An Investigator-Blinded Evaluation of Fluocinonide 0.1% Cream in the Treatment of Atopic Dermatitis and Psoriasis Vulgaris

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This article presents results from an investigator-blinded, randomized, split-body study completed in adult patients with atopic dermatitis, psoriasis vulgaris, and other corticosteroid-responsive dermatoses exhibiting symmetric involvement. In the psoriasis vulgaris group, results achieved with application of active treatment twice daily versus a designated emollient cream twice daily were compared over a 4-week duration. In the eczematous dermatoses group, results achieved with application of active treatment once daily or twice daily (depending on disease state treated) versus tacrolimus 0.1% ointment twice daily were compared over a study duration of up to 4 weeks.

Introduction

Fluocinonide 0.1% cream is a superpotent topical corticosteroid approved by the US Food and Drug Administration (FDA) for the treatment of atopic dermatitis, psoriasis vulgaris (plaque-type psoriasis), and other corticosteroid-responsive dermatoses. Clinical trials have been performed involving 443 patients with psoriasis vulgaris or atopic dermatitis treated once or twice daily for 2 weeks with fluocinonide 0.1% cream.

The designation of superpotent (class 1) topical corticosteroid was determined based on vasoconstrictor assay studies evaluating fluocinonide 0.1% cream.[1] Note that the 0.1% concentration of fluocinonide is 2-fold higher than conventional fluocinonide preparations (0.05%), which are primarily classified as high-potency formulations (class 2) and include creams, emollient creams, ointments, gels, and solutions. As the higher concentration of the active corticosteroid ingredient alone does not allow for superpotent activity based on vasoconstrictor assay, characteristics of the branded fluocinonide 0.1% cream vehicle contribute to the enhancement of active drug delivery into skin and the potency of the formulation.[1] The recommended maximum dosage of fluocinonide 0.1% cream is 60 g per week applied over a duration of 2 weeks.

Pivotal Trials Performed With Fluocinonide 0.1% Cream

In pivotal trials submitted to the FDA evaluating fluocinonide 0.1% cream for the treatment of atopic dermatitis, subjects (≥18 years of age) presenting with a rating of at least moderate severity applied the active cream once daily (n=109) or twice daily (n=102) versus vehicle cream once daily (n=50) or twice daily (n=52) for 14 consecutive days (body surface area range, 2%–10%).[1] Both once-daily and twice-daily regimens demonstrated that fluocinonide 0.1% cream was statistically superior to vehicle cream ($P<.001$); however, no difference was observed between once-daily and twice-daily applications.[1] The percentages of patients achieving treatment success, defined as cleared (no evidence of atopic dermatitis) or almost cleared (very minimal evidence of atopic dermatitis) after 2 weeks of application are presented in Table 1.

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TABLE 1

Patients With Atopic Dermatitis Achieving Treatment Success

Treatment	Patients Achieving Treatment Success, %*
Fluocinonide 0.1% cream once daily	59
Vehicle cream once daily	12
Fluocinonide 0.1% cream twice daily	57
Vehicle cream twice daily	19

*Treatment success defined as cleared (no evidence of atopic dermatitis) or almost cleared (very minimal evidence of atopic dermatitis).

TABLE 2

Patients With Psoriasis Vulgaris Achieving Treatment Success

Treatment	Patients Achieving Treatment Success, %*
Fluocinonide 0.1% cream once daily	18
Vehicle cream once daily	7
Fluocinonide 0.1% cream twice daily	31
Vehicle cream twice daily	6

*Treatment success defined as cleared (no evidence of psoriasis vulgaris) or almost cleared (very minimal evidence of psoriasis vulgaris).

In pivotal trials submitted to the FDA evaluating fluocinonide 0.1% cream for the treatment of psoriasis vulgaris (plaque-type psoriasis), subjects (≥18 years of age) applied the active cream once daily (n=107) or twice daily (n=107) versus vehicle cream once daily (n=54) or twice daily (n=55) for 14 consecutive days (body surface area range, 2%–10%).[1] Both once-daily and twice-daily regimens demonstrated that fluocinonide 0.1% cream was statistically superior to vehicle cream ($P<.001$).[1] The percentages of patients achieving treatment success, defined as cleared (no evidence of psoriasis vulgaris) or almost cleared (very minimal evidence of psoriasis vulgaris) after 2 weeks of application are presented in Table 2.

Significance of Primary End Point Assessments

Note that in the pivotal trials submitted to the FDA for evaluation for approval of fluocinonide 0.1% cream, the primary end point of treatment success after 2 weeks of active therapy was used in both the atopic dermatitis and psoriasis vulgaris studies. Treatment success in these trials was defined as the clinical determination of clear (no evidence of psoriasis or atopic dermatitis) or almost clear (very minimal evidence of psoriasis or atopic dermatitis) based on investigator assessment after 2 weeks of treatment. The investigator assessment is static, meaning that it is based on the presentation of the patient at that visit, not in comparison with baseline findings. The treatment success parameter is often used in recent studies based on FDA request and differs markedly from parameters that describe percent improvement as compared with baseline. Therefore, the reader is cautioned that comparison of results among different studies, especially when comparing different agents evaluated in separate trials, may be fraught with inaccuracy, as study criteria and assessment criteria may vary markedly among trials.

Current Clinical Trial

This article presents results from an investigator-blinded, randomized, split-body study completed in adult patients with atopic dermatitis, psoriasis vulgaris, and other corticosteroid-responsive dermatoses exhibiting symmetric involvement. In the psoriasis vulgaris group, results achieved with application of active treatment twice daily versus a designated emollient cream twice daily were compared over a 4-week duration. In the eczematous dermatoses group, results achieved with application of active treatment once daily or twice daily (depending on the disease state treated) versus tacrolimus 0.1% ointment twice daily were compared over a study duration of up to 4 weeks. Eczematous dermatoses included in the trial were atopic dermatitis, nummular eczema, and lichen simplex. Efficacy was assessed using a dichotomized investigator global assessment (IGA) and subject global assessment (SGA). Skin tolerability and safety assessments were also completed.

TABLE 3

Characteristics of Patients With Psoriasis Vulgaris or Eczematous Dermatoses Treated With Fluocinonide 0.1% Cream

Age, y	
	Mean, 39.8
	Range, 18–67
Gender, n	
	Male, 18
	Female, 12
Race, n	
	White, 20
	African American, 5
	Asian, 3
	Hispanic, 2

Patient Population

A total of 30 adult patients were included in an investigator-blinded, randomized, split-body evaluation of fluocinonide 0.1% cream used in the treatment of psoriasis vulgaris and corticosteroid-responsive eczematous dermatoses from 2 study sites. The study included 15 patients with psoriasis vulgaris, 7 with atopic dermatitis, 6 with nummular eczema, and 2 with lichen simplex. All patients presented with symmetric involvement of target areas for evaluation, mainly the extremities. None of the patients were undergoing use of a systemic or topical corticosteroid, topical calcineurin inhibitor, oral antihistamine, or any other medications that could affect study results (eg, cyclosporine, methotrexate, phototherapy, biologic agents) for at least 4 weeks prior to presentation. None of the patients with psoriasis vulgaris had previously received systemic retinoid therapy (eg, acitretin, etretinate, isotretinoin). Patient-related details are presented in Table 3.

Treatment Regimens

After initial assessment, target sites were determined in each patient prior to initiation of treatment based on symmetric involvement. All patients were instructed to apply only study medication and no other products (including moisturizers) to these regions.

Psoriasis Vulgaris

All patients were given a specified nonmedicated gentle skin cleanser to use during the trial. Patients were randomized to use fluocinonide 0.1% cream twice daily on one target side and a specified moisturizer cream on the other target side (control side) twice daily. Patients were followed at 1- to 2-week intervals, with the final visit at week 4. Therapy was continued for 4 weeks unless the investigator indicated otherwise at a follow-up visit during the trial.

Eczematous Dermatoses

This study group included subjects with atopic dermatitis, nummular eczema, and lichen simplex. All patients were given a specified nonmedicated gentle skin cleanser to use during the trial. Patients were randomized to use fluocinonide 0.1% cream once daily for atopic dermatitis, twice daily for nummular eczema, or twice daily for lichen simplex on one target side, and tacrolimus 0.1% ointment twice daily on the other target side. All patients included were rated to have disease of at least moderate severity at the target sites. Patients were followed at 1- to 2-week intervals, with the final visit at week 4. Therapy was continued for 4 weeks unless the investigator indicated otherwise at a follow-up visit during the trial.

Efficacy Assessments

Investigator Global Assessment

Investigators determined whether the condition of patients was completely cleared, almost cleared, moderately improved, minimally improved, unchanged, or worsened by treatment (Tables 4 and 5).

Representative cases of response to fluocinonide 0.1% cream for specific disease states are depicted in Figures 1 through 4.

Subject Global Assessment

Patients were asked to provide SGA based on determination of complete clearance, marked improvement, moderate improvement, minimal improvement, no improvement, or worsening. In addition, subjects treated in the eczematous dermatoses group were asked to record when pruritus resolved.

SGA of response in both the psoriasis vulgaris and eczematous dermatoses treatment groups was consistent with assessments completed by the investigators. No major differences were noted.

Evaluation of response of pruritus was not completed in the psoriasis vulgaris group, as this symptom was either absent or minimal. In the eczematous dermatoses group, the point (day) at which pruritus resolved

TABLE 4

Investigator Global Assessment in Subjects With Psoriasis Vulgaris

Psoriasis Group (n=15)	Fluocinonide Side	Control Side
Legs		
Patient 1, 37-year-old male		
Response week 2	Almost clear	Minimal improvement
Response week 4	Completely clear	Minimal improvement
Patient 2, 42-year-old male		
Response week 2	Almost clear	Minimal improvement
Response week 4	Almost clear	Worsened
Patient 7, 62-year-old male		
Response week 2	Minimal improvement	Unchanged
Response week 4	Moderate improvement	Minimal improvement
Patient 11, 55-year-old female		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Almost clear	Minimal improvement
Patient 13, 29-year-old female		
Response week 2	Moderate improvement	Unchanged
Response week 4	Almost clear	Unchanged
Patient 15, 27-year-old female		
Response week 2	Minimal improvement	Unchanged
Response week 4	Moderate improvement	Unchanged
Elbows		
Patient 3, 48-year-old female		
Response week 2	Moderate improvement	Unchanged
Response week 4	Almost clear	Minimal improvement
Patient 6, 52-year-old male		
Response week 2	Minimal improvement	Unchanged
Response week 4	Moderate improvement	Unchanged
Patient 9, 44-year-old male		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Almost clear	Minimal improvement
Patient 10, 37-year-old female		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Almost clear	Minimal improvement
Patient 12, 52-year-old male		
Response week 2	Minimal improvement	Unchanged
Response week 4	Moderate improvement	Minimal improvement
Patient 14, 28-year-old male		
Response week 2	Minimal improvement	Moderate improvement
Response week 4	Moderate improvement	Worsened
Knees		
Patient 4, 36-year-old female		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Almost clear	Minimal improvement
Patient 5, 51-year-old female		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Completely clear	Unchanged
Hands (dorsal)		
Patient 8, 50-year-old female		
Response week 2	Moderate improvement	Unchanged
Response week 4	Moderate improvement	Minimal improvement

TABLE 5

Investigator Global Assessment in Subjects With Eczematous Dermatoses*

Atopic Dermatitis Group (n=7)	Fluocinonide Side	Tacrolimus Side
Antecubital		
Patient 1, 18-year-old male		
Response week 2	Almost clear	Moderate improvement
Response week 4	Completely clear	Moderate improvement
Patient 2, 22-year-old female		
Response week 2	Completely clear	Moderate improvement
Response week 4	N/A	N/A
Patient 6, 18-year-old female		
Response week 2	Almost clear	Minimal improvement
Response week 4	Almost clear	Moderate improvement
Popliteal/legs		
Patient 3, 19-year-old female		
Response week 2	Moderate improvement	Minimal improvement
Response week 4	Completely clear	Almost clear
Patient 5, 22-year-old male		
Response week 2	Almost clear	Moderate improvement
Response week 4	Completely clear	Completely clear
Patient 7, 18-year-old male		
Response week 2	Completely clear	Moderate improvement
Response week 4	N/A	N/A
Arms/forearms		
Patient 4, 24-year-old female		
Response week 2	Completely clear	Moderate improvement
Response week 4	N/A	N/A
Nummular Eczema Group (n=6)	**Fluocinonide Side**	**Tacrolimus Side**
Ankles		
Patient 1, 52-year-old female		
Response week 2	Almost clear	Moderate improvement
Response week 4	Completely clear	Almost clear
Legs/ankles		
Patient 3, 67-year-old male		
Response week 2	Almost clear	Minimal improvement
Response week 4	Almost clear	Minimal improvement
Patient 4, 62-year-old female		
Response week 2	Almost clear	Minimal improvement
Response week 4	Completely clear	Moderate improvement
Legs		
Patient 5, 49-year-old male		
Response week 2	Completely clear	Moderate improvement
Response week 4	N/A	N/A
Patient 2, 57-year-old male		
Response week 2	Almost clear	Minimal improvement
Response week 4	Almost clear	Moderate improvement
Patient 6, 29-year-old female		
Response week 2	Completely clear	Moderate improvement
Response week 4	N/A	N/A

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TABLE 5 (CONTINUED)

Investigator Global Assessment in Subjects With Eczematous Dermatoses*

Lichen Simplex Group (n=2)	Fluocinonide Side	Tacrolimus Side
Foot/ankles (dorsal)		
Patient 1, 38-year-old female		
Response week 2	Almost clear	Minimal improvement
Response week 4	Almost clear	Moderate improvement
Ankles		
Patient 2, 51-year-old female		
Response week 2	Almost clear	Minimal improvement
Response week 4	Completely clear	Minimal improvement

*N/A indicates not applicable.

TABLE 6

Mean Time Until Complete Clearance of Pruritus in Patients With Eczematous Dermatoses*

Eczematous Dermatoses	Fluocinonide 0.1% Cream, d	Tacrolimus 0.1% Ointment, d
Atopic dermatitis (n=7)	5.42	13.71
Nummular eczema (n=6)	6.16	20.50†
Lichen simplex (n=2)	6.50	N/A‡

*N/A indicates not applicable.
†Based on 2 of 6 patients; pruritus was not cleared completely in the remaining 4 patients.
‡Pruritus was not cleared completely.

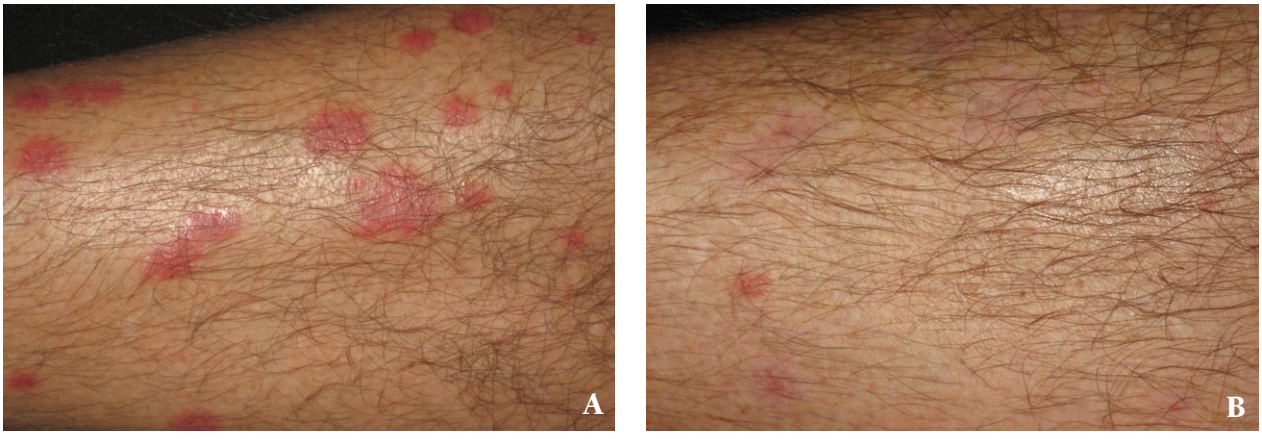

Figure 1. A 42-year-old male with plaque-type psoriasis on leg at baseline (A) and at end of study using fluocinonide 0.1% cream twice daily (B).

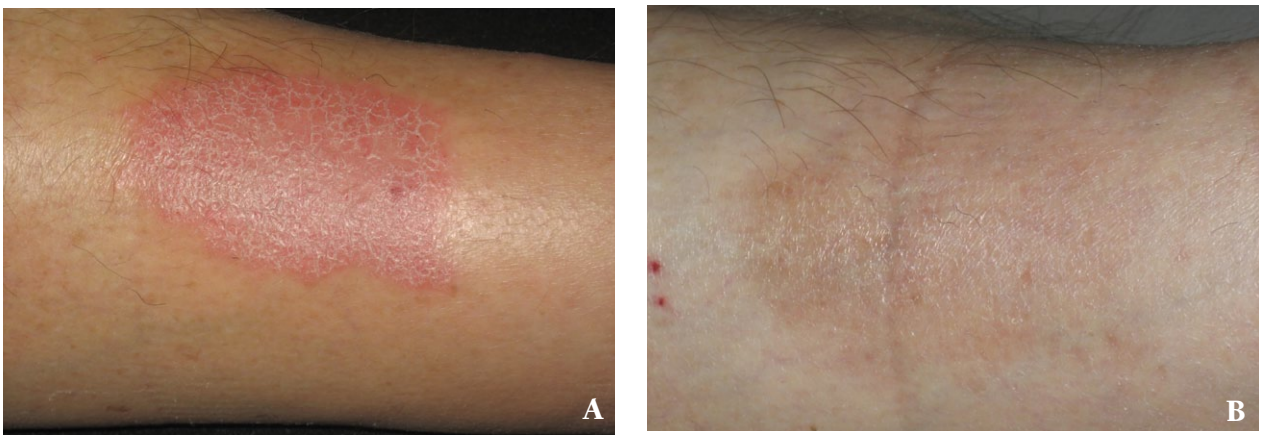

Figure 2. A 62-year-old male with plaque-type psoriasis on leg at baseline (A) and at end of study using fluocinonide 0.1% cream twice daily (B).

completely was recorded by the subjects. The mean time (number of days) until complete clearance of pruritus in the patients with eczematous dermatoses is presented in Table 6.

Safety Assessment

No serious adverse events occurred during the trial. All patients completed the trial, and none discontinued treatment. Two patients with atopic dermatitis and 1 patient with nummular eczema reported mild stinging after application of fluocinonide 0.1% cream over the first 2 to 3 days of use. The stinging was transient, with complete resolution within 1 to 2 minutes of application. One patient with atopic dermatitis treated with tacrolimus 0.1% ointment experienced mild, transient burning over the first 3 days of use, which resolved within a few minutes. No cases of cutaneous atrophy were noted.

Summary

Although statistical analysis was not completed owing to the small sample size, close prospective observation of results achieved in private practice, especially when potentially confounding variables are reasonably controlled, may provide clinically relevant information. The results observed in this investigator-blinded trial appeared to demonstrate that fluocinonide 0.1% cream produced better clinical results based on the evaluated parameters as compared with a designated control (branded moisturizer cream) used in the psoriasis vulgaris study group, or topical tacrolimus 0.1% ointment used in the eczematous dermatoses study group. All therapies were well tolerated.

Fluocinonide 0.1% cream applied twice daily for 4 weeks completely cleared 2 target areas, almost cleared 7 target areas, and moderately improved 6 target areas involving the extremities in 15 patients (15 target areas total) with psoriasis vulgaris. Among 7 target areas affected by at least moderately severe atopic dermatitis that were treated with fluocinonide 0.1% cream once daily, 3 target areas were completely cleared within 2 weeks, 3 target areas were completely cleared within 4 weeks, and 1 target area was almost cleared after 4 weeks of application.

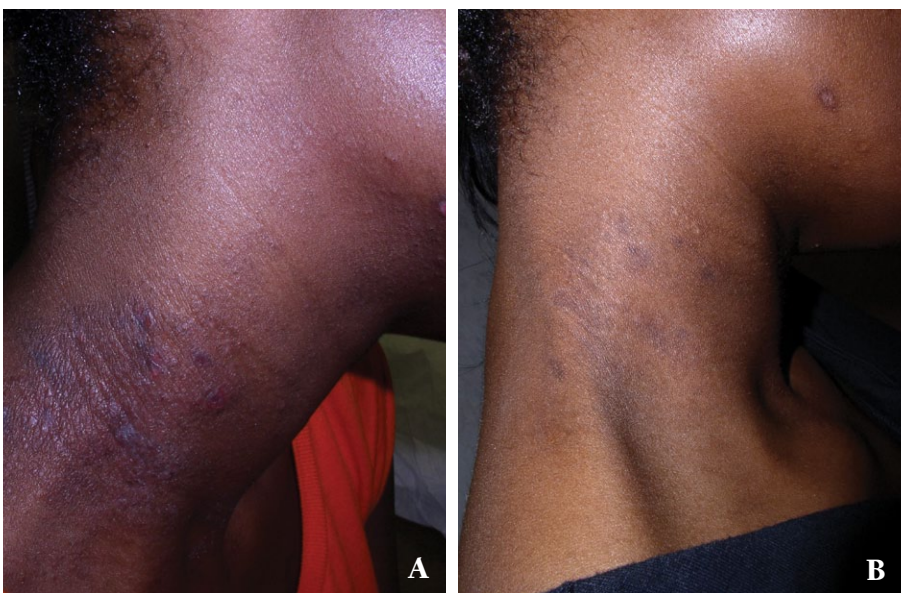

Figure 3. An 18-year-old female with atopic dermatitis on right lateral neck at baseline (A) and at end of study using fluocinonide 0.1% cream once daily (B).

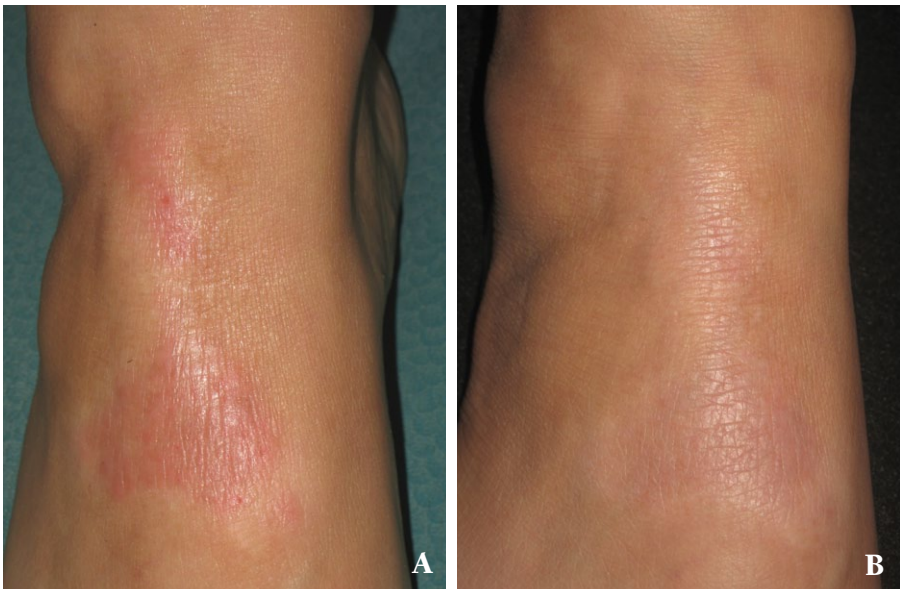

Figure 4. A 38-year-old female with lichen simplex on dorsal ankle at baseline (A) and at end of study using fluocinonide 0.1% cream twice daily (B).

Fluocinonide 0.1% cream applied twice daily for up to 4 weeks completely cleared 4 target areas and almost cleared 2 target areas in subjects (6 target areas total) treated for nummular eczema. In 2 subjects, both target areas treated with fluocinonide 0.1% cream twice daily were cleared completely within 2 weeks. Effective results were also noted in subjects treated for lichen simplex, with 2 target sites almost cleared within 2 weeks, followed by complete clearance at 1 target site by week 4.

In patients with eczematous dermatoses treated with fluocinonide 0.1% cream once or twice daily, the time until complete clearance of pruritus was 5.42 days in patients with atopic dermatitis, 6.16 days in patients with nummular eczema, and 6.5 days in patients with lichen simplex, as compared with 13.71 days, 20.5 days, and at least 28 days achieved with use of tacrolimus 0.1% ointment twice daily, respectively.

Fluocinonide 0.1% cream is a viable alternative for treatment of plaque-type psoriasis vulgaris and eczematous dermatoses. Relatively short courses of therapy (up to 4 weeks) produce complete or marked clearance in many patients. When treating psoriasis vulgaris, twice-daily application is suggested, as available data suggest better efficacy as compared with once-daily use. For atopic dermatitis, once-daily therapy appears to offer optimal benefit based on available data from pivotal trials, including comparison with twice-daily application. Data evaluating use of fluocinonide 0.1% cream for other corticosteroid-responsive eczematous dermatoses are limited. This trial indicates that fluocinonide 0.1% cream applied twice daily for up to 4 weeks is effective for treatment of nummular eczema and lichen simplex. As the number of treated patients was small, additional studies are warranted, especially evaluation of once-daily therapy for eczematous dermatoses other than atopic dermatitis.

Reference

1. Vanos (fluocinonide) cream 0.1% [package insert]. Scottsdale, Ariz: Medicis Pharmaceutical Corporation; 2006.