An open-label pilot study of apremilast for the treatment of moderate to severe lichen planus: A case series

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Background: Current treatments for chronic lichen planus (LP) are often ineffective and may have significant adverse side effects. An alternative safe and effective treatment for recalcitrant LP is needed.

Objectives: We sought to study the safety and efficacy of apremilast in the treatment of moderate to severe LP.

Methods: Ten patients with biopsy-proven LP received 20 mg of apremilast orally twice daily for 12 weeks with 4 weeks of treatment-free follow-up. The primary efficacy end point was the proportion of patients achieving a 2-grade or more improvement in the Physician Global Assessment (PGA) after 12 weeks of treatment.

Results: Three (30%) of the 10 patients achieved a 2-grade or more improvement in the PGA after 12 weeks of treatment; however, all patients demonstrated statistically significant clinical improvement with respect to secondary parameters between baseline and the end of treatment.

Limitations: It may be difficult to generalize the results of this study to a larger patient population with LP because of our small sample size and lack of a control group. In addition, a longer treatment period or higher dose may have been needed for therapeutic efficacy. The safety and efficacy of long-term apremilast therapy is currently unknown.

Conclusion: Apremilast may be efficacious in the treatment of LP, but double-blinded, controlled trials are necessary to thoroughly evaluate its safety and efficacy. (J Am Acad Dermatol 2013;68:255-61.)

Key words: apremilast; interferon-γ; interleukin; leukotriene B4; lichen planus; treatment; tumor necrosis factor-α.

Lichen planus (LP) is a chronic inflammatory disease that typically affects the skin, mucous membranes, and nails.[1-4] It frequently causes significant morbidity, including severe pruritus and pain. LP lesions can resolve spontaneously within a year; however, 15% to 20% of cases have a relapsing and remitting clinical course that is very difficult to treat.[5] Patients in the latter category have very few efficacious therapeutic options available to them, such as topical and oral corticosteroids, retinoids, cyclosporine, griseofulvin, dapsone, and phototherapy, and often with less than optimal results and

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significant adverse side effects.[6] Considering the paucity of available efficacious agents and the severity of clinical symptoms, the investigation of other medications in the treatment of LP is well merited.

The cause of LP is multifactorial, but predominantly involves skin and mucosal damage by T-cell-mediated inflammatory agents, such as tumor necrosis factor-α and interferon-γ. Apremilast is a novel phosphodiesterase type IV inhibitor, which promotes the accumulation of intracellular cyclic adenosine monophosphate.[7] Increased levels of cyclic adenosine monophosphate activate protein kinase A and effectively inhibit proinflammatory cytokine transcription and neutrophil degranulation, chemotaxis, and adhesion to endothelial cells.[8] Ultimately, apremilast inhibits the production of various inflammatory mediators, such as tumor necrosis factor-α, interferon-γ, leukotriene B4, and interleukin (IL)-2, IL-5, IL-8, and IL-12.[9] Thus, it is plausible that apremilast may be an effective treatment for LP.

CAPSULE SUMMARY

- There is a lack of effective therapies for the treatment of recalcitrant lichen planus.
- All study patients experienced statistically significant clinical improvement in secondary end points after 12 weeks of therapy with apremilast (20 mg orally twice a day).
- Apremilast was well tolerated, and no severe adverse events necessitating cessation or alteration of therapy were noted in this pilot study.

The primary objective of this study was to evaluate the overall efficacy of oral apremilast in patients with moderate to severe LP after 12 weeks of treatment. Secondary objectives included assessing the safety and toxicity of apremilast therapy, its efficacy for mucosal disease if present, and its effect on quality of life.

METHODS

Study patients

This was an investigator-initiated clinical trial approved by the institutional review board at Chesapeake Research Review Inc (Columbia, MD). Patients 18 years and older were recruited from the clinical practice of Pariser Dermatology Specialists (Norfolk, VA); the World Wide Web site of Virginia Clinical Research Inc, Norfolk (www.vcrinc.org); and referrals from community dermatologists. Written informed consent was obtained before study entry. In all, 28 adult patients were screened, and 10 were enrolled into the study (Fig 1). Patients were included if they had more than 20 distinct LP lesions and were appropriate candidates for systemic therapy (patients with a Physician Global Assessment [PGA] score >3 [moderate or severe], symptomatic [severe itching and/or pain that significantly interfered with activities of daily living], or refractory to treatment with topical corticosteroids [no improvement after at least 4 weeks of therapy]); patient exclusion criteria are available upon request.

Study design

This was a case series of an investigator-initiated, single-center, nonrandomized, open-label, pilot study of the safety and efficacy of apremilast in the treatment of moderate to severe LP (registered as NCT 01041625 on www.clinicaltrails.gov). The study was designed to have a 28-day screening period, 12-week open-label treatment phase, and 1 follow-up visit 28 days after the discontinuation of study medication. A total of 10 clinic visits were conducted over the course of 113 days.

Treatments and assessments

Study patients were treated with 20 mg of apremilast orally twice a day for 12 weeks. The PGA, PGA of Mucosal Disease (PGAMD), target area lesion count, Target Area Lesion Severity Score (TALSS), Subject Global Assessment (SGA), Subject Visual Analog Scale for Itch (SVAS), and Dermatology Life Quality Index (DLQI) questionnaires were performed at baseline (day 1; visit 2). The PGA was used to estimate the global burden of disease with respect to erythema, elevation, and pruritus at the time of evaluation, and the PGAMD assessed the extent of the patient's oral disease. "Target area" was defined as the part of the body with the greatest disease severity; its boundaries were clearly defined and documented at baseline to facilitate future assessments. The PGA, PGAMD, target lesion count, TALSS, SGA, SVAS, and DLQI questionnaires were also performed at 2-week intervals from baseline to the end of treatment (day 85; visit 9), and a final set of assessments were done at the end of the study (day 113; visit 10). A skin biopsy within the target area was performed at screening (day −34 to 0; visit 1) and the end of treatment.

Safety

Vital signs and physical examinations were performed at every office visit. Blood chemistry and hematology were assessed at every visit, except for visits 3 and 10. Serum antinuclear antibody (ANA) titers were assessed at screening (visit 1), and visits 6