

Clinical Dermatology

Topical tacrolimus improves vitiligo; adding sunlight may help even more

Degree of response from treatment seemed to depend on the application site and on the season it was applied

BY CHERYL GUTTMAN STAFF CORRESPONDENT

New Orleans — Results from an exploratory study indicate a potential role for topical tacrolimus in the management of vitiligo, Emil A. Tanghetti, M.D., said at the annual meeting of the American Academy of Dermatology.

He presented his experience having 15 patients with vitiligo apply tacrolimus 0.1 percent ointment (Protopic) as monotherapy twice a day for up to three months. The magnitude of responses varied, but 13 achieved at least partial improvement while two of those patients completely repigmented and another had a 50 percent to 75 percent response. The degree of response seemed to depend on the site of application and the season — patients achieving the greatest benefit had involvement of sun-



Dr. Tanghetti

exposed skin, i.e., face and neck, and used the ointment during the spring and summer months.

Results seen in six to eight weeks

The onset of response was typically noted within six to eight weeks.

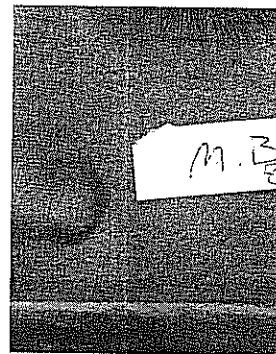
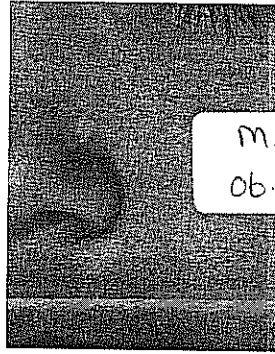
Treatment duration was between three and nine months but was at the lower end of that range in most patients. Use of topical tacrolimus resulted in no adverse events, Dr. Tanghetti reported.

"These results are certainly encouraging, even though they are not overwhelmingly positive," said Dr. Tanghetti, clinical professor of dermatology, University of California at Davis, and a private practitioner in Sacramento.

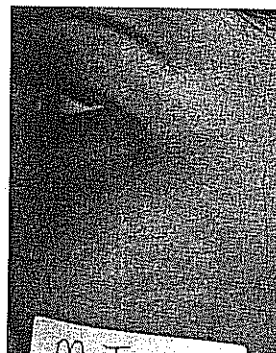
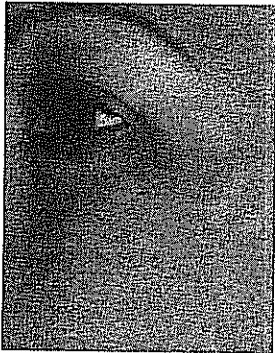
"However, they indicate that tacrolimus might work in some patients with vitiligo and particularly when combined with natural UV light," he said. "The findings in this study would support further investigation using tacrolimus and sun exposure in an additive approach for vitiligo."

Vitiligo: Tough to treat

According to Dr. Tanghetti, short of PUVA, there are few good treatments for the disease, "and perhaps it might be possible that tacrolimus could be used to enhance the response to PUVA, narrow



Vitiligo discolorations in nasal area at baseline (left) and two months topical tacrolimus posttreatment.



Vitiligo discolorations in cheek and eyebrow areas at baseline (left) and five months topical tacrolimus posttreatment.

band UVB, or the excimer laser. It might offer an opportunity for treating vitiligo with a combination of therapies. These would affect the immune system and disease pathophysiology in different ways, just as we approach the management of psoriasis and many other skin conditions."

Immunomodulator therapies

Describing tacrolimus as launching dermatology into a new era of immunomodulator drugs, Dr. Tanghetti noted he was intrigued by the possi-

bility of treating vitiligo, a disease characterized by an overactive immune system, with a topical drug other than corticosteroids.

"Current topical treatment of vitiligo is limited to corticosteroids, but the side effect profile of those drugs, especially the potential for atrophy, make corticosteroids an unattractive modality for long-term use, he said."

He emphasized that tacrolimus seemed a natural drug to consider as an alternative.

The first patient treated began apply-

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ing the tacrolimus ointment to the forehead in April and achieved complete repigmentation.

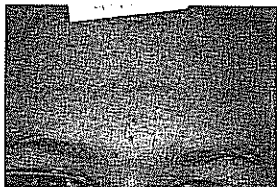
Treatments successful

Motivated by that outcome, 14 additional patients were entered into the open study. The other complete responder, as well as the patient with 50 percent to 75 percent improvement, used the treatment on the face and neck and began treatment in July. A fourth patient with facial vitiligo began treatment in June and had a 25 percent to 50 percent response.

Among the patients with a lesser response, only one other was applying the ointment to the face and neck exclu-



Patient presents scarring and hypopigmentation of forehead and brow area (left) caused by burns from topical psoralen administered by another physician. Repigmentation of all areas except scarred area (in pink) achieved eight months topical tacrolimus posttreatment. (All photographs courtesy of Emil Tanghetti, M.D.)



sively, but the treatment did not begin until August. Other patients with lesser responses were either treating the face

and hands or only extrafacial sites, including the knee, ankle, elbows, and hands.

Treatment sites for the two patients who

had no response were the face in one individual and the neck and chest in the other, but those patients used the ointment only during the late fall and winter months.

Dr. Tanghetti proposed that tacrolimus promotes repigmentation in patients with vitiligo by down-regulating overactive T-cell function. However, since the immunological basis of that disease is not completely elucidated, neither can the exact mechanism(s) of action of tacrolimus be determined.

He noted that because tacrolimus is a large molecule, it does not penetrate well through intact skin, and that feature might be a limiting factor in its efficacy in vitiligo. The addition of sunlight might improve treatment responses by altering permeability characteristics to enhance drug penetration or by affecting the immunological abnormality through a different pathway than tacrolimus.

More evaluation would be beneficial

"Further study seems worthwhile to evaluate disease response to a combination regimen consisting of tacrolimus plus sunlight or other UV exposure. However, another dual therapy option to consider is using tacrolimus with a treat-

"Since poor absorption through intact skin may be an impediment to efficacy, perhaps tacrolimus might be used together with a topical retinoid."

Emil Tanghetti, M.D.

Clinical professor of dermatology,
University of California at Davis

ment that changes the barrier characteristics of the skin," Dr. Tanghetti said.

"Since poor absorption through intact skin may be an impediment to efficacy, perhaps tacrolimus might be used together with a topical retinoid," he said. "The latter drug would thin the horny layer of the skin and allow better cutaneous penetration of tacrolimus."

Warning on label

He added that the labeling information for tacrolimus ointment includes the precautionary statement that it is prudent for patients to minimize or avoid natural or artificial sunlight exposure.

Tacrolimus was observed to shorten the time to skin tumor formation in an animal photocarcinogenicity study. Whether this has a significant role in humans remains to be seen.

More study of this topic is essential to permit further exploration of combination studies with tacrolimus and ultraviolet light.

Protopic is a product of Fujisawa Inc. Dr. Tanghetti has no financial interest in the company and received no funding for his study. DT

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