# Clobetasol Propionate Lotion in the Treatment of Moderate to Severe Plaque-Type Psoriasis

Jacques Decroix, MD; Henrik Pres, MD; Nicolaï Tsankov, MD; Michel Poncet, PhD; Stéphanie Arsonnaud

*Owing to its anti-inflammatory, antipruritic, vasoconstrictive, and immune-modulating properties, clobetasol propionate is used to treat psoriasis. This study was conducted to evaluate the efficacy, safety, and cosmetic acceptability of clobetasol propionate lotion compared with its vehicle and with clobetasol propionate cream in the treatment of moderate to severe plaque-type psoriasis.*

*A total of 222 patients were treated. After 4 weeks of treatment, clobetasol propionate lotion was more efficient than vehicle lotion and of equivalent efficacy as clobetasol propionate cream. Cosmetic acceptability was significantly better with clobetasol propionate lotion than with clobetasol propionate cream. Clobetasol propionate lotion was efficient, safe, and well tolerated and offers a significantly higher cosmetic advantage in the treatment of moderate to severe plaque-type psoriasis compared with clobetasol propionate cream.*

*Cutis*. 2004;74:201-206.

Accepted for publication March 22, 2004.

Dr. Decroix is in private practice, Moucron, Belgium. Dr. Pres is in private practice, Berlin, Germany. Dr. Tsankov is from the Department of Dermatology and Venereology, Alexander's University Hospital, Sofia, Bulgaria. Dr. Poncet is from Galderma R&D, Sophia Antipolis, France. Ms. Arsonnaud is from Galderma R&D, Cranbury, New Jersey.

This study was funded by Galderma R&D, Sophia Antipolis, France. The investigating authors received payments for the conduct of this research. Dr. Poncet and Ms. Arsonnaud are employees of Galderma R&D.

Reprints: Stéphanie Arsonnaud, Galderma R&D, 5 Cedar Brook Dr, Cranbury, NJ 08512 (e-mail: stephanie.arsonnaud@galderma.com).

Psoriasis is a lifelong condition, with onset occurring at any time throughout life. It affects men and women equally, and almost all races in varying rates of frequency are affected. Psoriasis usually first appears between the ages of 15 and 30 years and may occur anywhere on the body.

Psoriasis is an inherited condition; however, both genetic and environmental factors play an important role in its onset and course. The condition has a considerable impact on quality of life, with patients complaining about the messiness of the topical agents used to treat the condition and the profound psychological impact of the treatments and the condition.[1-5]

Clobetasol propionate is known for its anti-inflammatory, antipruritic, vasoconstrictive, and immune-modulating properties and is currently used in the treatment of certain hyperproliferative or inflammatory dermatoses, including psoriasis and atopic dermatitis. Its safety and efficacy are well-defined in the medical literature.[6] Available in the United States and Europe, clobetasol propionate is the most common corticosteroid used to treat moderate to severe plaque-type psoriasis.[7]

Different formulations of clobetasol propionate are available. These creams and ointments, however, have disadvantages: they are greasy and difficult to apply on large areas, and may, for these reasons, have an impact on the patient's quality of life. In the past, different vehicles, such as foams and solutions, have been evaluated, and results showed that patients preferred foam and solution over cream, gel, and ointment. These results suggest that the characteristics of solution and foam may favor improved adherence to topical therapy.[8] Hence, it was thought that a new clobetasol propionate

formulation, such as a lotion, would provide an additional use in patients with moderate to severe plaque-type psoriasis while showing the same efficacy and safety profile as currently available formulations.

## Materials and Methods

This was a multicenter, randomized, investigator-masked, active-controlled and vehicle-controlled, parallel group study. It was conducted according to the Declaration of Helsinki and good clinical practice. Before any study procedures, independent ethics committee approvals for all study sites were obtained, and patients provided written informed consent.

*Patients*—Patients of any gender and race, 18 years or older, with stable, moderate to severe plaque-type psoriasis were eligible to enroll in the study. The target lesion had to measure at least 3 to 4 cm in diameter and not be localized to the scalp, face, hands, or feet. Patients had to have at least a 10% body surface area (BSA) involvement. Female patients had to have a negative urine pregnancy test at the beginning of the study.

There was a 4-week washout period for topical psoriasis treatments (ie, corticosteroids, other anti-inflammatory drugs, anthralin, UV-light therapy [including sunbathing], retinoids, or vitamin D analogs); a 2- to 16-week washout period for systemic psoriasis medications; and a 2-week washout period for patients who had regular sun exposure.

*Test Material*—Patients were randomized to receive clobetasol propionate lotion, its vehicle, or clobetasol propionate cream in a 3:1:3 ratio. Test materials were applied twice daily for 4 weeks. The study was investigator masked because 2 different types of formulation were used. Appropriate procedures were applied to ensure investigator blinding.

*Clinical Assessments*—Evaluation visits took place at baseline and at weeks 1, 2, and 4. Erythema, plaque elevation, scaling, pruritus, and global improvement were evaluated for target lesions. Global severity and BSA were evaluated for all treated areas.

Evaluation scores ranged from 0 (none) to 4 (severe) for erythema, plaque elevation, scaling, pruritus, and global severity. The dermatologic sum score (DSS) was defined as the sum of erythema, plaque elevation, and scaling for the target lesions. Global severity was dichotomized as "success" or "failure," where success was defined by a global severity score (GSS) of 0, 0.5, or 1, and failure was defined by a GSS of 2, 3, or 4. Global improvement was rated by investigators and by patients on a scale of -1 (worse) to 5 (clear) at week 4 only. The percentage of the BSA involved and treated was estimated and recorded at each visit using the rule of nines. Safety was monitored through skin evaluation of telangiectasia and skin atrophy, as well as adverse events. Telangiectasia and skin atrophy at all application sites were scored on a 0 (none) to 3 (severe) scale. A survey concerning the cosmetic acceptability of the products was completed by each patient at the end of treatment.

*Statistics*—The main objectives of the study were to show the noninferior efficacy of clobetasol propionate lotion to clobetasol propionate cream and the superior efficacy of clobetasol propionate lotion to its vehicle. The noninferiority of clobetasol propionate lotion versus cream was assessed by using a 95% confidence interval (CI) approach. To conclude noninferiority, the difference in DSS between the 2 drugs could not exceed 1 point, and the difference in GSS could not exceed 0.5 point.

Both the per protocol population, with observed cases, and the intent-to-treat (ITT) population, with missing data inputted using the last observation carried forward, were analyzed for efficacy.

Analysis for efficacy variables and BSA were performed at all visits using an analysis of covariance. Tests were 2 sided, and the 0.05 level was used to declare significance. To assess noninferiority, 95% CI of the difference in least square means between both active drugs were calculated.

Global improvement, scores of telangiectasia and skin atrophy, and each item of the cosmetic acceptability survey were analyzed using the log-rank test.

## Results

*Demographics and Baseline Data*—A total of 222 patients were recruited in Germany, Bulgaria, Belgium, and France, with 94 patients in the clobetasol propionate lotion group, 95 patients in the clobetasol propionate cream group, and 33 patients in the clobetasol propionate lotion vehicle group; 213 patients completed the study. Nine patients withdrew from the study: 2 in the clobetasol propionate cream group for cleared conditions; 1 in the lotion vehicle group for lack of efficacy; 1 in the clobetasol propionate lotion group for an adverse event; and, by request, 2 patients in the clobetasol propionate lotion group and 3 patients in the lotion vehicle group.

All patients had moderate to severe psoriasis at baseline, with at least 20% BSA involved. Patient characteristics at baseline are provided in the Table.

*Treatment Compliance*—The easiness of use of clobetasol propionate lotion did not enhance an excessive application on the areas to be treated compared with clobetasol propionate cream. Study drug compliance reached more than 97% in all treatment groups.

*Efficacy*—In the ITT population, the DSS and GSS decreased over time in both active treatment groups (Figures 1 and 2). The upper limit of the 95% CI for these differences after 4 weeks of treatment were inferior to the prespecified noninferiority margins of 1 point and 0.5 point, respectively (0.82 for the DSS and 0.24 for the GSS). Clobetasol propionate lotion was shown to be as effective as clobetasol propionate cream. Results for the DSS and GSS were statistically significantly better ($P<.001$) with clobetasol propionate lotion compared with its vehicle.

Erythema, plaque elevation, scaling, and pruritus decreased over time in all treatment groups. There was a notable difference between both clobetasol propionate formulations and the lotion vehicle.

At the end of the study, the condition improved significantly ($P<.001$) in more than 70% (70/94; 74/95) of patients receiving clobetasol propionate lotion or cream compared with 15% (5/33) of patients in the lotion vehicle group. There was no significant difference between clobetasol propionate lotion and clobetasol propionate cream (Figure 3). These results were confirmed by the patient's assessment.

The BSA involved in both active treatment groups decreased significantly (more than 94% at week 4; $P<.001$) and remained unchanged in the clobetasol propionate lotion vehicle group.

A statistically significant difference in favor of clobetasol propionate lotion compared with clobetasol propionate cream was observed for the following items of the cosmetic acceptability survey: displays satisfactory penetration time ($P=.043$), dries quickly ($P=.002$), feels greasy ($P<.001$), possesses a pleasing aspect and perfume ($P=.001$), and leaves a film on the skin ($P=.017$)(Figure 4).

*Safety*—Thirteen patients experienced at least one adverse event: 7 (7.4%) patients in the clobetasol propionate lotion group, 5 (5.3%) patients in the

## Patient Baseline Characteristics

| | Clobetasol Propionate | | |
|---|---|---|---|
| | Lotion (n=94) | Cream (n=95) | Lotion Vehicle (n=33) |
| Mean age±SD, y | 48.71±14.08 | 47.29±15.90 | 50.94±14.61 |
| Gender, n (%) | | | |
| Male | 47 (50%) | 56 (58.9%) | 21 (63.6%) |
| Female | 47 (50%) | 39 (41.1%) | 12 (36.4%) |
| Race, n (%) | | | |
| White | 94 (100%) | 95 (100%) | 33 (100%) |
| Previous psoriasis therapy, n (%) | 73 (77.7%) | 79 (83.2%) | 21 (63.6%) |
| Dermatologic sum score±SD* | 8.49±1.45 | 8.33±1.36 | 8.61±1.71 |
| Skin atrophy† | | | |
| 1 | 93 (98.9%) | 94 (98.9%) | 33 (100%) |
| 2 | 1 (1.1%) | — | — |
| 3 | — | 1 (1.1%) | — |
| Telangiectasia† | | | |
| 0 | 94 (100%) | 93 (97.9%) | 33 (100%) |
| 1 | — | 1 (1.1%) | — |
| 2 | — | 1 (1.1%) | — |

*Scale 0–12.
†Scale 0–3.

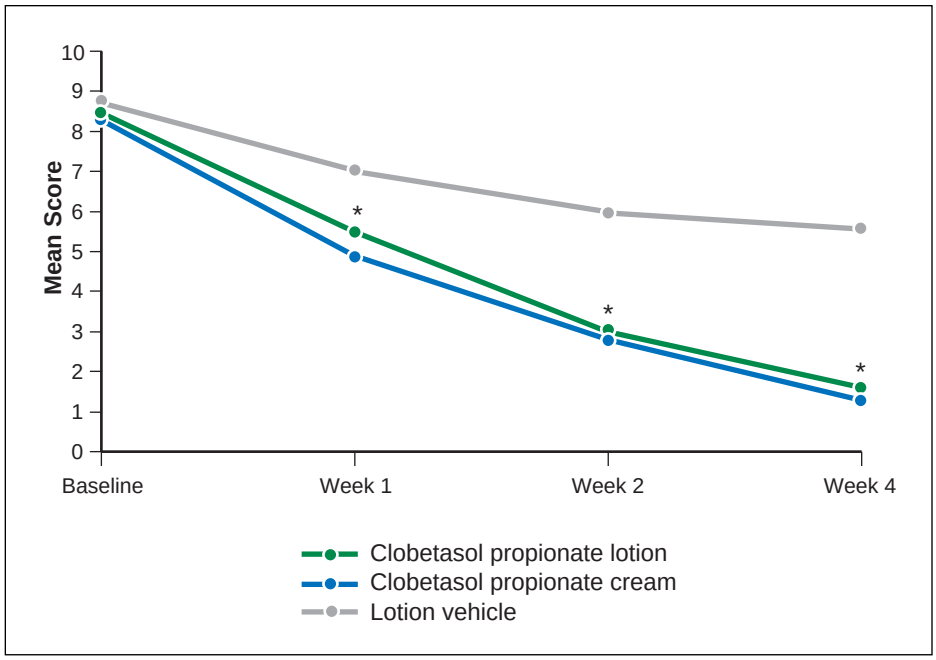


**Figure 1.** Dermatologic sum scores in the intent-to-treat population. Asterisk indicates $P<.001$ vs clobetasol propionate lotion vehicle. No statistical difference could be shown between both active treatments.

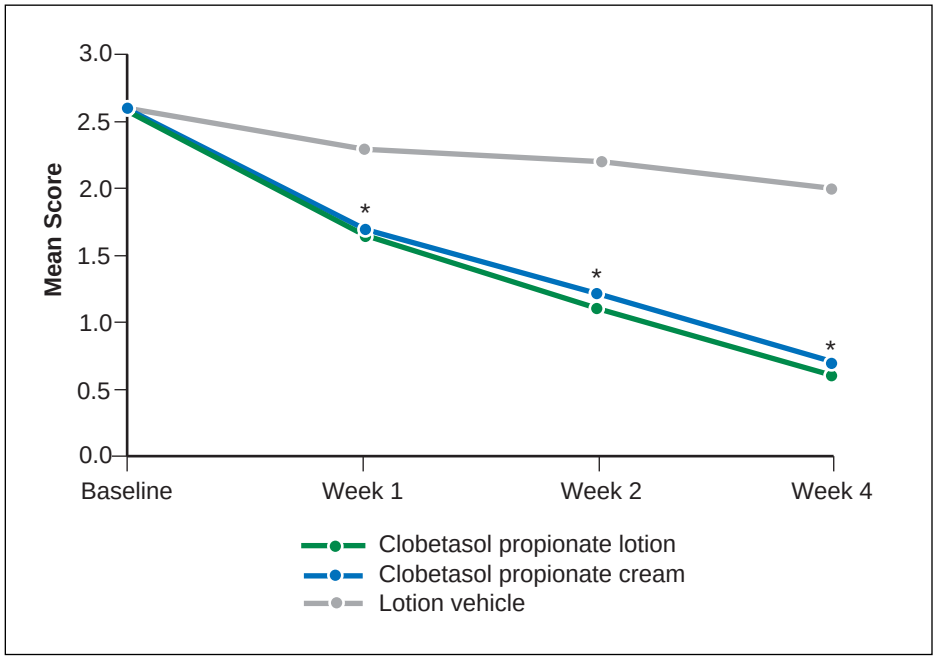


**Figure 2.** Global severity scores in the intent-to-treat population. Asterisk indicates $P<.001$ vs clobetasol propionate lotion vehicle. No statistical difference could be shown between both active treatments.

clobetasol propionate cream group, and 1 (3.0%) patient in the clobetasol propionate lotion vehicle group. Four adverse events (2 in each active group) reported by 2 patients were considered drug related. Only one adverse event (lung edema) not related to the study drugs led to the withdrawal of one patient in the clobetasol propionate lotion group.

After 4 weeks of treatment, no notable differences in the incidence of telangiectasia or skin atrophy were observed between the 2 active treatment groups. Three subjects in each group experienced mild to moderate telangiectasis; 3 subjects in the clobetasol propionate lotion group and 4 in the clobetasol propionate cream group experienced mild to moderate skin atrophy. No severe cases were observed.

## Comment

The use of topical corticosteroid preparations in psoriasis is well established with clobetasol propionate, the highest potency topical steroid available for use in patients with psoriasis.[9] The present study shows that, in patients with moderate to severe

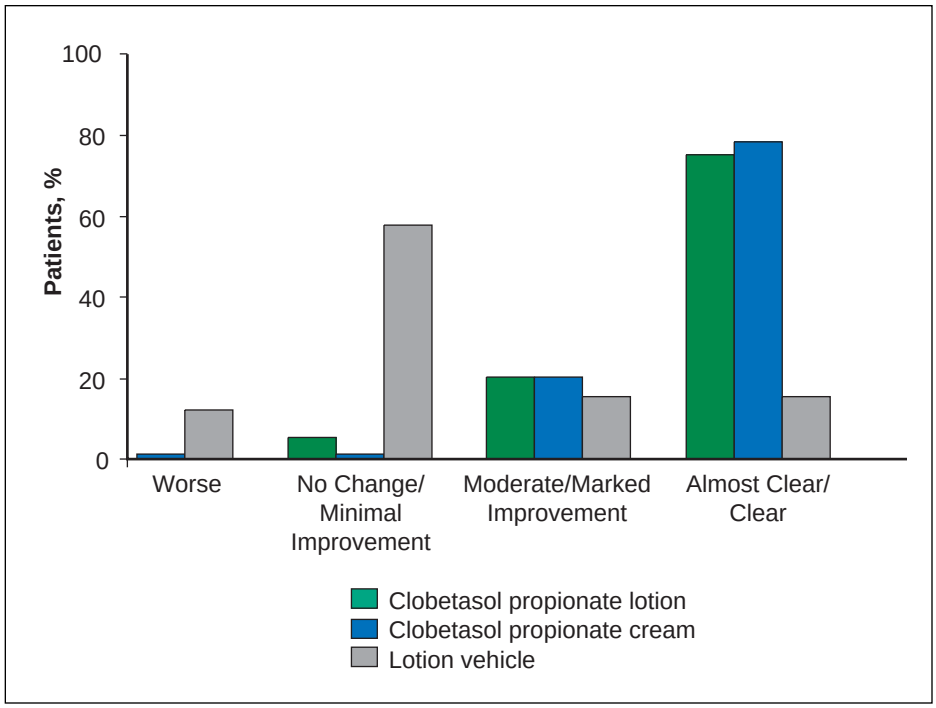


**Figure 3.** Global improvement at week 4 as rated by the investigator.

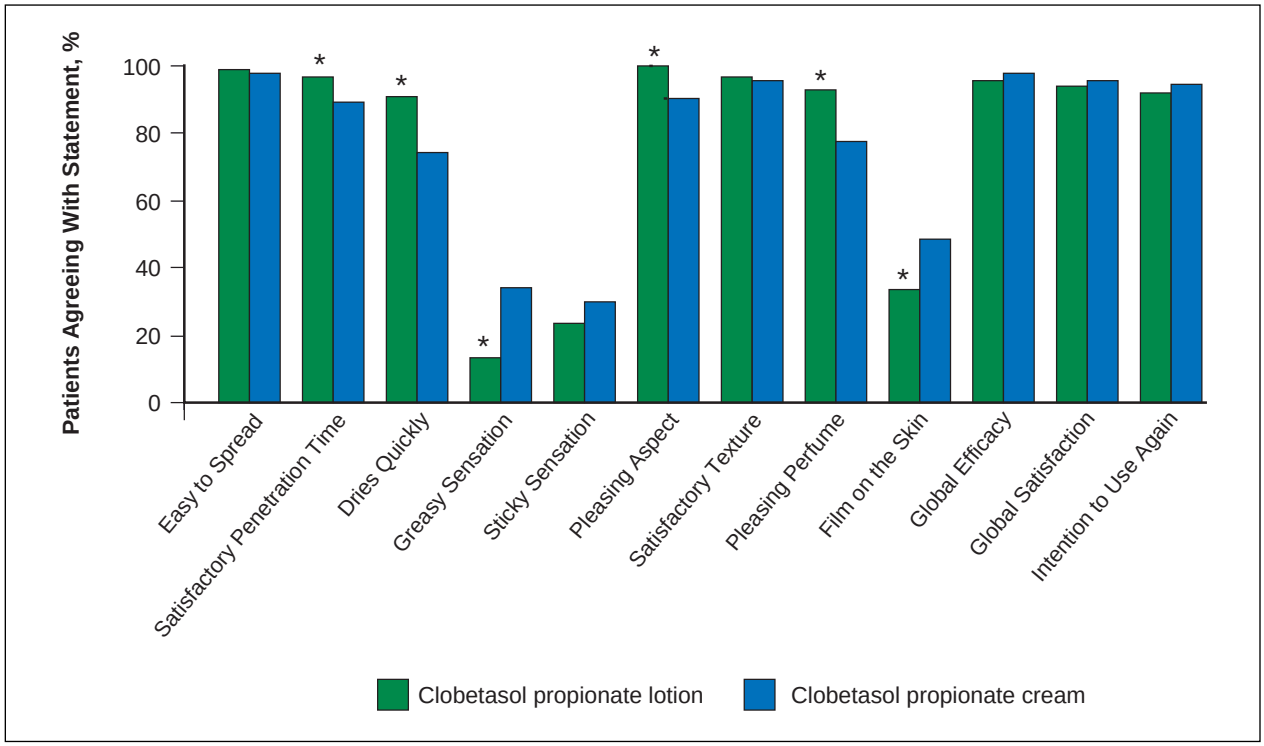


**Figure 4.** Cosmetic acceptability survey as rated by the patients at the end of treatment. Asterisk indicates $P<.05$ vs clobetasol propionate cream.

plaque-type psoriasis, the different formulations of clobetasol propionate (lotion and cream) do not affect efficacy and safety.

Results of the 2 primary efficacy criteria, the DSS and GSS, showed that clobetasol propionate lotion was as efficient as its active comparator. All evaluated psoriasis signs (erythema, plaque elevation, scaling, and pruritus) improved in both treatment groups.

The BSA involved and treated in both populations significantly decreased over time with both

active drugs and remained constant in the clobetasol propionate lotion vehicle group. The analysis of the investigators' and patients' global assessment of improvement showed similar results. The percentage of patients with almost cleared and cleared condition in both active treatment groups was similar and was greater than in the clobetasol propionate lotion vehicle group.

Despite the similar efficacy results, statistically significant differences for the patient-rated cosmetic acceptability was shown in favor of the new lotion formulation of clobetasol propionate versus the cream formulation. This observation underlines that an efficient and well-known treatment such as clobetasol propionate provides a certain comfort to patients with this condition in their daily quality of life.[6,10]

During the course of the study, treatment compliance for the different products investigated was similar and reached more than 97%, emphasizing that an easy-to-spread formulation, such as a lotion, does not necessarily encourage an excessive use of the medication and thus does not increase the number or the distribution of known or expected adverse events of clobetasol propionate.

## Conclusion

Clobetasol propionate lotion, a new formulation, provides a convenient and highly accepted cosmetic profile compared with clobetasol propionate cream, while offering similar efficacy and safety characteristics. Clobetasol propionate available as a lotion improves the daily quality of life of patients with moderate to severe plaque-type psoriasis.

*Acknowledgments*—The authors would like to thank the investigators who took part in this clinical study and Patrick Göritz at Galderma Laboratories for his assistance in the drafting of this article.

## REFERENCES

1. Koo J. Population-based epidemiologic study of psoriasis with emphasis on quality of life assessment. *Dermatol Clin*. 1996;14:485-496.
2. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes much disability as other major medical diseases. *J Am Acad Dermatol*. 1999;41(suppl 3, pt 1):401-410.
3. Lebwohl M, Sherer D, Washenik K, et al. A randomized, double-blind, placebo-controlled study of clobetasol propionate 0.05% foam in the treatment of nonscalp psoriasis. *Int J Dermatol*. 2002;41:269-274.
4. Rapp SR, Feldman SR, Fleischer AB Jr, et al. Health related quality of life in psoriasis: a biopsychosocial model and measures. In: Rajagopalan R, Sheretz EF, Anderson R, eds. *Care Management of Skin Diseases: Life Quality and Economic Impact*. New York, NY: Marcel Dekker; 1998:125-145.
5. Arruda LH, De Moraes AP. The impact of psoriasis on quality of life. *Br J Dermatol*. 2001;144(suppl 58):33-36.
6. Amin S, Cornell RC, Soughton RB, et al. Topical corticosteroids. In: Roenigk HH Jr, Maibach HI, eds. *Psoriasis*. 3rd ed. New York, NY: Marcel Dekker; 1998:453-467.
7. Al Suwaidan SN, Feldman SR. Clearance is not a realistic expectation of psoriasis treatment. *J Am Acad Dermatol*. 2000;42:796-802.
8. Housman TS, Mellen BG, Rapp SR, et al. Patients with psoriasis prefer solution and foam vehicles: a quantitative assessment of vehicle preference. *Cutis*. 2002;70:327-332.
9. Katz HI, Ngo TH, Prawer SE, et al. Superpotents steroid treatment of psoriasis vulgaris—clinical efficacy and adrenal function. *J Am Acad Dermatol*. 1987;16:804-811.
10. Weiss SC, Kimball AB, Liewehr DJ, et al. Quantifying the harmful effect of psoriasis on health-related quality of life. *J Am Acad Dermatol*. 2002;47:512-518.