

---

# Efficacy and safety of mycophenolate mofetil for lichen planopilaris

Bryan K. Cho, MD, PhD,<sup>a</sup> Deborah Sah, MD,<sup>b</sup> Jennifer Chwalek, MD,<sup>c</sup> Ingrid Roseborough, MD,<sup>d</sup> Blanca Ochoa, MD,<sup>e</sup> Charles Chiang, MD,<sup>f</sup> and Vera H. Price, MD<sup>f</sup>  
*Mountain View, Fremont, Union City, and San Francisco, California; Iowa City, Iowa; and Houston, Texas*

*See commentary on page 398*

**Background:** Lichen planopilaris (LPP) is a chronic inflammatory disorder that causes permanent scalp hair loss and significant patient discomfort.

**Objectives:** We sought to determine the efficacy and safety of mycophenolate mofetil (MMF) for treatment of LPP in patients who had failed prior topical, intralesional, or oral anti-inflammatory medications such as hydroxychloroquine or cyclosporine.

**Methods:** We conducted a retrospective chart review of 16 adult patients with LPP treated with at least 6 months of MMF in an open-label, single-center study from 2003 to 2007. Subjective and objective end points were quantified using the LPP Activity Index (LPPAI) and scores before and after treatment were assessed using a paired *t* test. Adverse events were monitored.

**Results:** Patients who completed treatment with MMF had significantly decreased signs and symptoms of active LPP despite having failed multiple prior therapies ( $P < .005$ ). Five of 12 patients were complete responders (LPPAI score decreased  $>85\%$ ), 5 of 12 patients were partial responders (LPPAI score decreased 25%-85%), and two of 12 patients were treatment failures (LPPAI score decreased  $<25\%$ ). Four patients withdrew from the trial because of adverse events.

**Limitations:** Retrospective analysis and small sample size were limitations.

**Conclusions:** MMF was effective at reducing the signs and symptoms of active LPP in 83% of patients (10 of 12) who had failed multiple prior treatments after at least 6 months of treatment. (*J Am Acad Dermatol* 2010;62:393-7.)

**Key words:** lichen planopilaris; Lichen Planopilaris Activity Index; mycophenolate mofetil.

**L**ichen planopilaris (LPP) is a rare cicatricial alopecia characterized by chronic lymphocytic inflammation in the upper third of the

From the Department of Dermatology, Palo Alto Medical Foundation, Mountain View<sup>a</sup>; Urgent Care, Palo Alto Medical Foundation, Fremont<sup>b</sup>; Department of Dermatology, Kaiser Medical Group, Union City<sup>c</sup>; Department of Dermatology, University of Iowa Hospitals and Clinics<sup>d</sup>; Department of Dermatology, Baylor College of Medicine, Houston<sup>e</sup>; and Department of Dermatology, University of California, San Francisco.<sup>f</sup>

Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication May 3, 2009.

Reprint requests: Vera H. Price, MD, Department of Dermatology, University of California, San Francisco, 1701 Divisadero St, Third Floor, San Francisco, CA 94143. E-mail: [pricev@derm.ucsf.edu](mailto:pricev@derm.ucsf.edu).

Published online January 11, 2010.

0190-9622/\$36.00

© 2009 by the American Academy of Dermatology, Inc.

doi:10.1016/j.jaad.2009.05.018

#### *Abbreviations used:*

LPP: lichen planopilaris  
LPPAI: Lichen Planopilaris Activity Index  
MMF: mycophenolate mofetil

hair follicle leading to scarring and destruction of the follicle and follicular stem cells.<sup>1</sup> The disease presents as patchy or diffuse scalp hair loss with perifollicular erythema and scaling.<sup>2</sup> Active LPP will have a positive pull test for anagen hairs.<sup>3</sup> The disease is most common in women age 30 to 60 years.

Topical or intralesional corticosteroids and topical immune modulators (pimecrolimus, tacrolimus) are not effective as monotherapy. Most patients require oral immunosuppression.<sup>1</sup> Hydroxychloroquine is used most commonly, but is not always effective.<sup>4,5</sup> For those who fail antimalarials, treatment options are

limited. Cyclosporine is helpful but its use is limited by its side effects.<sup>3</sup> Acitretin has been used for lichen planus on glabrous skin, but can cause a telogen effluvium that is poorly tolerated by patients with existing hair loss.<sup>6</sup> Therefore, there is an unmet need for a therapy that arrests LPP in patients who have failed current treatments.

Mycophenolate mofetil (MMF) is an antimetabolite approved for the treatment and prevention of organ rejection in patients with transplantation. It specifically inhibits activated lymphocytes, and is well tolerated with few effects on other rapidly dividing cells.<sup>7</sup> As lymphocytes likely play a central role in the inflammatory process underlying lichen planus and LPP, the aim of this study is to determine if MMF could safely induce a remission in patients with severe, recalcitrant LPP and prevent further hair loss.

## METHODS

The medical records and pathology reports of 16 patients with MMF treated at the University of California, San Francisco Hair Center between 2004 and 2007 were reviewed after receiving institutional review board approval. Study participants had biopsy-verified LPP less than 6 months before start of MMF and failed one or more prior systemic treatments (doxycycline, antimalarials, or cyclosporine). Patients excluded were those treated with systemic immunosuppressants less than 30 days before the first dose of MMF, prior hair transplantation, or pregnant/breast-feeding women. From the medical records, demographics, disease duration, scalp biopsy results, laboratory studies, and prior treatments were obtained. [Table I](#) shows patient demographics and [Table II](#) summarizes prior treatments.

Patients received 0.5 g of MMF orally twice daily for 4 weeks, then 1 g of MMF twice daily for at least 20 weeks although some patients were continued on MMF for up to 1 year. At roughly 12-week intervals, patients taking MMF were assessed using a standardized cicatricial alopecia flow chart<sup>3</sup> that scored subjective (itch, pain, and burning) and objective (scalp erythema, perifollicular erythema, perifollicular scale, anagen pull test, disease spreading) criteria. Laboratory testing (complete blood cell count, liver function tests) was assessed pretreatment, at 4 weeks, and every 12 weeks thereafter.

To quantify pretreatment and posttreatment responses to MMF, several subjective and objective

surrogate markers were analyzed using the LPP Activity Index (LPPAI). The index score ranges from 0 (no evidence of clinically active disease) to 10 (most severe). This index has been previously validated to correlate with clinical responses (see Chiang et al this issue\*) and allows statistical comparison. The surrogate markers were measured on a scale ranging from absent (0), mild (1), moderate (2), to severe (3). The anagen pull test was scored as negative (0) or positive (1). Assessment of disease spreading was measured on a scale ranging from inactive (0), indeterminate (1), to active spreading (2). LPPAI values were calculated using the following equation:

$$LPPAI = (itch + pain + burn) / 3 + (scalp\ erythema + perifollicular\ erythema + perifollicular\ scale) / 3 + 2.5(pull\ test) + 1.5(spreading / 2)$$

The pre-MMF and post-MMF LPPAI scores were compared using a paired *t* test to determine if there was a significant improvement. Statistical significance was assumed for *P* value less than .05. Statistical analysis was performed by the University of California, San Francisco Clinical and Translational Science Institute Epidemiology Department.

To help stratify the clinical effectiveness of MMF treatment, the changes in LPPAI scores were arbitrarily divided into complete responders (>85% LPPAI score improvement), partial responders (25%-85% LPPAI score improvement), or treatment failures (<25% LPPAI score improvement).

## RESULTS

### Patient demographics

In this study, the overall average age of onset was 51.5 years, with the majority of patients being Caucasian and female ([Table I](#)). The onset in male patients occurred at a younger age (46.2 years) than that of female patients (54.7 years). Four patients had lichen planus diagnosed at other sites (25%) similar to the prevalence of non-scalp lichen planus in patients with LPP (28%) reported by Tan et al.<sup>8</sup>

\*Chiang C, Sah D, Cho BK, Ochoa BE, Price VH. Hydroxychloroquine and lichen planopilaris: Efficacy and introduction of Lichen Planopilaris Activity Index scoring system. *J Am Acad Dermatol* 10.1016/j.jaad.2009.08.054.

## CAPSULE SUMMARY

- Mycophenolate mofetil is significantly effective in decreasing symptoms and signs of active lichen planopilaris in patients who have failed multiple prior treatments.
- Improvement in responders is apparent within 6 months.

**Table I.** Patient demographics

Patient	Sex	Race	Age at study, y	Age at onset, y	Duration of prior Tx	Other LP
1	F	Latino	74	66	8	No
2	F	Caucasian	59	52	7	No
3	M	Caucasian	53	49	4	No
4	M	Caucasian	60	55	5	No
5	F	Caucasian	60	57	3	No
6	F	Caucasian	68	57	11	No
7	M	Caucasian	40	32	8	Oral
8	F	Caucasian	54	51	1.5	No
9	F	Caucasian	54	36	18	No
10	M	Caucasian	46	42	4	No
11	M	Caucasian	57	55	2	No
12	F	Caucasian	54	53	2	No
13	F	Caucasian	58	56	1	Cutaneous
14	F	Asian/Pacific Islander	57	54	2	Cutaneous
15	M	Jewish (Sephardic)	52	44	4	Cutaneous
16	F	Caucasian	67	65	2	No
	10F		Mean	Mean	Mean	4/16
	6M		57.1	51.5	5.2	

F, Female; LP, lichen planus; M, male; Tx, treatment.

**Table II.** Treatments before mycophenolate mofetil

Hydroxychloroquine	Cyclosporine	Other oral*	Intralesional <sup>†</sup>	Topical <sup>‡</sup>	Total prior Tx
15/16	7/16	5/16	7/16	11/16	45
94%	44%	31%	44%	69%	

Average prior Tx/patient (45/16) = 2.8.

Tx, Treatment.

\*Quinacrine, acitretin, doxycycline, clindamycin, rifampin.

<sup>†</sup>Intralesional Kenalog.

<sup>‡</sup>Betamethasone foam, clobetasol solution, tacrolimus, pimecrolimus, fluocinonide oil, Dovonex solution.

Overall, the patient demographics of this study agreed well with published characteristics of patients with LPP.<sup>3</sup>

All participants in this study previously failed hydroxychloroquine except one who did not use this medication because of prior retinal disease. Most patients had failed additional oral, intralesional, or topical interventions (Table II). Overall, enrolled patients had used an average of 2.8 prior treatments during the past 5.2 years.

### Efficacy of MMF for recalcitrant LPP

Twelve patients completed the study. The pre-MMF and post-MMF LPPAI scores were compared using a paired *t* test and showed significant improvement (*P* value < .005) indicating that, as a group, patients treated with at least 6 months of MMF had reduced symptoms and signs of LPP (Table III).

Patients were also stratified into complete responders, partial responders, or treatment failures by calculating the percent improvement in LPPAI scores pre-MMF and post-MMF (see “Methods”).

Greater than 83% of patients improved with treatment. Five of 12 patients were complete responders, five of 12 were partial responders, and two of 12 were treatment failures (Fig 1).

Improvement with MMF was apparent in all complete and partial responders within 6 months. Lengthening the therapy duration beyond 6 months did not appear to increase the likelihood of responding (Fig 1).

### Adverse events

Four patients withdrew from the study because of adverse events and were not included in the statistical analysis. Two of these events were expected based on published studies with MMF and included herpes zoster and gastrointestinal disturbance. Two patients withdrew because of unexpected but mild (grade 1) hand/foot swelling that resolved after MMF was discontinued. Edema is not a commonly reported side effect of MMF and it is unclear why it developed in these patients. Routine laboratory screening did not detect any electrolyte or kidney

**Table III.** Summary of pretreatment and posttreatment Lichen Planopilaris Activity Index

Patient	LPPAI (pre)	LPPAI (post)	
1	8.3	0.0	
2	2.5		AE hand/foot swelling
3	6.0	1.0	
4	6.7	0.7	
5	4.7		AE zoster
6	5.5	1.5	
7	2.8	7.7	
8	6.2	1.3	
9	1.7		AE hand/foot swelling
10	7.0	6.3	
11	6.7	1.0	
12	4.0		AE myalgias and gastrointestinal
13	5.9	2.5	
14	5.3	1.5	
15	5.7	0.7	
16	4.9	0.7	

AE, Adverse event; LPPAI, Lichen Planopilaris Activity Index.

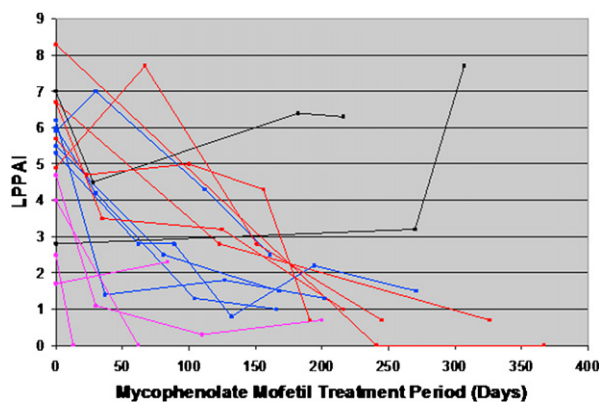
dysfunction. After MMF was discontinued, the hand and foot edema resolved. All adverse events occurred within an average of 2 months after starting MMF (range: 13-100 days).

All other study participants tolerated MMF well without significant symptoms. Laboratory analyses in all patients were routinely performed and showed no abnormalities. There were no reports of serious infections, hospitalizations, or cancers during the course of the study.

## DISCUSSION

This study provides an evidence-based approach to assess whether MMF is effective in treating cases of LPP that have failed multiple prior therapies. By quantifying patient symptoms and signs of disease progression using the LPPAI scoring system, a statistically significant improvement ( $P$  value < .005) could be demonstrated after 6 months of MMF. Of the treated patients, 42% were complete responders, 42% were partial responders, and 16% were treatment failures. Although 4 of 16 patients withdrew because of adverse events, these events were mild (grade 1) and required no special treatment or intervention.

MMF is widely considered a safe and tolerable immunosuppressive.<sup>9</sup> A recent study compared the long-term safety of MMF with cyclosporine and concluded MMF has less long-term risk for cancer or end-organ damage compared with cyclosporine.<sup>7</sup> Its effectiveness and safety profile have made it the antimetabolite of choice, replacing azathioprine in the treatment of many autoimmune and



**Fig 1.** Treatment of recalcitrant lichen planopilaris (LPP) with mycophenolate mofetil (MMF). Patients with LPP who failed multiple prior treatments were treated with MMF for 6 to 12 months. Pretreatment and posttreatment symptoms and signs were quantified using LPP Activity Index (LPPAI). Twelve patients completed study. Five of 12 patients were complete responders (LPPAI score decreased >85%; red line); 5 of 12 patients were partial responders (LPPAI score decreased 25%-85%; blue line); and two of 12 patients were treatment failures (LPPAI score decreased <25%; black line). Four patients discontinued MMF because of adverse effects (purple line).

inflammatory disorders. Within dermatology, MMF is becoming more widely used as a steroid-sparing agent in a variety of disorders such as pemphigus vulgaris, bullous pemphigoid, atopic dermatitis, and psoriasis.<sup>10</sup> Recent studies have suggested MMF may be helpful for other forms of lichen planus.<sup>11-14</sup>

## Summary

Results from a small, retrospective study such as this must be interpreted with caution. However, several reports have found MMF helpful for other forms of lichen planus suggesting that MMF may find applicability to all lichen planus-related conditions. It is also noteworthy that greater than 83% of treated patients benefited from treatment (either complete or partial responders) despite having failed at least one, or in many cases, multiple systemic treatments previously. As current treatments for LPP are largely based on case reports or case series, this study represents a significant step forward in level of evidence because the LPPAI scoring system allows statistical comparison and calculation of significance ( $P$  values). Based on these findings, we suggest that MMF may be an effective and safe treatment for recalcitrant LPP.

We would like to thank Kari Connolly, MD, for her expertise regarding use of MMF and Lee Zane, MD, for his helpful suggestions for our statistical analysis.

**REFERENCES**

1. Whiting DA. Cicatricial alopecia: clinico-pathological findings and treatment. *Clin Dermatol* 2001;19:211-25.
2. Mehregan DA, Van Hale HM, Muller SA. Lichen planopilaris: clinical and pathologic study of forty-five patients. *J Am Acad Dermatol* 1992;27:935-42.
3. Mirmirani P, Willey A, Price VH. Short course of oral cyclosporine in lichen planopilaris. *J Am Acad Dermatol* 2003;49:667-71.
4. Ho VC, Gupta AK, Ellis CN, Nickoloff BJ, Voorhees JJ. Treatment of severe lichen planus with cyclosporine. *J Am Acad Dermatol* 1990;22:64-8.
5. Price VH. The medical treatment of cicatricial alopecia. *Semin Cutan Med Surg* 2006;25:56-9.
6. Cribier B, Frances C, Chosidow O. Treatment of lichen planus: an evidence-based medicine analysis of efficacy. *Arch Dermatol* 1998;134:1521-30.
7. Buell C, Koo J. Long-term safety of mycophenolate mofetil and cyclosporine: a review. *J Drugs Dermatol* 2008;7:741-8.
8. Tan E, Martinka M, Ball N, Shapiro J. Primary cicatricial alopecias: clinicopathology of 112 cases. *J Am Acad Dermatol* 2004;50:25-32.
9. Zwerner J, Fiorentino D. Mycophenolate mofetil. *Dermatol Ther* 2007;20:229-38.
10. Liu V, Mackool BT. Mycophenolate in dermatology. *J Dermatolog Treat* 2003;14:203-11.
11. Dalmau J, Puig L, Roe E, Peramiqel L, Campos M, Alomar A. Successful treatment of oral erosive lichen planus with mycophenolate mofetil. *J Eur Acad Dermatol Venereol* 2007;21:259-60.
12. Nousari HC, Goyal S, Anhalt GJ. Successful treatment of resistant hypertrophic and bullous lichen planus with mycophenolate mofetil. *Arch Dermatol* 1999;135:1420-1.
13. Frieling U, Bonsmann G, Schwarz T, Luger TA, Beissert S. Treatment of severe lichen planus with mycophenolate mofetil. *J Am Acad Dermatol* 2003;49:1063-6.
14. Tursen U, Api H, Kaya T, Ikizoglu G. Treatment of lichen planopilaris with mycophenolate mofetil. *Dermatol Online J* 2004;10:24.