Clobetasol Propionate Shampoo 0.05% Is Efficacious and Safe for Long-term Control of Scalp Psoriasis

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Clobetasol propionate (CP) shampoo 0.05% is an efficacious and safe treatment for scalp psoriasis. The aim of this double-blind, randomized, placebo-controlled study was to determine if CP shampoo is suitable for long-term disease control. Participants with moderate to severe scalp psoriasis (global severity score [GSS] of 3 or 4 on a scale of 0 [clear] to 5 [very severe]) first received once daily CP shampoo treatment for up to 4 weeks. Responders were subsequently randomized to receive the CP shampoo or vehicle twice weekly maintenance regimen for up to 6 months. When relapse occurred (defined as GSS>2), participants resumed once daily CP shampoo treatment; when symptoms diminished (GSS≤2), they readopted the twice weekly maintenance regimen. At all visits significantly more participants treated with CP shampoo did not relapse compared with participants treated with vehicle (P<.001). Only approximately one-third of participants treated with vehicle remained relapse free at 1 month, while this rate was observed approximately 3.5 months later (4.5 months after baseline of maintenance phase) in the CP shampoo group. After 6 months 31.1% (33/106) of participants in the CP shampoo group were still relapse free versus 8.1% (9/111) of participants in the vehicle group. There was no greater incidence of skin atrophy, telangiectasia, or hypothalamic-pituitary-adrenal (HPA) axis suppression in the CP shampoo group compared with the vehicle group. Clobetasol propionate shampoo is efficacious and safe for acute management and long-term maintenance of moderate to severe scalp psoriasis.

Cutis. 2010;85:43-50.

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This study was funded by Galderma R&D. The clinical investigators received fees for the conduct of this study. Dr. Poulin received a research grant from Galderma R&D. Drs. Papp and Guenther report no additional conflicts of interest. Dr. Bissonnette has received grants and honoraria from and has been a consultant and investigator for Galderma R&D and LEO Pharma. Dr. Tan has served as advisor, consultant, and speaker for Galderma R&D. Dr. Lynde is on the advisory board for and received a research grant from Galderma R&D. Mr. Kerrouche is an employee and Mr. Villemagne was an employee of Galderma R&D until study completion.

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Psoriasis is a chronic recurrent inflammatory disease that commonly involves the scalp.[1] Because of frequent relapses and concern regarding cosmetic acceptability of topical agents, treatment of scalp psoriasis is a challenge for patients and physicians.[2,3] A suitable treatment should have minimal side effects and be adaptable to both acute management for rapid disease control and long-term maintenance.

Topical agents remain the mainstay of scalp psoriasis treatment, though the outcomes often are less than ideal.[4-7] Topical corticosteroids most commonly

are used, despite potential side effects.[8-10] Only a few reports have been published on safe and efficacious long-term treatment strategies for psoriasis. Among them is pulse therapy (weekend therapy), which includes a clearing phase with a superpotent corticosteroid administered daily followed by a transitional phase with medication applied only on weekends.[11,12]

Clobetasol propionate (CP) shampoo 0.05% was developed to incorporate the most potent topical corticosteroid as a once daily short-contact treatment to maximize efficacy and reduce side effects. It was shown to be efficacious, safe, and convenient for 4-week treatment of moderate to severe scalp psoriasis.[13-16] Based on its established risk-benefit profile, we hypothesized that CP shampoo could be optimized to manage the entire treatment cycle of scalp psoriasis for both acute management and long-term maintenance.

Methods

This double-blind, randomized, placebo-controlled study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and in compliance with local regulatory requirements. The study was reviewed and approved by institutional review boards. All participants provided written informed consent prior to entering the study.

Study Design and Treatment—Participants 18 years or older with moderate to severe scalp psoriasis (global severity score [GSS] of 3 or 4 on a scale of 0 [clear] to 5 [very severe]) were enrolled in 12 centers in Canada. Specified washout periods were required for participants using systemic treatments or certain topical treatments on the scalp. Clobetasol propionate shampoo or its vehicle was applied onto dry scalp in a thin film and left in place for 15 minutes before lathering and rinsing. During the study, all topical treatments, except superpotent corticosteroids, were allowed for treatment of body psoriasis. Individuals who needed systemic treatment for their body psoriasis as well as females who were pregnant or planning a pregnancy were excluded from the study.

The study design is depicted in Figure 1. Participants entered an initial open-label phase in which CP shampoo was applied to affected areas once daily for up to 4 weeks. Participants achieving a GSS of 2 or less (ie, clear, very mild, or mild scalp psoriasis) at the end of the initial phase subsequently entered a double-blind maintenance phase in which they were randomized to either CP shampoo or vehicle twice weekly (3–4 days apart) on the entire scalp for up to 6 months. Relapse was defined as having moderate, severe, or very severe scalp psoriasis (GSS>2) during the maintenance

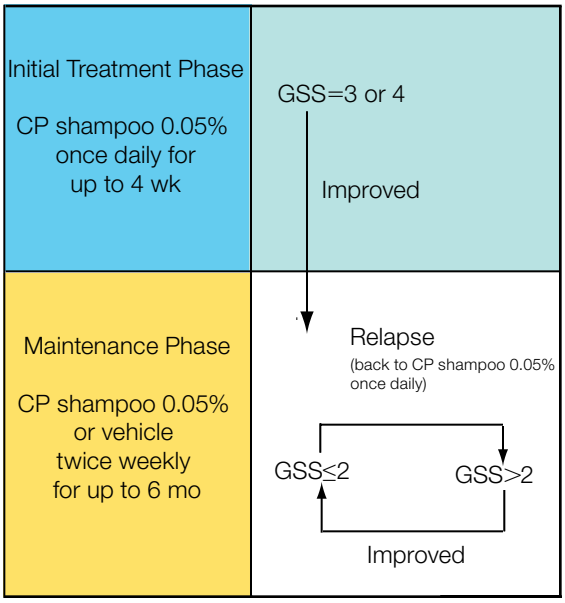

Figure 1. Study design. The global severity score (GSS) was evaluated on a 6-point scale (0=clear; 1=very mild; 2=mild; 3=moderate; 4=severe; 5=very severe). CP indicates clobetasol propionate.

period. When relapse occurred, participants resumed once daily treatment with CP shampoo for 4 weeks. If disease control was regained (GSS≤2) after 4 weeks, participants re-entered the twice weekly maintenance regimen according to the original randomization scheme, otherwise they exited the study.

Assessments—Every 4 weeks, investigators assessed GSS and individual sign scores, including erythema (E), scaling (S), and plaque thickening (P) on a scale of 0 (none) to 4 (very severe), as well as the extent of the disease (Ex) on a scale of 0 (none) to 5 (80%–100%). Modified psoriasis area and severity index (MPASI) score was calculated as MPASI=(E+S+P)Ex.[17] Participants also evaluated pruritus intensity on a scale of 0 (none) to 3 (severe).

The percentage of participants with rebound at the time of first relapse also was determined. Rebound was defined as an MPASI score during relapse of at least 125% of the baseline score (MPASI−125).[18]

Safety variables included assessment of adverse events (AEs), burning sensation, skin atrophy, and telangiectasia at each study visit, as well as hypothalamic-pituitary-adrenal (HPA) axis activity at the end of the study using morning assay of serum cortisol at the last study visit with a 5 µg/dL threshold.

A satisfaction questionnaire was completed by participants at the end of the study.

Statistical Analysis—The percentage of participants who did not relapse during the maintenance phase was assessed using the Cochran-Mantel-Haenszel (CMH) test stratified by center for the entire population. Participants who prematurely discontinued before the first relapse were considered as having relapsed at the subsequent visit (intention-to-treat [ITT]/worst-case population). The distribution of participants for GSS, individual sign scores, and pruritus intensity scores during first relapse were descriptively analyzed. The incidence of AEs was descriptively analyzed. The worst scores for burning sensation, skin atrophy, and telangiectasia after baseline, as well as cases of HPA axis suppression at the last study visit, were analyzed by CMH test for the safety population, which included all participants who had applied the treatment at least once. Every item of the satisfaction questionnaire completed by the participant was submitted to the CMH test. Every test was 2-tailed at $\alpha = .05$.

Results

Participant disposition of the ITT population is shown in Figure 2. After the initial treatment phase, 225 (78.1%) of 288 enrolled participants had a GSS of 2 or less, and 217 (96.4%) were randomized in the maintenance phase to receive either CP shampoo or vehicle twice weekly. Demographic and disease characteristics were similar between the 2 groups at baseline of the maintenance phase (Table 1), with more than 75% of participants having none to mild disease symptoms. Fewer participants from the CP shampoo group (16/106 [15.1%]) discontinued from the study compared with the vehicle group (29/111 [26.1%]).

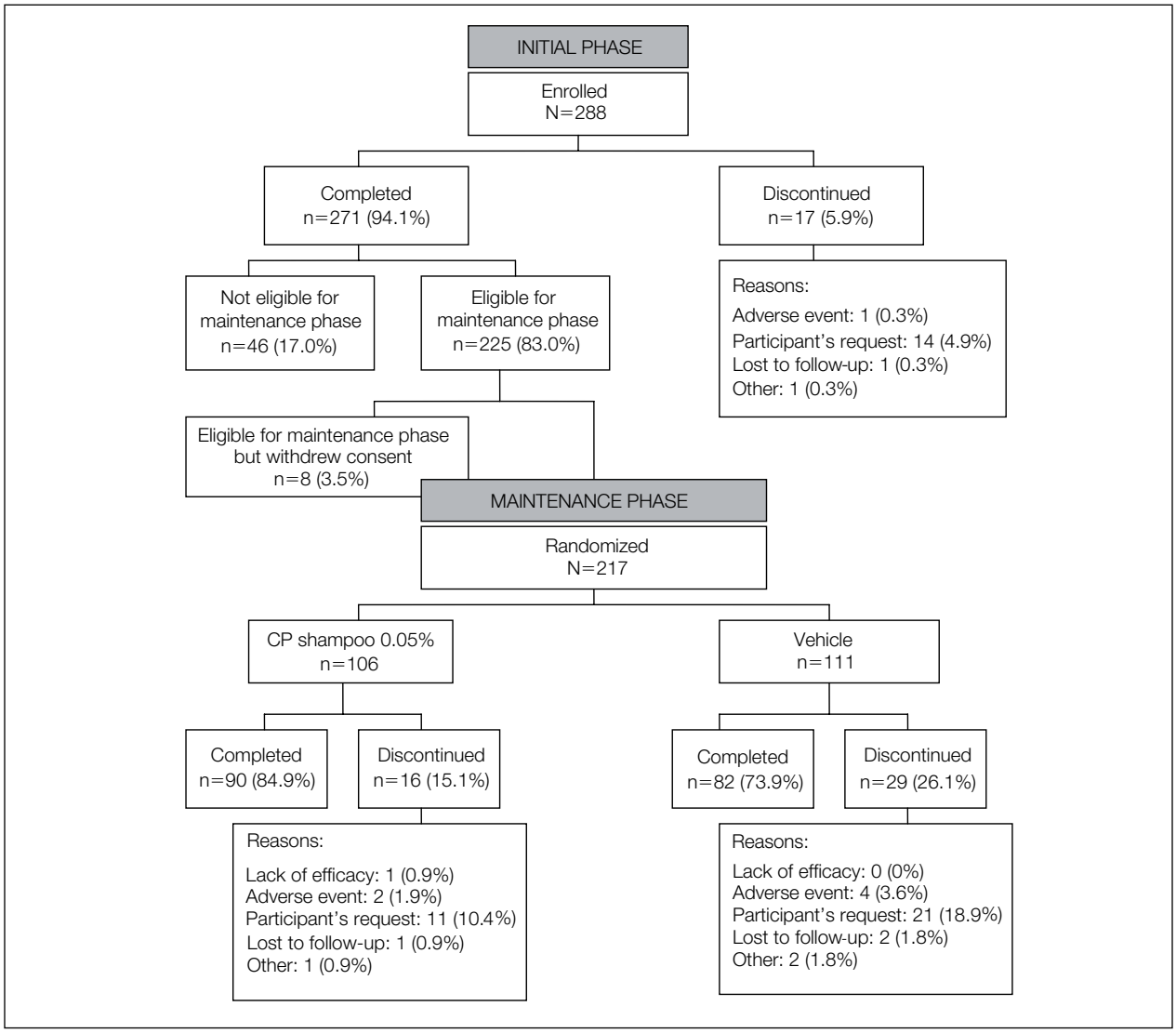

Figure 2. Flowchart of participant disposition (intention-to-treat population). CP indicates clobetasol propionate.

Table 1.

Demographics and Disease Characteristics at Baseline of the Maintenance Phase (Week 4)(ITT Population)

	CP Shampoo 0.05% (n=106)	Vehicle (n=111)	Total (N=217)
Gender, n (%)			
Female	57 (53.8)	63 (56.8)	120 (55.3)
Male	49 (46.2)	48 (43.2)	97 (44.7)
Age, y			
Mean	49.3	51.5	50.4
Min, Max	19, 79	18, 82	18, 82
Race, n (%)			
White	97 (91.5)	101 (91.0)	198 (91.2)
Global severity score, n (%)			
0 (clear)	11 (10.4)	11 (9.9)	22 (10.1)
1 (very mild)	36 (34.0)	37 (33.3)	73 (33.7)
2 (mild)	59 (55.6)	63 (56.8)	122 (56.2)
Erythema, n (%)			
0–1 (none–mild)	85 (80.2)	86 (77.5)	171 (78.8)
2 (moderate)	21 (19.8)	23 (20.7)	44 (20.3)
3 (severe)	0 (0)	2 (1.8)	2 (0.9)
Scaling, n (%)			
0–1 (none–mild)	87 (82.1)	84 (75.7)	171 (78.8)
2 (moderate)	19 (17.9)	27 (24.3)	46 (21.2)
Plaque thickening, n (%)			
0–1 (none–mild)	99 (93.4)	96 (86.5)	195 (89.8)
2 (moderate)	6 (5.7)	15 (13.5)	21 (9.7)
3–4 (severe–very severe)	1 (0.9)	0 (0)	1 (0.5)
Extent of the disease, n (%)			
0–1 (none–19%)	80 (75.5)	86 (77.5)	166 (76.5)
2–3 (20%–59%)	23 (21.7)	21 (18.9)	44 (20.3)
4–5 (60%–100%)	3 (2.8)	4 (3.6)	7 (3.2)
Pruritus, n (%)			
0–1 (none–mild)	99 (93.4)	104 (93.7)	203 (93.6)
2 (moderate)	6 (5.7)	6 (5.4)	12 (5.5)
3 (severe)	1 (0.9)	1 (0.9)	2 (0.9)
MPASI			
Mean (SD)	3.9 (3.6)	4.6 (4.7)	4.2 (4.2)

Abbreviations: ITT, intention to treat; CP, clobetasol propionate; MPASI, modified psoriasis area and severity index; SD, standard deviation.

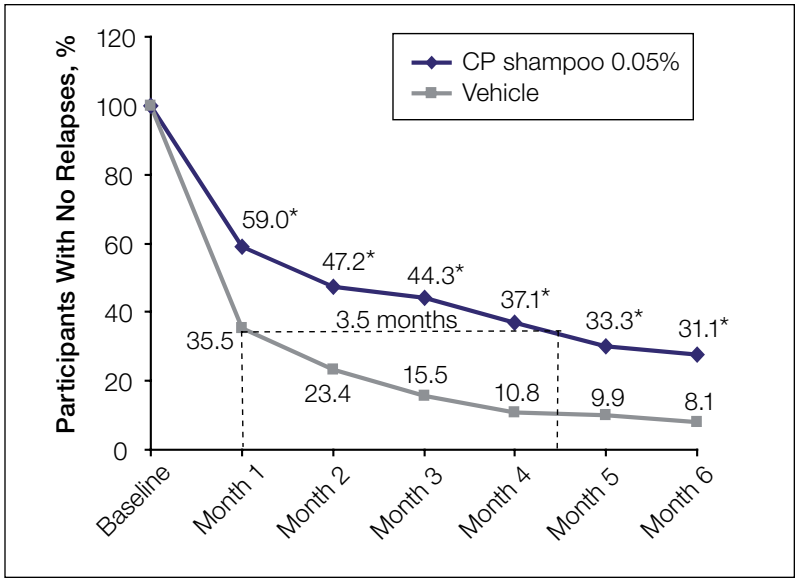

Figure 3. Percentage of participants with no relapses during the study (intention-to-treat/worst-case population; N=217). Participants who prematurely discontinued before the first relapse were considered as having relapsed at the subsequent visit. CP indicates clobetasol propionate. Asterisk indicates $P<.001$ at all time points.

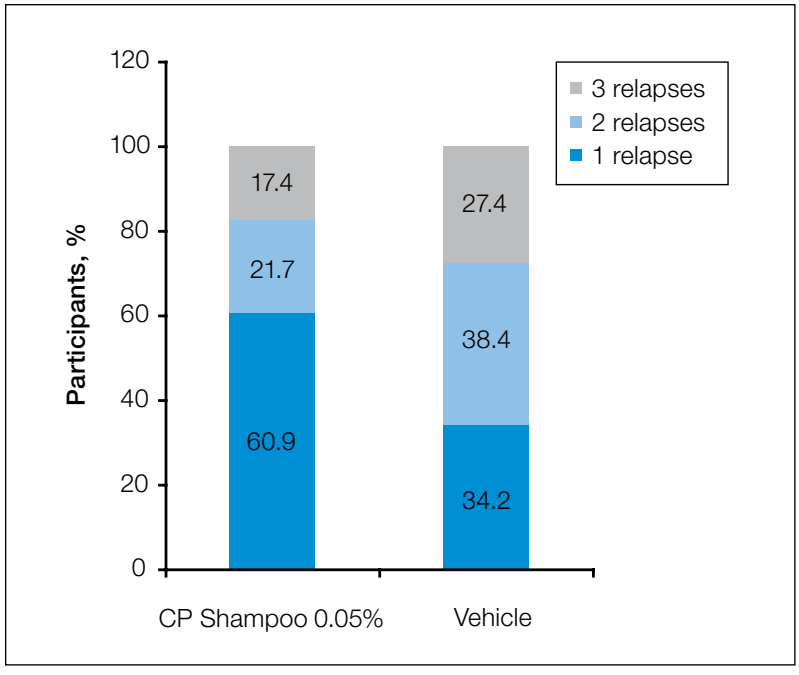

Figure 4. Distribution of participants who underwent alternate treatment cycles during the study (intention-to-treat/worst-case population)(n=46 in the CP shampoo group; n=73 in the vehicle group). $P=.004$ vs vehicle. CP indicates clobetasol propionate.

Efficacy—Efficacy of the twice weekly maintenance regimen was evaluated by the percentage of participants who did not relapse over 6 months in the ITT/worst-case population. At each time point significantly more participants in the CP shampoo group did not relapse compared with the vehicle group ($P<.001$)(Figure 3). Only approximately one-third of participants remained relapse free in the vehicle group at 1 month, while this rate was observed approximately 3.5 months later (4.5 months after baseline of maintenance phase) in the CP shampoo group, indicating that twice weekly treatment with CP shampoo prolonged disease control after the initial treatment phase. After 6 months the relapse-free rates were 31.1% (33/106) for the CP shampoo group and 8.1% (9/111) for the vehicle group. Relapses occurred as soon as the initial once daily treatment was terminated; 64.5% (71/110) of participants in the vehicle group experienced relapse by 1 month.

During the first relapse, rebound was assessed as the percentage of participants with MPASI−125. Fourteen of 97 participants (14.4%) who had relapse in the vehicle group versus 5 of 68 participants (7.3%) who had relapse in the CP shampoo group fulfilled the criterion for rebound. Disease

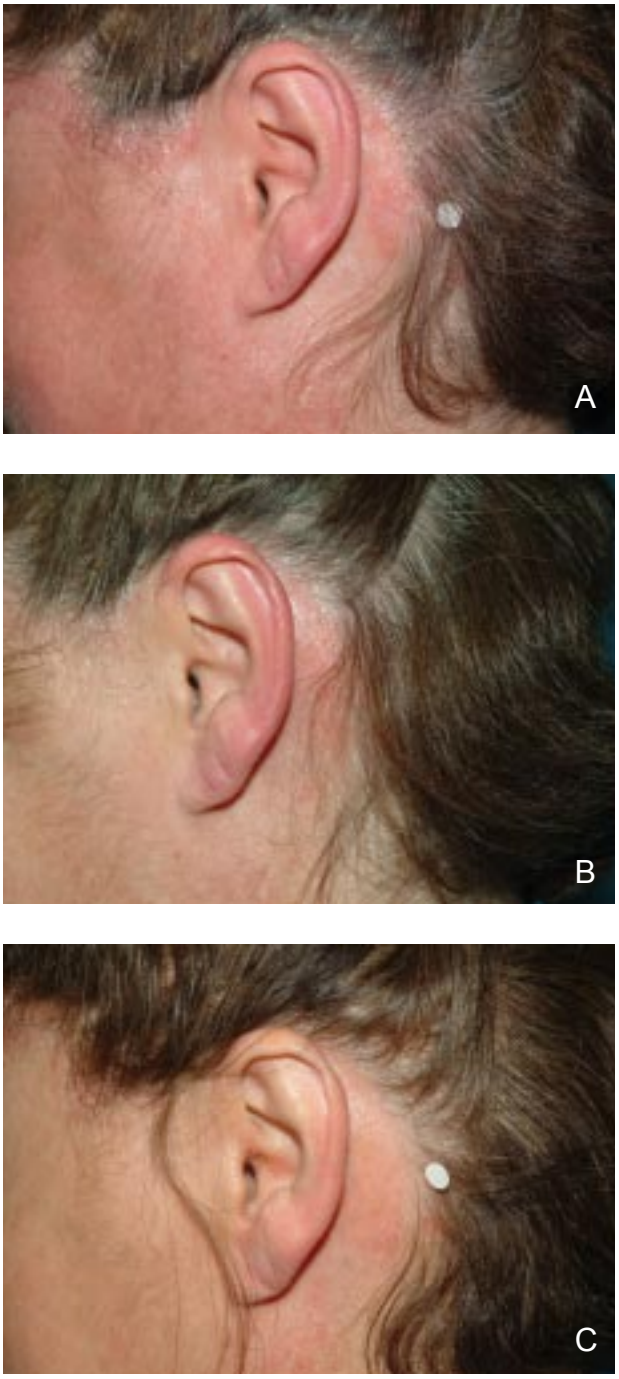

Figure 5. Effect of 6 months' maintenance therapy with clobetasol propionate shampoo 0.05% in a participant with severe scalp psoriasis (baseline [A], after 4 weeks of once daily treatment [baseline of maintenance phase][B], and after 6 months of maintenance treatment with twice weekly application [C]).

severity during the first relapse was similar in both groups while disease extent differed (44.1% [30/68] of participants in the CP shampoo group had <20% affected scalp vs 28.9% [28/97] of the vehicle group).

To regain disease control after relapse participants were re-treated with once daily CP shampoo. The efficacy of CP shampoo treatment was assessed by the total number of relapses. Among the participants who underwent alternate treatment cycles, 60.9% (28/46) of the CP shampoo group had only one relapse compared with 34.2% (25/73) of the vehicle group (Figure 4). The distribution was significantly different for the 2 groups (P=.004), suggesting that the maintenance treatment with CP shampoo was efficacious in preventing future relapses and reducing the number of treatment cycles.

Figure 5 illustrates the effect of 6 months' twice weekly maintenance treatment with CP shampoo following 4 weeks of once daily treatment (initial phase).

Safety—During the 7-month study period (196 days), CP shampoo was applied on average for 80.5 days in the CP shampoo group and 60.3 days in the vehicle group. Because participants in the vehicle group received CP shampoo during relapse, the average exposure to CP shampoo in the vehicle group was not much lower than the CP shampoo group.

Participants in the CP shampoo and vehicle groups had similar local safety profiles, with more than 80% reported to have no burning sensation, skin atrophy, or telangiectasia (Table 2). When skin atrophy and telangiectasia were observed, they either already existed at baseline and did not worsen or were transient. Only one participant experienced moderate telangiectasia in the vehicle group at the last study visit. No effect of the CP shampoo on HPA axis activity was observed, as only one participant in the vehicle group had results of the morning serum cortisol assay above the threshold. A total of 5 and 6 treatment-related AEs were reported in the CP shampoo and vehicle groups, respectively; only one was of severe intensity (asthma in the CP shampoo group).

Participant Satisfaction—More than 80% of participants reported the treatment regimen was easy to incorporate into their daily routine. Significantly more participants in the CP shampoo group (67.4% [60/89]) than the vehicle group (50.5% [46/91]) preferred using the twice weekly maintenance regimen for an extended period rather than once daily treatment only when symptoms reoccurred (P=.017). Most participants wished to use such a maintenance regimen for 6 to 12 months to avoid reoccurring symptoms. Finally, 73.6% (67/91) of participants in the CP shampoo group preferred to continue treating their scalp psoriasis with the maintenance regimen compared with 57.1% (52/91) of the vehicle group (P=.018).

Table 2.

Cutaneous Tolerance: Worst Scores During the Whole Study (Safety Population; N=217)

	CP Shampoo 0.05%, n (%) (n=106)	Vehicle, n (%) (n=111)	*P* Value
Burning sensation (worst score)			.557
None	87 (82.0)	89 (80.2)	
Mild	15 (14.2)	17 (15.3)	
Moderate	4 (3.8)	5 (4.5)	
Skin atrophy (worst score)			.931
None	105 (99.1)	110 (99.1)	
Mild	1 (0.9)	1 (0.9)	
Telangiectasia (worst score)			.403
None	104 (98.1)	107 (96.4)	
Mild	2 (1.9)	3 (2.7)	
Moderate	0 (0)	1 (0.9)	

Abbreviation: CP, clobetasol propionate.

Comment

Because of its chronic nature, scalp psoriasis mandates long-term management that should provide rapid control when symptoms occur and a safe convenient therapy when symptoms diminish. In this study, approximately two-thirds of participants in the vehicle group relapsed 1 month after treatment was discontinued, supporting the concept that maintenance therapy is required for continued control. This study supports the efficacy and safety of twice weekly maintenance treatment with CP shampoo, with once daily treatment of relapses. Since most relapses occurred during the first 4 weeks of treatment, a more gradual tapering of the initial dose (ie, 3 applications per week for 1 month) might have been more beneficial.

No severe burning sensation, skin atrophy, or telangiectasia was reported during the entire study. Over 7 months' duration in the CP shampoo group there was 1 case of mild atrophy (compared to 1 in the vehicle group), 2 cases of mild telangiectasia (versus 3 mild and 1 moderate in the vehicle group), and no cases of HPA axis suppression (versus 1 in the vehicle group). Considering participants could have received up to 4 months of once daily CP shampoo treatment during the 7-month study period, these results suggest that long-term chronic use of CP shampoo was safe and well tolerated.

Participant satisfaction is important because up to 40% of participants with psoriasis treated with topical corticosteroids are nonadherent.[19,20] In this study, participants were satisfied with both the cosmetic properties of CP shampoo as previously reported[21] and the treatment regimen. The high participant satisfaction observed in this study should encourage adherence and promote improved outcomes of the treatment regimen.

Conclusion

This study suggests that CP shampoo is efficacious, safe, and convenient for complete care of scalp psoriasis, from control of acute flares to long-term maintenance.

Acknowledgments—The authors would like to thank the other investigators who participated in the study (all from Canada): Kirk Barber, MD, Calgary, Alberta; David Gratton, MD, Montreal, Québec; Harvey Lui, MD, Vancouver, British Columbia; Richard Thomas, MD, Vancouver, British Columbia; Ronald Vender, MD, Hamilton, Ontario; and Beatrice Wang, MD, Montreal, Québec. The authors also thank Y. May Ma, PhD, and Zeina Saab, PharmD, medical writers, Galderma R&D, Sophia Antipolis, France, for their editorial assistance.

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