

Vitiligo and Beyond: Tacrolimus and Pimecrolimus Find New Roles for Children

Dermatologists continue to find new applications for TCIs. A pediatric dermatologist reviews new and future treatment trends.

By Angela Battluck, Associate Editor

To say the introduction of tacrolimus and pimecrolimus has been an important step in pediatric dermatology would be an understatement. Tacrolimus (Protopic, Fujisawa) and pimecrolimus (Elidel, Novartis) have revolutionized the management of atopic dermatitis and are proving to play an important role in the management of other autoimmune skin conditions that affect children. In fact, numerous case reports suggesting novel uses of topical calcineurin inhibitors, ranging from cutaneous lupus erythematosus to lichen sclerosus, are appearing in the literature.

In particular, TCIs are proving to be a significant advancement in the management of vitiligo. In fact, according to Nanette Silverberg, MD, Director of Pediatric Dermatology at St. Luke's-Roosevelt Hospital Center in New York, tacrolimus has become first-line therapy for childhood vitiligo. Let's look a little more closely at how the management of vitiligo has changed and how first-line treatment of other autoimmune skin conditions may also change in the near future, thanks to tacrolimus and pimecrolimus.

Vitiligo: New Treatment Trends

For years, dermatologists considered topical corticosteroids and phototherapy first-line treatment for childhood vitiligo. Although helpful for some children, these options were ineffective for a significant percentage of children, while other children were denied treatment

due to disease location, such as the intertriginous areas. "Even the best of studies have suggested that the response to topical corticosteroids is only about 64 percent in children," notes Dr. Silverberg. "Thirty-six percent is a big group of patients that wouldn't repigment or didn't repigment fully."

Shortly after Protopic received FDA-approval for atopic dermatitis in 2000, reports¹⁻⁴ began to emerge suggesting topical tacrolimus produces repigmentation in vitiligo patients, and more recent reports suggest pimecrolimus has a similar effect.⁵ To determine the safety and efficacy of tacrolimus for childhood vitiligo, Dr. Silverberg and colleagues recently reviewed⁶ 57 pediatric vitiligo cases managed with tacrolimus ointment alone, which only provided further evidence that this topical immunomodulator was a safe and effective alternative to topical steroids.

In fact, Dr. Silverberg and colleagues found 89 percent of children with vitiligo on the head or neck responded to a once- or twice-daily treatment with tacrolimus ointment, while 63 percent of children with vitiligo on the trunk or extremities responded to therapy. "This is clearly the highest response rate in

terms of vitiligo of the head and neck and in terms of overall response rates by patient to any therapy because there was an overall 84 percent response rate," says Dr. Silverberg. "That is clearly the highest response rate that's been seen with

any topical therapy for vitiligo." In addition, she notes that although segmental vitiligo tends to respond poorly to therapy, "Patients with segmental vitiligo on the face had a 94 percent response rate to tacrolimus, which was incredibly high."

"Patients with segmental vitiligo on the face had a 94 percent response rate to tacrolimus, which was incredibly high."

Dr. Silverberg explains that the treatment regimen with tacrolimus ointment for vitiligo is very similar to that for atopic dermatitis. Specifically, she notes that children were able to achieve a high response rate while staying within the age-appropriate dosing regimens (tacrolimus 0.03% for children 15 and younger and 0.1% for children older than 15). "The patients who were treated with twice daily tacrolimus did much better than once daily," explains Dr. Silverberg. Treatment was for at least a three month period.

Tacrolimus therapy allows for repigmentation on multiple levels, according to Dr. Silverberg. On one level it inhibits the autoimmune inflammatory process that is destroying the

melanocytes, and on another level it re-stimulates melanocytes that had previously been dysfunctional but still capable of repigmentation. "With tacrolimus therapy you are going to get repigmentation from the hair follicles, but you will also get a diffuse repigmentation, which usually conceptually means that the patients have had some resurgence of activity of melanocytes that had stopped functioning," Dr. Silverberg explains. Because tacrolimus does not interfere with collagen production, Dr. Silverberg notes this agent does not have atrophogenic potential, which means it can be safely used in the intertriginous areas. "It now opens up the possibility for patients who were previously untreated to be treated safely and for longer time periods," says Dr. Silverberg.

Despite tacrolimus' high efficacy rate, topical steroids still play a role for some children. Even for children who fail topical steroids, Dr. Silverberg does not always immediately end steroid therapy to introduce tacrolimus ointment. Instead, for some children, she adds Dovonex (calcipotriene, Bristol-Myers Squibb/Warner Chilcott) to the regimen. "There are certainly patients who we still treat with topical steroids, and if they should fail, rather than stopping

the topical steroid that is still being used, we can drop the steroid down to once a day, add in topical calcipotriene, and get an adjuvant effect that rescues these children," explains Dr. Silverberg. Because this combination regimen reduces steroid exposure to once a day, it is a safer option for children, similar to tacrolimus.

With tacrolimus therapy—as well as all vitiligo treatments—small amounts of natural sunlight often enhance repigmentation. "The patients should get some sun exposure during this time period," recommends Dr. Silverberg. "We don't want to burn our patients or give them skin cancer, but a small amount is similar in activity to getting phototherapy."

Beyond Vitiligo

Additional reports are also appearing in the literature suggesting other roles for tacrolimus, such as contact dermatitis. Dr. Silverberg reports, "I have had good response when patients have a chronic eruption, particularly from nickel contact dermatitis. They can do very nicely with topical tacrolimus." In addition, Dr. Silverberg notes good experience using topical tacrolimus for children with cutaneous lupus erythematosus,

cutaneous morphea, and lichen sclerosus. Reports also suggest pimecrolimus is a safe and effective treatment option for contact dermatitis, cutaneous lupus erythematosus, and lichen sclerosus.⁷⁻⁹

A Giant Leap

Without doubt, tacrolimus and pimecrolimus have proven to be a huge advancement in pediatric dermatology and not just in the management of atopic dermatitis. Thanks to the TCIs, children with vitiligo now have a safe and effective alternative to high potency topical steroid therapy. In the future months and years, dermatologists will likely find additional roles for tacrolimus and pimecrolimus, and similar to vitiligo therapy, these agents may even one day become the treatment of choice for other pediatric skin conditions. ■

1. Grimes PE, Soriano T, Dytoc MT. Topical tacrolimus for repigmentation of vitiligo. *J Am Acad Dermatol*. 2002 Nov;47(5):789-91.
2. Smith DA, Tofte SJ, Hanifan JM. Repigmentation of vitiligo with topical tacrolimus. *Dermatology*. 2002;205(3):301-3.
3. Tanghetti EA. Tacrolimus ointment 0.1% produces repigmentation in patients with vitiligo: results of a prospective patient series. *Cutis*. 2003 Feb;71(2):158-62.
4. Travis LB, Weinberg JM, Silverberg NB. Successful treatment of vitiligo with 0.1% tacrolimus ointment. 2003 May;139(5):571-4.
5. Mayoral FA, Gonzalez C, Shah NS, Arciniegas C. Repigmentation of vitiligo with pimecrolimus cream: a case report. *Dermatology*. 2003;207(3):322-3.
6. Silverberg NB, Lin P, Travis L, Farley-Li J, Mancini AJ, Wagner AM, Chamlin SL, Paller AS. Tacrolimus ointment promotes repigmentation of vitiligo in children: a review of 57 cases.
7. Queille-Roussel C, Graeber M, Thurston M, Lachapelle JM, Decroix J, de Cuyper C, Ortonne JP. SDZ ASM 981 is the first non-steroid that suppresses established nickel contact dermatitis elicited by allergen challenge. *Contact Dermatitis* 2000 Jun;42(6):349-50.
8. Kreuter A, Gambichler T, Breuckmann F, Pawlak FM, Stucker M, Bader A, Altmeyer P, Freitag M. Pimecrolimus 1% cream for cutaneous lupus erythematosus. *J Am Acad Dermatol*. 2004 Sep;51(3):407-10.
9. Boms S, Gambichler T, Freitag M, Altmeyer, Kreuter A. Pimecrolimus 1% cream for anogenital lichen sclerosus in childhood. *BMC Dermatol*. 2004 Oct 14;4(1):14.

New in Your Practice

Around the World. Neither ethnic origin of a child with atopic dermatitis nor baseline disease severity appears to impact the efficacy of pimecrolimus cream 1% (Elidel), according to a recent study in *International Journal of Dermatology* (44:70). In fact, the study found that all children with mild to moderate atopic dermatitis responded well to pimecrolimus. The study, which involved 589 children ranging in age from three months to 17 years, also notes a twice-daily treatment with pimecrolimus appears to be safe and well tolerated.

Class of Its Own. Clobetasol may soon be available as an aerosol spray. CutiCeuticals recently announced. Modeled after Kenalog spray and Skin-Cap spray, CutiCort Spray contains 0.05% clobetasol formulated in oil and alcohol with a standard propellant and has been described by the manufacturer as working "like a class zero steroid." Studies involving over 2,000 patients show CutiCort clears limited plaque psoriasis in seven to 21 days and is not associated with any adverse reactions. CutiCort is undergoing several FDA-required evaluations and is not yet available.