

Tacrolimus, Pimecrolimus Eyed for Off-Label Use

The drugs are seen as good potential alternatives to mid- to high-potency topical steroids.

BY BRUCE JANCIN
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VIENNA — The topical calcineurin inhibitors constitute the most important advance in topical therapy of inflammatory dermatoses in half a century, Thomas A. Luger, M.D., said at a satellite symposium held in conjunction with the annual meeting of the European Society for Dermatological Research.

Topical tacrolimus (Protopic) and pimecrolimus (Elidel) are approved only for the treatment of atopic dermatitis. But investigations are underway for their use in a wide range of other inflammatory skin diseases. These agents are attractive alternatives to corticosteroids because they exhibit efficacy akin to that of mid- to high-potency topical steroids, but without the classic steroid side effects of skin atrophy and suppression of the hypothalamic-pituitary-adrenal axis. Pimecrolimus is marketed by Novartis, sponsor of the satellite symposium.

Here are some of the skin diseases where the early off-label clinical experi-

ence with the topical calcineurin inhibitors appears to be favorable, although it must be stressed that randomized controlled trials will be required to establish which patients are best treated with these agents, added Dr. Luger, professor and chair of dermatology at the University of Münster (Germany);

► **Cutaneous lupus erythematosus.** A recent 11-patient series reported by investigators at Ruhr University in Bochum, Germany, concluded that 3 weeks of twice-daily 1% pimecrolimus cream, with the second application followed by overnight occlusion, resulted in excellent results in all patients, with the benefits being sustained in most patients during 8 weeks of follow-up off treatment (*J. Am. Acad. Dermatol.* 2004;51:407-10). The investigators found that the skin lesions of systemic lupus erythematosus (SLE) and subacute cutaneous lupus erythematosus (LE) responded better than those of longstanding discoid LE, which tend to be more hyperkeratotic and therefore resistant to transdermal drug penetration.

Topical tacrolimus appears to be effective as well. Investigators at St. Thomas' Hospital, London, have reported that 6 of 11 LE patients with resistant cutaneous lesions showed clear improvement in their skin lesions in response to a minimum of 6 weeks of 0.1% tacrolimus ointment. Among the responders were patients with discoid LE, subacute cutaneous LE, and SLE (*Rheumatology* 2004;43:1383-5).

Dr. Luger added that he, too, has had favorable clinical experiences using topical tacrolimus, particularly in patients with cutaneous LE of the face.

► **Netherton syndrome.** Dr. Luger and colleagues have obtained gratifying results using 1% pimecrolimus cream to treat a series of patients with this disorder. Systemic absorption wasn't a problem with pimecrolimus cream, unlike topical tacrolimus, which permeates skin more efficiently. Other investigators have reported that topical tacrolimus therapy in Netherton syndrome patients often results in therapeutic blood levels.

"We treated 99% of the body surface area with pimecrolimus in some of our patients with Netherton syndrome, yet their blood levels after 3 weeks of therapy were still only one-tenth of what's needed for a systemic effect," Dr. Luger said.

► **Psoriasis.** The topical calcineurin in-

hibitors are quite effective for facial lesions and for the intertriginous lesions of psoriasis inversa. These are sites where the skin is relatively thin. In contrast, neither topical agent is effective in chronic plaque-type psoriasis because the drugs can't penetrate the thick hyperkeratotic skin.

► **Lichen sclerosus.** Dr. Luger and his associates have reported complete resolution of anogenital lichen sclerosus with once-daily tacrolimus ointment in three prepubertal girls and three adults, with remissions lasting for up to 1 year and no noteworthy adverse effects (*Arch. Dermatol.* 2003;139:922-4). The pain and itching prominent in the disorder resolved completely in the first 2-3 weeks; fissuring, erythema, and other physical changes responded more slowly.

Other investigators recently reported that 3-4 months of pimecrolimus cream resulted in almost complete remission of severe anogenital lichen sclerosus in four prepubertal girls (*BMC Dermatol.* 2004;4:4).

► **Other applications.** Promising results have been reported with use of topical calcineurin inhibitors are perioral dermatitis; the skin lesions of dermatomyositis, vitiligo, steroid-induced rosacea, alopecia areata; and seborrheic dermatitis. ■

Child's Dermatitis, Family's Quality of Life Improve With Pimecrolimus Treatment

BY DIANA MAHONEY
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BOSTON — Pimecrolimus cream for atopic dermatitis leads to itch-free kids and happier parents, a study has shown.

In a randomized, double-blind trial enrolling 275 children from 3 months to 11 years old with moderate to severe atopic dermatitis, the parents of those children treated with a 1% strength of the topical immunomodulator pimecrolimus (Elidel) reported substantially improved quality of life, compared with parents of children treated with topical corticosteroids, Jennifer Sung, M.D., said at the annual meeting of the American College of Allergy, Asthma, and Immunology.

All of the parents whose children were enrolled in the multicenter vehicle-controlled investigation completed a patient gender-specific version of the Parent's Index of Quality of Life in Atopic Dermatitis (PIQoL-AD) at base-

line, week 12, and at the end of the study at week 24.

The questionnaire, which is the only survey specifically designed for parents of children aged 3 months to 12 years, contains 28 true/not true items and has been shown to have good psychometric properties, said Dr. Sung, a clinical investigator at Novartis Pharmaceuticals, East Hanover, N.J., the manufacturer of Elidel.

The questionnaire includes items addressing parents' concerns about their children's appearance, the effort required to prevent itching and provide appropriate care, and the stress of worrying about the condition and the effect of treatments.

Responses are numbered and summed. Scores range from 0 to 28, with higher scores indicating a poorer quality of life. The investigators used an analysis of covariance model to compare changes in scores from baseline to the end of the study, controlling for treatment, center, and baseline score.

At baseline, all mean demographic and clinical characteristics between the pimecrolimus-based therapy and the 92 who received corticosteroid-based treatment were the same.

In both groups, atopic dermatitis affected at least 5% of each subject's total body surface area.

All of the children in the study received emollients for dry skin and either pimecrolimus cream 1% or corticosteroid twice daily at any sign of active atopic dermatitis.

Corticosteroid subjects who experienced severe flares were given a mid-potency topical corticosteroid for evening use until complete resolution, for a maximum of 3 weeks.

The baseline PIQoL-AD score for parents of children in the pimecrolimus and corticosteroid groups, respectively, was 8.4 and 9.3.

At 24 weeks, the respective scores were 4.9 and 6.3, representing an improvement from baseline of 37.6% for the pimecrolimus group and 26.8% for the corticosteroid group, Dr. Sung reported.

"A number of studies have already shown [pimecrolimus] to be a safe, effective, nonsteroidal option for these kids. This study tells us that there's a beneficial effect on their parents' quality of life also," Dr. Sung said. "Parents are especially relieved not to have to worry about corticosteroid-related side effects." ■

Topical Imiquimod Useful for Treatment Of Lentigo Maligna

VIENNA — Imiquimod appears to be an excellent off-label treatment option in selected patients with lentigo maligna, Ingrid H. Wolf, M.D., said at the annual meeting of the European Society for Dermatological Research.

She reported on five patients with biopsy-proven lentigo maligna on the face and/or shoulder who underwent a course of imiquimod therapy because they had contraindications for surgery, the standard first-line treatment. The participants self-applied 5% imiquimod cream once daily for 5-13 weeks.

All five patients experienced a complete clinical and histopathologic response. They have now been followed for 7-22 months with no evidence of recurrence, said Dr. Wolf of the University of Graz (Austria).

The only significant side effect was the occurrence of erythema and erosions at the treatment site in all of the patients 2-4 weeks after the start of therapy.

Immunohistologic assessment performed at several time points during treatment suggested the topical agent induced a cytotoxic T-cell-mediated immune response, she continued.

The predominant finding was an inflammatory cell infiltrate comprised of helper T cells that were mixed in with monocytes, macrophages, and cytotoxic cells.

Situations in which it would be appropriate for dermatologists to consider turning to imiquimod for the treatment of patients with lentigo maligna include large lesions, advanced patient age, ill-defined lesional margins, a cosmetically precarious anatomic location, and comorbid systemic illness that increases surgical risk, Dr. Wolf said.

—Bruce Jancin

