

sis. Neither Williams-Beuren syndrome nor rheumatic purpura has been described in association with tufted folliculitis. This association seems to be coincidental in our patient.

Cyclosporine stimulates the anagen stage of the hair cycle in mice⁷ and humans.⁸ In vitro, low concentrations of cyclosporine induce keratinocyte proliferation and morphological alterations (enlargement and vacuolization), whereas higher concentrations provoke keratinocyte death.⁹ Because cyclosporine provokes keratinocyte proliferation, hypertrichosis, and folliculitis, we assume that in our patient tufted folliculitis was an adverse effect of cyclosporine treatment. To our knowledge, no similar cases have been reported. Our observation may lead to other reports, which are necessary to confirm tufted folliculitis as a cutaneous adverse effect of treatment with cyclosporine.

David Farhi, MD
Valérie Buffard, MD
Nicolas Ortonne, MD
Jean Revuz, MD, PhD

Correspondence: Dr Farhi, 58 rue Traversière, 75012 Paris, France (farhidavid@yahoo.fr).

Financial Disclosure: None.

1. Bencini PL, Montagnino G, Sala F, De Vecchi A, Crosti C, Tarantino A. Cutaneous lesions in 67 cyclosporin-treated renal transplant recipients. *Dermatologica*. 1986;172:24-30.
2. Heaphy MR, Shamma HN, Hickmann M, White MJ. Cyclosporine-induced folliculodystrophy. *J Am Acad Dermatol*. 2004;50:310-315.
3. Smith NP, Sanderson KV. Tufted folliculitis of the scalp. *J R Soc Med*. 1978;71:606-608.
4. Powell JJ, Dawber RPR, Gatter K. Folliculitis decalvans including tufted folliculitis: clinical, histological and therapeutic findings. *Br J Dermatol*. 1999;140:328-333.
5. Annessi G. Tufted folliculitis of the scalp: a distinctive clinicohistological variant of folliculitis decalvans. *Br J Dermatol*. 1998;138:799-805.
6. Luz Ramos M, Muñoz-Pérez MA, Pons A, Ortega M, Camacho F. Acne keloidalis nuchae and tufted hair folliculitis. *Dermatology*. 1997;194:71-73.
7. Paus R, Stenn KS, Link RE. The induction of anagen hair growth in telogen mouse skin by cyclosporin A administration. *Lab Invest*. 1989;60:365-369.
8. Taylor M, Ashcroft ATT, Messenger AG. Cyclosporin A prolongs human hair growth in vitro. *J Invest Dermatol*. 1993;100:237-239.
9. Takahashi T, Kamimura A. Cyclosporin A promotes hair epithelial cell proliferation and modulates protein kinase C expression and translocation in hair epithelial cells. *J Invest Dermatol*. 2001;117:605-611.

Lack of Efficacy of Tacrolimus in the Treatment of Vitiligo in the Absence of UV-B Exposure

The best results in vitiligo treatment with tacrolimus ointment have been obtained in summer and on UV light-exposed areas, which suggests that UV light enhances the efficacy of tacrolimus ointment.¹⁻⁵ We performed a prospective intra-individual left/right comparison pilot study to evaluate the efficacy of 0.1% tacrolimus ointment as true monotherapy with no UV light exposure (artificial or natural).

Methods. Nine consecutive patients, each with at least 1 pair of symmetrical patches of vitiligo with similar evolution, were included in the study (**Table 1**). For each patient, 2 symmetrical target lesions were chosen in areas cov-

Table 1. Characteristics of the Study Population

Patient No./Sex/Age, y	Skin Type	Vitiligo Site	Vitiligo Duration, y
1/F/14	2	Leg	3
2/F/56	2	Wrist	11
3/F/33	4	Wrist	19
4/F/52	2	Elbow	17
5/F/30	2	Thigh	18
6/F/60	2	Wrist	10
7/F/43	3	Knee	6
8/F/44	3	Thigh	25
9/F/61	2	Forearm	22



Figure 1. Vitiligo patches on forearms before treatment (patient 9).



Figure 2. The same vitiligo patches from patient 9 pictured in Figure 1 after 12 weeks of treatment with tacrolimus ointment alone (left) and combination therapy (right).

ered by clothes and protected from UV exposure. The entire study was performed in winter (December to February), and patients were asked to avoid UV exposure on the treated areas during the entire length of the study. Each lesion was treated twice daily with the 0.1% tacrolimus ointment (Protopic; Fujisawa Healthcare Inc, Deerfield, Ill) for a total of 12 weeks. In each patient, 1 of the 2 symmetrical target lesions also received treatment twice a week with 308-nm excimer laser (TALOS; WaveLight Laser Technology AG, Erlangen, Germany). Initial fluences were 50 mJ/cm², less than the minimal erythema dose in vitiliginous skin. Fluences were increased by intervals of 50 mJ/cm² every second session. In the presence of erythema lasting more than 8 hours over the treated lesions, treatment was withheld and resumed after resolution at the last dose that did not prompt adverse reaction.

Tolerance was evaluated using a visual analog scale. Efficacy was evaluated by 2 independent physicians blinded to the treatment using direct digital light photographs (Fujifilm Finepix S1 Pro; Tokyo LTD, Tokyo Japan) taken before and at the end of treatment. Repigmentation was graded on a 6-point scale (0, no repigmentation; 1, 1%-24% repigmentation; 2, 25%-

Table 2. Results After 12 Weeks of Treatment With 0.1% Tacrolimus Ointment With and Without UV-B Laser Therapy

Patient, No.	Repigmentation Score*		Treatment Session at Which Repigmentation First Appeared, No.	Cumulative Dose of UV-B at the Onset of Repigmentation, J/cm ²	Patient Satisfaction With Tacrolimus Alone	Patient Satisfaction With Combination Treatment
	Tacrolimus Alone	Tacrolimus Plus UV-B				
1	0	3	13	2.2	Poor	Good
2	0	1	8	2.3	Poor	Moderate
3	0	2	7	2.1	Poor	Good
4	0	4	7	1.3	Poor	Excellent
5	0	4	8	1.5	Poor	Excellent
6	0	2	9	2.7	Poor	Good
7	0	2	13	5.4	Poor	Good
8	0	4	10	3	Poor	Excellent
9	0	3	13	3.9	Poor	Good

*Higher score indicates greater repigmentation. For a full description of the 6-point scale, see the "Methods" section.

49% repigmentation; 3, 50%-74% repigmentation; 4, 75%-99% repigmentation; and 5, total repigmentation). At the final visit, the patients' opinions about treatment effectiveness were recorded.

Results. After 12 weeks of treatment, all of the vitiliginous patches that were treated with the combination therapy were partially repigmented, with scores ranging from 1 to 4 (**Figure 1** and **Figure 2**). Conversely, none of the opposite site patches that were treated with tacrolimus ointment alone showed any repigmentation (**Table 2**). No adverse effects were noted with tacrolimus monotherapy; however, mild-to-moderate erythema was observed with combination treatment. The tolerance of both treatments was good.

Comment. Our results do not support the efficacy of tacrolimus when used as monotherapy in the treatment of vitiligo. Owing to the design of the study (intra-individual left/right), we could not add an arm with laser treatment only. However, in a previous study our research team has shown that tacrolimus ointment plus excimer laser was more effective than laser alone,⁶ supporting the hypothesis that the repigmentation observed in the present study was not only owing to laser treatment. Previous reports have provided some positive results in the treatment of vitiligo with tacrolimus ointment.¹⁻⁵ Interestingly, in most of the cases reported, the concomitant action of UV exposure cannot be ruled out and is sometimes underlined as a possible factor in good results. The synergistic action of this association has already been emphasized.^{6,7} Such a synergistic effect also has been shown with the combination of topical steroid and UV-A.⁸ Optimal repigmentation of vitiligo macules might have 2 requirements: first, an immunomodulation to halt the disease process, which could be provided by the tacrolimus ointment; then, repigmentation might require or at least be enhanced by stimulation of the proliferation and migration of melanoblasts induced by the UV light.

Our study does not determine if longer applications of tacrolimus ointment monotherapy would finally induce a repigmentation. Moreover, the sites chosen for this study, such as knee and elbow, are usually very difficult areas to treat. This could explain the complete absence of repigmentation with tacrolimus alone. Although results of combination therapy are very encouraging, carcinogenic adverse effects cannot be ruled out, and long-term follow-up is still required. Nonetheless, further prospective studies without any source of UV exposure should be performed to determine the true efficacy of tacrolimus ointment monotherapy in vitiligo.

Nima Ostovari, MD
Thierry Passeron, MD
Jean-Philippe Lacour, MD
Jean-Paul Ortonne, MD

Correspondence: Dr Passeron, Department of Dermatology, Archet-2 hospital, BP 3079, 06202 Nice CEDEX 3, France (t.passeron@free.fr).

Financial Disclosure: None.

1. Smith DA, Tofte SJ, Hanifin JM. Repigmentation of vitiligo with topical tacrolimus. *Dermatology*. 2002;205:301-303.
2. Grimes PE, Soriano T, Dytoc MT. Topical tacrolimus for repigmentation of vitiligo. *J Am Acad Dermatol*. 2002;47:789-791.
3. Travis LB, Weinberg JM, Silverberg NB. Successful treatment of vitiligo with 0.1% tacrolimus ointment. *Arch Dermatol*. 2003;139:571-574.
4. Lepe V, Moncada B, Castanedo-Cazares JP, Torres-Alvarez MB, Ortiz CA, Torres-Rubalcava AA. Double-blind randomized trial of 0.1% tacrolimus vs 0.05% clobetasol for the treatment of childhood vitiligo. *Arch Dermatol*. 2003;139:581-585.
5. Tanghetti EA. Tacrolimus ointment 0.1% produces repigmentation in patients with vitiligo: results of a prospective patient series. *Cutis*. 2003;71:158-162.
6. Passeron T, Ostovari N, Zakaria W, et al. Topical tacrolimus and the 308-nm excimer laser: a synergistic combination for the treatment of vitiligo. *Arch Dermatol*. 2004;140:1065-1069.
7. Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. *Dermatol Surg*. 2004;30:130-135.
8. Westerhof W, Nieuweboer-Krobotova L, Mulder PG, Glazenburg EJ. Left-right comparison study of the combination of fluticasone propionate and UV-A vs either fluticasone propionate or UV-A alone for the long-term treatment of vitiligo. *Arch Dermatol*. 1999;135:1061-1066.