 0.6 |
| Patient satisfaction (%) | — | — | 74.0 | 81.0 | 87.0 | 70.0 |

Scores are on a 0–3 scale (mean values, n = 50 per group at baseline; n = 47 per group at 1 and 3 months). Group A = Pimecrolimus; Group B = Clobetasone.

**Disease Recurrence:** Disease recurrence, defined as return of symptoms necessitating re-treatment, was assessed at the six-month follow-up. The recurrence rate was lower in Group A compared with Group B (12.8% versus 31.9%, respectively; p = 0.02). This finding suggests a more durable remission achieved by pimecrolimus relative to the topical corticosteroid.

**Patient Satisfaction:** Patient satisfaction scores on the VAS were comparable between groups at one month. At the three-month and six-month assessments, satisfaction scores were numerically higher in Group A, reflecting the sustained clinical benefit and absence of steroid-related side effects in the pimecrolimus group (8.7 versus 7.0 out of 10 at six months; p = 0.01).

**Adverse Effects:** Mild transient burning or stinging at the site of application was reported by 9 patients (18.0%) in Group A during the first one to two weeks of treatment; this was uniformly self-resolving and did not lead to treatment discontinuation. In Group B, prolonged topical corticosteroid application was associated with local dryness and mild irritation in 14 patients (28.0%), particularly at the three- and six-month assessments. Symptoms suggestive of rebound inflammation following treatment cessation were observed in 11 patients (22.0%) in Group B compared with 3 patients (6.0%) in Group A. No systemic adverse effects attributable to either preparation were documented. Table 3 summarises the adverse effect profiles.

**Table 3: Summary of Adverse Effects Observed During the Study Period**

| Adverse Effect | Group A – Pimecrolimus | Group B – Clobetasone |
|---|---|---|
| Transient burning sensation | Mild; self-resolving | Not reported |
| Local dryness / irritation | Not prominent | Observed in prolonged use |
| Cutaneous atrophy (suspected) | Not observed | 3 patients (6.0%) |
| Rebound inflammation | Lower incidence | Observed on discontinuation |
| Recurrence at 6 months | Lower | Higher |

Group A = Pimecrolimus 1% cream; Group B = Clobetasone butyrate 0.05% cream.

## Discussion

This randomised comparative study evaluated the clinical performance of topical pimecrolimus 1% cream against clobetasone butyrate 0.05% cream in patients with chronic seborrheic eczematous otitis externa. The key finding is that, while clobetasone afforded faster early symptomatic relief, pimecrolimus demonstrated superior long-term disease control and a more favourable adverse-effect profile, particularly with respect to treatment-emergent local tolerability and recurrence rates on sustained use.

The observed early advantage of clobetasone is consistent with the established pharmacodynamics of topical corticosteroids. By directly suppressing nuclear factor-kappa B (NF-κB) and glucocorticoid response element-mediated transcription, corticosteroids achieve rapid downregulation of pro-inflammatory mediators, clinically translating into swift reduction in erythema and pruritus. [22] This attribute makes low-potency topical steroids such as clobetasone the pragmatic first-choice agent for acute flares. However, the inherent chronicity and relapsing nature of seborrheic dermatitis mandates a more sustained treatment strategy, and it is in this context that the limitations of topical corticosteroids become clinically relevant.

The long-term superiority of pimecrolimus observed in the present study aligns with the pharmacological mechanism of calcineurin inhibitors. Pimecrolimus selectively binds to the intracellular receptor macrophilin-12 (FKBP-12 analogue), thereby inhibiting the phosphatase activity of calcineurin and preventing dephosphorylation of the nuclear factor of activated T cells (NFAT). [21] This

selective immunomodulatory effect restricts the synthesis and secretion of cytokines including IL-2, IL-4, IL-10, IL-13, TNF-α, and IFN-γ, without affecting collagen-synthesising fibroblasts. [20] The structural integrity of the canal epithelium is thereby preserved during prolonged therapy — a particularly important consideration in the confined, cartilaginous microenvironment of the EAC.

Prior published evidence supports the role of TCIs in seborrheic dermatitis affecting facial and scalp regions. Cicek et al. demonstrated in a randomised clinical study that pimecrolimus 1% cream achieved comparable efficacy to methylprednisolone aceponate 0.1% cream and was particularly effective in patients refractory to corticosteroid therapy. [15] Similarly, Warshaw et al. reported sustained disease control with pimecrolimus 1% cream in adult facial seborrheic dermatitis in a vehicle-controlled trial.[14] The present study extends this evidence base to the EAC, a site where the risk-benefit calculus strongly favours steroid-sparing alternatives given the occlusive anatomical configuration and heightened cutaneous sensitivity.

Mild transient burning following pimecrolimus application, as reported in Group A, is a well-characterised class effect of topical calcineurin inhibitors, generally attributed to local sensory nerve stimulation during the initial days of therapy. [20,21] This phenomenon is typically self-limiting and resolves within the first two weeks of therapy. In the present study, no patient in Group A discontinued therapy due to this side effect, corroborating the generally acceptable tolerability profile of the agent.

The higher recurrence rate in Group B upon treatment cessation is consistent with the concept of tachyphylaxis and rebound hyperresponsiveness associated with topical corticosteroid withdrawal. [22] Chronic steroid use may also alter the local microbiome within the EAC, potentially facilitating secondary colonisation by Malassezia or commensal bacteria, which in turn perpetuates the inflammatory cascade. The absence of such a phenomenon in the pimecrolimus group further underscores the potential of calcineurin inhibitors as maintenance therapy in this clinical setting.

It is important to contextualise these findings within the broader debate regarding the risk of cutaneous malignancy associated with long-term TCI use. Although the United States Food and Drug Administration (FDA) issued a black-box warning in 2006 cautioning about a theoretical risk of lymphoma and skin cancer with topical TCIs, [25] subsequent systematic reviews and long-term epidemiological data have not substantiated this concern at the doses used for dermatological indications. [25] Notwithstanding, clinicians should apply the principle of minimum effective duration, particularly in paediatric populations, and ensure appropriate patient counselling.

**Strengths and Limitations:** The present study contributes to a relatively sparse literature on the pharmacological management of chronic seborrheic eczematous otitis externa by providing prospective, randomised comparative data over a six-month period — a duration sufficient to assess both short-term efficacy and longer-term disease control and safety. The use of validated, standardised symptom scoring instruments and the inclusion of patient-reported satisfaction scores add clinical relevance to the findings.

Several limitations merit acknowledgment. First, the study employed an open-label design; although outcome assessors were blinded where feasible, the lack of double-blinding may have introduced performance or detection bias. Second, although the sample size of 100 patients permitted adequately powered comparisons for the primary endpoints, larger multicentre cohorts would strengthen the generalisability of the recurrence and safety findings. Third, the study did not include microbiological assessments of the EAC microbiome at different time points, which might have provided mechanistic insights into the differential recurrence rates observed between groups. Fourth, the study population was drawn from a single centre, which may limit the generalisability of findings to broader or more ethnically diverse populations. Finally, data beyond six months were not captured, precluding assessment of very long-term outcomes.

Future multicentre, double-blind, placebo-controlled trials incorporating larger sample sizes, objective biomarker endpoints, and extended follow-up periods are warranted to confirm and expand upon these findings.

## Conclusion

Topical pimecrolimus 1% cream represents a clinically effective, safe, and well-tolerated alternative to topical corticosteroids in the management of chronic seborrheic eczematous otitis externa. While clobetasone butyrate 0.05% offers a more rapid onset of symptomatic relief, pimecrolimus provides superior sustained disease control over six months, with a lower recurrence rate and a more favourable tolerability profile during prolonged use. In patients who require repeated or long-term topical therapy — a common scenario in the chronically relapsing nature of this condition — pimecrolimus offers a meaningful steroid-sparing option that circumvents the risks of cutaneous atrophy and rebound inflammation associated with extended corticosteroid application within the external auditory canal.

**Acknowledgements:** The authors wish to acknowledge the faculty, residents, and nursing staff of the Departments of Dermatology and ENT for their assistance in patient recruitment and data collection. We are grateful to all participants who contributed their time to this study.

**Funding Statement:** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The funding source had no role in study design, data collection, analysis, interpretation, or the decision to submit for publication.

**Conflict of Interest**

The authors declare that they have no conflicts of interest relevant to the subject matter or materials discussed in this manuscript. [If applicable, disclose specific financial relationships or affiliations.]

**Author Contributions**

**Dr. Bhawesh Rajak:** Conceptualization, study design, patient recruitment, data acquisition, manuscript drafting.
**Dr. Sanjay Kumar:** Patient recruitment, clinical assessment, data analysis, manuscript review.
**Dr. Anwar Kabir:** Statistical analysis, critical revision of the manuscript.

All authors have read and approved the final version of the manuscript and accept accountabilities for all aspects of the work.

**References**

1. Borda LJ, Wikramanayake TC. Seborrheic dermatitis and dandruff: a comprehensive review. J Clin Investig Dermatol. 2015;3(2):10.13188/2373-1044.1000019.
2. Wikramanayake TC, Borda LJ, Miteva M, Paus R. Seborrheic dermatitis-looking beyond Malassezia. Exp Dermatol. 2019;28(9):991-1001. doi:10.1111/exd.14006. PMID: 31310695.
3. Turchin I, et al. Current understanding of seborrheic dermatitis: epidemiology, burden of disease, and pathophysiology. J Cutan Med Surg. 2025;29(4_suppl):5S-15S. doi:10.1177/12034754251368840. PMID: 40965103.
4. Saunte DML, Gaitanis G, Hay RJ. Malassezia-associated skin diseases, the use of diagnostics and treatment. Front Cell Infect Microbiol. 2020;10:112. PMID: 32391275.
5. Naldi L. Seborrhoeic dermatitis. BMJ Clin Evid. 2010;2010:1713.
6. Gupta AK, Bluhm R, Cooper EA, Summerbell RC, Batra R. Seborrheic dermatitis. Dermatol Clin. 2003;21(3):401-412.
7. Borda LJ, Perper M, Keri JE. Treatment of seborrheic dermatitis: a comprehensive review. J Dermatolog Treat. 2019;30(2):158-169. doi:10.1080/09546634.2018.1473554.
8. Schaefer P, Baugh RF. Acute otitis externa: an update. Am Fam Physician. 2012;86(11):1055-1061. PMID: 23198673.
9. Rosenfeld RM, Schwartz SR, Cannon CR, et al. Clinical practice guideline: acute otitis externa. Otolaryngol Head Neck Surg. 2014;150(1 Suppl):S1-S24. doi:10.1177/0194599813517083. PMID: 24491310.
10. Roland PS, Stroman DW. Microbiology of acute otitis externa. Laryngoscope. 2002;112(7 Pt 1):1166-1177.
11. Caffier PP, Harth W, Mayelzadeh B, Haupt H, Sedlmaier B. Tacrolimus: a new option in therapy-resistant chronic external otitis. Laryngoscope. 2007;117(6):1046-1052.
12. Montoro V, Asensio C, Martínez Á, et al. Efficacy and safety of fluocinolone acetonide 0.025% otic solution in patients with otic eczema: a randomized, double-blind, placebo-controlled clinical trial. J Int Med Res. 2018;46(10):4050-4060. doi:10.1177/0300060518786755.
13. Successful treatment of erythematous-squamous disorders of the external auditory canal with tacrolimus and clotrimazole in otic oil: our experience in 25 patients. J Dermatolog Treat. 2021;32(6):673-678. doi:10.1080/09546634.2020.1737638. PMID: 33112026.
14. Warshaw EM, Wohlhuter RJ, Liu A, et al. Results of a randomized, double-blind, vehicle-controlled efficacy trial of pimecrolimus cream 1% for the treatment of moderate to severe facial seborrheic dermatitis. J Am Acad Dermatol. 2007;57(2):257-264. doi:10.1016/j.jaad.2006.11.007. PMID: 17188780.
15. Cicek D, Kandi B, Bakar S, Turgut D. Pimecrolimus 1% cream, methylprednisolone aceponate 0.1% cream and metronidazole 0.75% gel in the treatment of seborrhoeic dermatitis: a randomized clinical study. J Dermatolog Treat. 2009;20(6):344-349. doi:10.3109/09546630802687349. PMID: 19954391.
16. Koc E, Arca E, Kose O, Akar A. An open, randomized, prospective, comparative study of topical pimecrolimus 1% cream and topical ketoconazole 2% cream in the treatment of seborrheic dermatitis. J Dermatolog Treat. 2009;20(1):4-9. doi:10.1080/09546630802286993. PMID: 18677657.
17. Zhao J, Sun W, Zhang C, et al. Comparison of different regimens of pimecrolimus 1% cream in the treatment of facial seborrheic dermatitis.

J Cosmet Dermatol. 2018;17(1):90-94. doi:10.1111/jocd.12353. PMID: 28589618.
18. Goldust M, Rezaee E, Raghifar R. Treatment of seborrheic dermatitis: comparison of sertaconazole 2% cream versus pimecrolimus 1% cream. Ir J Med Sci. 2013;182(4):703-706. doi:10.1007/s11845-013-0960-8. PMID: 23715821.
19. Alsmeirat O, Lakhani S, Egaimi M, Idris O, Elkhalifa M. The efficacy and safety of pimecrolimus in patients with facial seborrheic dermatitis: a systematic review of randomized controlled trials. Cureus. 2022;14(8):e27622. doi:10.7759/cureus.27622. PMID: 36072203.
20. Cook BA, Warshaw EM. Role of topical calcineurin inhibitors in the treatment of seborrheic dermatitis: a review of pathophysiology, safety, and efficacy. Am J Clin Dermatol. 2009;10(2):103- 118. doi:10.2165/00128071-200910020-00003. PMID: 19222250.
21. Wollina U. Tacrolimus and pimecrolimus: from clever prokaryotes to inhibiting calcineurin and treating atopic dermatitis. J Eur Acad Dermatol Venereol. 2002;16(2):105-106. PMID: 11807435.
22. Barnes L, Kaya G, Rollason V. Topical corticosteroid-induced skin atrophy: a comprehensive review. Drug Saf. 2015;38(5):493-509. doi:10.1007/s40264-015-0287-7.
23. Ricardo JW, Gosch M, Wang F, et al. Risk of skin atrophy induced by short-term topical corticosteroid use in atopic dermatitis lesional skin: a systematic review. J Am Acad Dermatol. 2023. doi:10.1016/j.jaad.2023.06.030. PMC10338287.
24. Siegfried EC, Jaworski JC, Kaiser JD, Hebert AA. Systematic review of published trials: long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. BMC Pediatr. 2016;16:75. PMID: 27268321. PMC4895880.
25. Devasenapathy N, Chu A, Wong M, et al. Cancer risk with topical calcineurin inhibitors, pimecrolimus and tacrolimus, for atopic dermatitis: a systematic review and meta-analysis. Lancet Child Adolesc Health. 2023;7(1):13-25. doi:10.1016/S2352-4642(22)00283-8. PMID: 36370744.