Correspondence

Usage and safety of topical tacrolimus in patients with mycosis fungoides

doi: 10.1111/ced.15162

Dear Editor,

Tacrolimus is a calcineurin inhibitor, which in topical formulation is used to treat a variety of skin conditions, including eczema and psoriasis. Tacrolimus has an antiproliferative effect on T lymphocytes, a function that has the potential to treat cutaneous T-cell lymphoma (CTCL). However, tacrolimus is also immunosuppressive and systemic tacrolimus has itself been associated with CTCL and is therefore avoided in patients with CTCL.[1] Unlike systemic tacrolimus, topical tacrolimus has not been clearly associated with CTCL.[2,3] As topical tacrolimus is not commonly used in patients with CTCL, there is limited information on its usage and safety in this unique population.

We conducted a retrospective study at the Hospital of the University of Pennsylvania of patients with mycosis fungoides (MF) who had received topical tacrolimus for any indication over the past 20 years. We collected data on the indication for and usage of topical tacrolimus, the course of MF, and rates of progression-free survival (PFS) and overall survival (OS). Disease progression was defined by the 2011 criteria from the Cutaneous Lymphoma Task Force of the European Organization for Research and Treatment of Cancer.[4]

In total, 13 patients meeting the criteria were identified, with a median age of 68 years (range 21–92 years) (Table 1). In most patients, topical tacrolimus was used

Table 1 Characteristics of patients with mycosis fungoides who received topical tacrolimus.

	CTCL presentation at start of topical usage, tacrolimus		Topical tacrolimus treatment course			Disease progression	
Patient	Stage	Location	Indication	Location	Length of usage, months (frequency)	Progression	Description
1	IA (T1N0M0B0)	Back, right hand	Seborrhoeic dermatitis	Eyelids	11.4 (twice daily)	No	NA
2	IA (T1N0M0B0a)	Back, thighs	Atopic dermatitis	Around mouth	20.8 (once daily)	No	NA
3	IA (T1N0M0B0)	Neck	Not recorded	Not recorded	30.8 (once daily)	No	NA
4	IA (T1N0M0B0)	Thighs	Seborrhoeic dermatitis	Face	41.1 (twice daily)	No	NA
5	IA (T1N0M0B0)	Axillae	Perioral dermatitis	Around mouth	30.3 (once daily)	No	NA
6	IA (T1N0M0B0)	Back	Granuloma annulare	Dorsal hands	25.2 (once daily)	No	NA
7	Remission	NA	Chronic dermatitis	Axillae	2.3 (once daily)	No	NA
8	Remission	NA	Paraneoplastic hypersensitivity reaction to mantle cell lymphoma	Knees	3 (twice daily)	No	NA
9	Remission	NA	Lichen planopilaris	Scalp	10 (once daily)	No	NA
10	Remission	NA	Seborrhoeic dermatitis	Behind ears	54.7 (twice daily)	No	NA
11	Not yet diagnosed	NA	Seborrhoeic dermatitis	Face	76 (twice daily)	Yes[a]	MF has fluctuated between IA and IB
12	Not yet diagnosed	Neck	Dermatitis (later diagnosed as MF)	Neck	12.2 (twice daily)	No	NA
13	Not yet diagnosed	Arms, legs	Dermatitis (later diagnosed as MF)	Arms	9 (twice daily)	No	NA

CTCL, cutaneous T-cell lymphoma; MF, mycosis fungoides; NA, not available. [a]Of the 13 patients with cutaneous T-cell lymphoma who received topical tacrolimus, only 1 had progression of disease.

to treat a condition other than MF, most commonly for suspected concurrent eczema or seborrhoeic dermatitis. Of the 13 patients, 6 patients with active MF (all Stage IA) received topical tacrolimus, while 4 patients received topical tacrolimus during MF remission and 3 received topical tacrolimus both before and after diagnosis of MF. Topical tacrolimus 0.1% ointment was prescribed for daily or twice-daily use for a median of 20.8 months (range 2.3–76 months). The medication was applied to a median body surface area of 2% (range 1–10%), usually to sites uninvolved with known MF. Progression of MF occurred in only 1 of 13 patients (7.6%), and the 12-month PFS and 12-month OS were 100%. All other patients either remained in remission or had stable disease for median follow-up of 45 months (range 10–165 months). The one patient who progressed has skin involvement that has fluctuated between Stages IA and IB.

In this retrospective study at a single institution, we did not observe worsening or recurrence of MF over several years of follow-up in the large majority of patients who were prescribed topical tacrolimus for other conditions. Although one patient's disease progressed, it is unclear whether the condition was exacerbated by topical tacrolimus as their MF lesions have continued to wax and wane since stopping the medication.

In meta-analyses of patients with skin conditions such as vitiligo and atopic dermatitis, topical tacrolimus has generally not increased the risk of CTCL or other skin cancers even when applied to a more widespread body surface area.[2,3] A previous case report also suggested that topical tacrolimus can help treat early-stage MF in some cases.[5]

To our knowledge, the current study is the first to describe the usage patterns and safety of topical tacrolimus in patients with CTCL. In the future, more large-scale research will help definitively characterize the effects of topical tacrolimus in this patient population.

David M. Weiner,[1] Ashley K. Clark,[2] Rahul S. Bhansali,[3] Lisa Pappas-Taffer,[2] Stefan K. Barta,[3] Jennifer Villasenor-Park,[2] Paul L. Haun,[2] Carmela C. Vittorio,[2] Alain H. Rook,[2] Ellen J. Kim[2] and Sara S. Samimi[2]

[1]*Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; Department of* [2]*Dermatology and* [3]*Hematology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA*

E-mail: david.weiner@pennmedicine.upenn.edu

Conflict of interest: The authors declare that they have no conflicts of interest.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Accepted for publication 27 February 2022

References

1 Pomerantz RG, Campbell LS, Jukic DM, Geskin LJ. Posttransplant cutaneous T-cell lymphoma: case reports and review of the association of calcineurin inhibitor use with posttransplant lymphoproliferative disease risk. *Arch Dermatol* 2010; **146**: 513–16.

2 Ju HJ, Han JH, Kim MS *et al*. The long-term risk of lymphoma and skin cancer did not increase after topical calcineurin inhibitor use and phototherapy in a cohort of 25,694 patients with vitiligo. *J Am Acad Dermatol* 2021; **84**: 1619–27.

3 Paller AS, Fölster-Holst R, Chen SC *et al*. No evidence of increased cancer incidence in children using topical tacrolimus for atopic dermatitis. *J Am Acad Dermatol* 2020; **83**: 375–81.

4 Olsen EA, Whittaker S, Kim YH *et al*. Clinical end points and response criteria in mycosis fungoides and Sézary syndrome: a consensus statement of the International Society for Cutaneous Lymphomas, the United States Cutaneous Lymphoma Consortium, and the Cutaneous Lymphoma Task Force of the European Organisation for Research and Treatment of Cancer. *J Clin Oncol* 2011; **29**: 2598–607.

5 Rallis E, Economidi A, Verros C, Papadakis P. Successful treatment of patch type mycosis fungoides with tacrolimus ointment 0.1%. *J Drugs Dermatol* 2006; **5**: 906–7.