An Open-Label, Multicenter Study of the Efficacy and Safety of an AM/PM Treatment Regimen With Clobetasol Propionate Spray 0.05% and Calcitriol Ointment 3 μg/g in the Management of Plaque Psoriasis

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Psoriasis is a chronic condition with serious quality-of-life ramifications. Dermatologists seek alternative treatments of patients with plaque psoriasis that provide both efficacy and safety while minimizing exposure to high-potency steroids that can have adverse effects following long-term use. We report an open-label, multicenter study designed to evaluate a morning/evening (AM/PM) treatment regimen involving clobetasol propionate spray 0.05% and calcitriol ointment 3 μg/g for moderate plaque psoriasis. Participants applied clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 μg/g in the evening for up to 4 weeks. Participants were evaluated at baseline, week 2, and week 4. The results of this study indicate that a 4-week regimen of clobetasol propionate spray 0.05% treatment in the morning and calcitriol ointment 3 μg/g in the evening is efficacious and without unexpected safety issues for the management of moderate plaque psoriasis.

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Topical steroids are the most commonly prescribed psoriasis medications, and in recent years, physicians are prescribing even more potent corticosteroids.[1] Topical corticosteroids have several mechanisms of action including anti-inflammatory, immunosuppressive, and antiproliferative effects. These multiple mechanisms of action make them highly effective in treating psoriasis. However, there are adverse side effects associated with long-term use of high-potency topical steroids including skin atrophy, striae, telangiectases, and hypothalamic-pituitary-adrenal axis suppression.[2,3] The severity of these side effects is determined by the potency of the steroid, frequency of application, and duration of use.[2] Thus consensus guidelines recommend combining high-potency steroids with nonsteroid-containing products such as topical vitamin D agents for the long-term management of psoriasis.[3] Vitamin D analogs have been successfully used to treat mild to moderate plaque psoriasis since the early 1990s and are now a mainstay in topical treatment of psoriasis due to their efficacy and favorable tolerability profile. Vitamin D analogs act differently from corticosteroids by inhibiting keratinocyte proliferation and normalizing cellular differentiation.[4] A number of studies have demonstrated success when combining high-potency steroids with vitamin D analogs, and treatment regimens that utilize rotational or sequential regimens to limit exposure to high-potency topical steroids during long-term disease management commonly are used in clinical practice.[5-7]

Clobetasol propionate spray 0.05%, a super high–potency steroid, is indicated for the treatment of moderate to severe plaque psoriasis for up to 4 consecutive weeks of therapy.[8] Calcitriol ointment 3 μg/g, which contains the naturally occurring and biologically active metabolite of vitamin D_3, has been developed for the treatment of mild to moderate plaque psoriasis and has been shown to be effective and well-tolerated when used for up to 1 year.[9,10] The objective of this study was to evaluate a morning/evening (AM/PM) dosing regimen involving clobetasol propionate spray 0.05% and calcitriol ointment 3 μg/g for participants with moderate plaque psoriasis. Eligible participants applied clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 μg/g in the evening for up to 4 weeks.

Methods

The study was conducted in accordance with the Declaration of Helsinki, Finland (1964), and its Tokyo, Japan (1975); Venice, Italy (1983); Hong Kong (1989); Somerset West, South Africa (1996); and Edinburgh, Scotland (2000) amendments, as well as the International Conference on Harmonisation Good Clinical Practice principles, US Food and Drug Administration Code of Federal Regulations, Health Insurance Portability and Accountability Act, and local regulatory requirements.

Study Design and Treatment—This open-label, multicenter study was conducted in participants aged 18 to 80 years inclusive with moderate plaque psoriasis. For inclusion in this study, female participants of childbearing potential must have had a negative urine pregnancy test at the beginning of the study and must have agreed to practice an effective method of contraception for the duration of the study. Participants with 3% to 10% treatable body surface area (most areas were treated with the exception of the face, scalp, groin, axillae, and other intertriginous areas) also were included in this study. Participants using medication(s) to treat a concurrent medical condition were allowed to participate in the study if the type and dose of the medication(s) were stable for at least 3 months prior to study entry and were not expected to change during the study. Participants receiving treatment with beta-blockers or lithium, whose dose had been stable for at least 6 months and who had shown no worsening of their psoriasis, were included in the study at the discretion of the investigator. Participants meeting the specific enrollment criteria followed an AM/PM treatment regimen, applying clobetasol propionate spray 0.05% each morning and calcitriol ointment 3 μg/g each evening for 28 days.

Female participants who were pregnant, nursing, or planning a pregnancy during the study were excluded from this study. Participants with a known allergy to any of the components of the study products, participants with intakes of more than 50 μg per day of vitamin D and/or more than 1000 mg per day of calcium; participants who foresaw intensive UV exposure during the study; and participants whose psoriasis involved only the face, scalp, groin, axillae, and/or other intertriginous areas also were excluded from this study. Participants with a wash-out period for topical treatment (any steroid containing medication, calcipotriene, anthralin, tar, and/or UVB treatment) less than 30 days and a wash-out period for systemic treatment (corticosteroids, biologics, and/or psoralen plus UVA treatment) less than 12 weeks also were excluded from this study.

Assessments—Participants were evaluated at each visit for overall disease severity (ODS), signs of psoriasis (erythema, scaling, and plaque elevation), and percentage treatable body surface area (BSA). The primary efficacy parameter was the ODS score at week 4 (intent-to-treat [ITT] population). The secondary end points included the ODS score at week 2 (ITT population), global assessment

Table 1.

Participant Demographics

	ITT Population (N=68)
Age, y	
Mean (SD)	44.5 (14.4)
Median	45.0
Minimum, Maximum	18.0, 80.0
Gender, n (%)	
Male	44 (65)
Female	24 (35)
Race, n (%)	
White	64 (94)
Black	2 (3)
Other or mixed	2 (3)
Fitzpatrick skin type, n (%)	
I	2 (3)
I	16 (24)
III	30 (44)
IV	11 (16)
V	6 (9)
VI	3 (4)
History of psoriasis, y	
Mean (SD)	16.2 (14.9)
Treatable BSA at baseline, %	
Mean (SD)	5.8 (2.2)

Abbreviations: ITT, intent to treat; SD, standard deviation; BSA, body surface area.

of improvement (GAI) scores at weeks 2 and 4, signs of psoriasis at weeks 2 and 4, and percentage change from baseline in percentage treatable BSA at weeks 2 and 4.

Safety evaluation included tolerability assessments and incidence of adverse events (AEs). For the tolerability assessments, pruritus, telangiectases, skin atrophy, burning/stinging, and folliculitis were evaluated at each visit.

At week 4, participants completed a satisfaction survey.

Statistical Analysis—Descriptive statistics were provided to summarize demographic data, efficacy end points, tolerability end points, AEs, and participant satisfaction at all applicable visits. For the primary end point, the full-scale ODS scores at week 4 were compared to baseline using the Cochran-Mantel-Haenszel test after ridit transformation. For the secondary end points, the full-scale ODS scores at week 2 were compared to baseline using the Cochran-Mantel-Haenszel

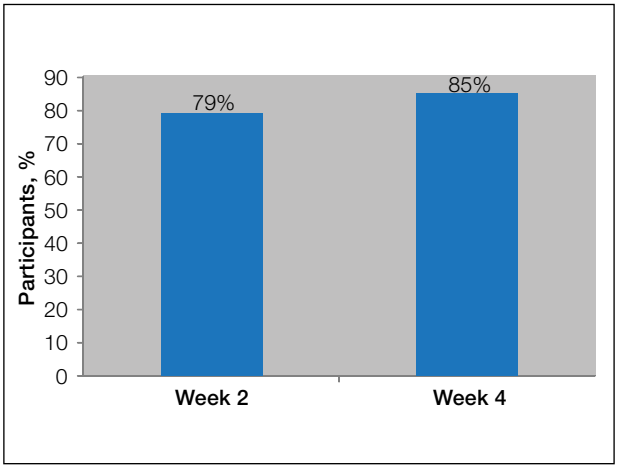

Figure 1. Percentage of participants who achieved overall disease severity scores of clear, almost clear, or mild at weeks 2 and 4 of treatment with clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 µg/g in the evening (N=68).

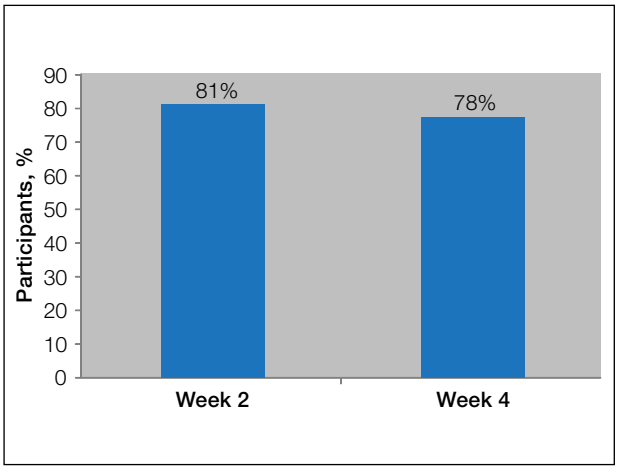

Figure 2. Percentage of participants with global assessment of improvement of definite improvement, considerable improvement, and clearing at weeks 2 and 4 of treatment with clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 µg/g in the evening (N=68).

test after ridit transformation. Additionally, the percentage change from baseline in percentage treatable BSA was summarized at weeks 2 and 4.

The GAI scores were summarized at weeks 2 and 4. Signs of psoriasis and participant satisfaction were summarized at each applicable time point with frequency tables. No statistical analyses were conducted for these variables. Adverse events, tolerability, and compliance data were summarized using descriptive statistics on the safety population. No statistical analyses were conducted for these variables.

Results

Demographics—The participant demographics for the ITT population (N=68) are shown in Table 1. The majority of the participants were male (44/68 [65%]) and white (64/68 [94%]) with Fitzpatrick skin types II (16/68 [24%]) or III (30/68 [44%]). The mean age (standard deviation [SD]) was 44.5 (14.4) years with a mean (SD) history of psoriasis of 16.2 (14.9) years and a mean (SD) percentage treatable BSA at baseline of 5.8% (2.2%).

Primary Efficacy Assessment—The study results indicate that the treatment regimen was efficacious with a significant improvement in ODS at week 4 of the treatment regimen ($P<.001$)(Figure 1). At baseline, all participants had ODS scores of moderate (68/68 [100%])(not shown); at week 4, 85% (58/68) of participants were clear, almost clear, or mild.

Secondary Efficacy Assessments—Figure 1 also shows the improvement in ODS at week 2. At week 2, 79% (54/68) of participants were clear, almost clear, or mild. The ODS distribution was significantly different between baseline and week 2 ($P<.001$).

At weeks 2 and 4, 81% (55/68) and 78% (53/68) of participants, respectively, had GAI scores of definite improvement, considerable improvement, and clearing (Figure 2).

Signs of psoriasis at weeks 2 and 4 also were evaluated. At baseline, 19% (13/68), 9% (6/68), and 6% (4/68) of participants had clear, almost clear, or mild scores for scaling, erythema, and plaque elevation, respectively. At week 2, 91% (62/68), 60% (41/68), and 88% (60/68) had clear, almost clear, or mild scores for scaling, erythema, and plaque elevation, respectively, while at week 4, 93% (63/68), 75% (51/68), and 90% (61/68) had clear, almost clear, or mild scores for scaling, erythema, and plaque elevation, respectively. The distribution of scores for each of the signs of psoriasis was significantly different between baseline and week 2 ($P<.001$) as well as baseline and week 4 ($P<.001$).

The median percentage change from baseline in percentage treatable BSA at weeks 2 and 4 for participants on the AM/PM regimen was −25% and −50%, respectively (Figure 3), which was significantly different at each week ($P<.001$ for both) compared to baseline.

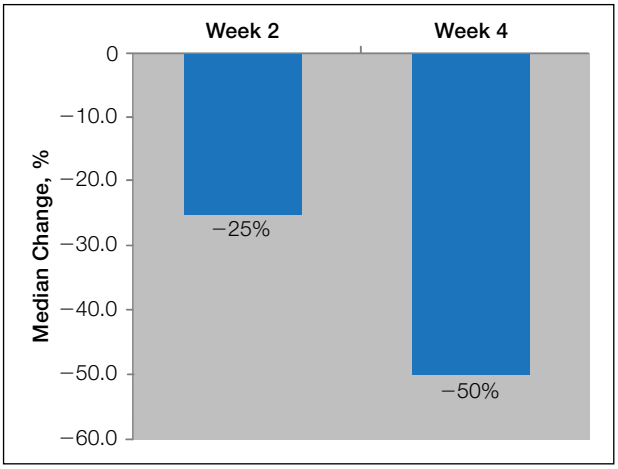

Figure 3. Median percentage change from baseline in percentage treatable body surface area at weeks 2 and 4 of treatment with clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 μg/g in the evening (N=68).

Safety Assessments—At week 4, there were no reports of telangiectases or folliculitis, and the majority of participants had no pruritus (47/68 [69%]), no burning/stinging (54/68 [79%]), and no skin atrophy (64/68 [94%])(Table 2).

There were 17 AEs reported by 11 participants on the AM/PM regimen, all mild or moderate in severity (17/17 [100%]). Adverse events included 1 report each of application-site dermatitis, gastroenteritis, viral gastroenteritis, sinusitis, upper respiratory tract infection, contusion, nasal congestion, pulmonary congestion, pain of skin, psoriasis, and rash. There were 2 reports of headache, 3 reports of nasopharyngitis, and 1 report of dermatitis. Most of the AEs definitely were unrelated or unlikely related (15/17 [88%]) to the study medication. There were no serious AEs reported in this study.

Participant Satisfaction—The results of the participant satisfaction survey at week 4 (safety population; N=68) are summarized in Table 3. Almost all participants on the AM/PM regimen strongly agreed or moderately agreed that the treatment program was easy to follow (67/68 [99%]). The majority of participants strongly agreed or moderately agreed that they were satisfied with their appearance and were satisfied with the results of the treatment program (57/68 [84%] and 62/68 [91%], respectively). The majority of participants also strongly agreed or moderately agreed that they would use the treatment program again (66/68 [97%]).

Table 2.

Tolerability Assessments (Safety Population; N=68)[a,b]

Tolerability Assessments	Participants, n (%)				
	None	Mild	Moderate	Severe	Present
Baseline					
Pruritus	5 (7)	18 (26)	36 (53)	9 (13)	
Telangiectases	66 (97)	2 (3)	0 (0)	0 (0)	
Burning/stinging	43 (63)	9 (13)	13 (19)	3 (4)	
Skin atrophy					1 (1)
Folliculitis					0 (0)
Week 2					
Pruritus	38 (56)	20 (29)	9 (13)	0 (0)	
Telangiectases	66 (97)	1 (1)	0 (0)	0 (0)	
Burning/stinging	51 (75)	14 (21)	1 (1)	1 (1)	
Skin atrophy					0 (0)
Folliculitis					0 (0)
Week 4					
Pruritus	47 (69)	11 (16)	7 (10)	0 (0)	
Telangiectases	65 (96)	0 (0)	0 (0)	0 (0)	
Burning/stinging	54 (79)	8 (12)	3 (4)	0 (0)	
Skin atrophy					1 (1)
Folliculitis					0 (0)

[a]Tolerability assessments are reported for the safety population, which includes all participants who received at least 1 dose of any of the study products. Percentages may not add up to 100% due to missing assessments and/or rounding.

[b]Tolerability assessments of pruritus, telangiectases, and burning/stinging were rated as none, mild, moderate, or severe; skin atrophy and folliculitis were considered present (or not present [not shown]).

Comment

Long-term use of high-potency topical steroids is associated with AEs such as striae, telangiectases, and skin atrophy. Psoriasis treatment guidelines, therefore, recommend using high-potency steroids with intermittent use of nonsteroid therapies.[3] Reports in the medical literature have demonstrated successful combination regimens of high-potency steroids with vitamin D agents, which have a different mechanism of action than corticosteroids. This combination has been shown to be well-tolerated and effective for long-term disease management, thus providing a useful therapeutic option for physicians.[5-7]

This study reports the efficacy and safety of an alternative regimen for the treatment of moderate plaque psoriasis consisting of clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 µg/g in the evening. A significant improvement in ODS was observed at the end of the 4-week study period ($P<.001$), along with improved GAI scores and significantly reduced signs of psoriasis ($P<.001$). Clinical benefit also was observed by week 2

Table 3.

Participant Satisfaction Survey at Week 4 (Safety Population; N=68)

Survey Statement	Response	Participants, n (%)
The treatment program was easy to follow.	Strongly agree/moderately agree	67 (99)
I am satisfied with my appearance.	Strongly agree/moderately agree	57 (84)
I am satisfied with the results of the treatment program.	Strongly agree/moderately agree	62 (91)
I would use this treatment program again.	Strongly agree/moderately agree	66 (97)

of the regimen. Additionally, the AM/PM regimen was well-tolerated and no serious AEs were reported; however, due to the short duration of the study, it would be unlikely to see skin-related side effects with once-daily use of clobetasol propionate. Importantly, the high participant satisfaction suggests that there would be high compliance with this treatment regimen.

Limitations of this study are the relatively low number of participants and the lack of a comparator arm. However, the results of this study demonstrate that this particular combination regimen is well-tolerated and may be a useful option in the management of plaque psoriasis.

Conclusion

The treatment regimen of clobetasol propionate spray 0.05% in the morning and calcitriol ointment 3 µg/g in the evening was efficacious and well-tolerated in the treatment of moderate plaque psoriasis and resulted in high participant satisfaction. Therefore, this treatment regimen offers physicians an alternative treatment option for patients with moderate plaque psoriasis that is effective and may allow for reduced high-potency topical steroid usage.

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