Rosacea Management:
Guide Patients Path to Control



Dermatologists who keep an open mind and tailor the regimen to each individual can help steer patients toward long-term control of rosacea symptoms.

By Paul Winnington, Editor-in-Chief



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Management of rosacea continues to evolve, with new topical and systemic treatment options emerging recently. Perhaps the biggest news in rosacea therapy is the launch of Oracea (CollaGenex), a once-daily formulation of subantimicrobial dose doxycycline indicated to manage the inflammatory component of rosacea. With its apparently low rate of adverse events and the elimination of concerns regarding antibiotic resistance, Oracea (as discussed in this month's Acne/Rosacea Advances, p. 20) may become a popular choice of systemic therapy among dermatologists.

However, topical therapy remains an important element of therapy for a number of rosacea patients, whether as the primary intervention or for long-term maintenance. Dermatologists are familiar with the available options but may not always consider alternative regimens or combinations that may optimize therapy and speed their patients along the road to control.

General Guidelines

With relatively new treatments indicated for rosacea, such as once-daily metronidazole 1% (Metro1, Galderma) and reports of certain topical therapies successfully used off-label for rosacea, dermatologists have a large and expanding palette of options from which to choose when building the treatment regimen. Though clinicians may have certain preferred agents or regimens, it's important to, "Be open-minded and consider a wide array of treatment options, including topical antibiotics, TCIs, azelaic acid, and oral antibiotics," says Kevin M. Crawford, MD, a dermatologist at Emory University Medical Center in Atlanta. Then, he says, dermatologists must use the appropriate agent(s) "in whatever combination seems most feasible."

Head off possible patient frustration by letting them know that a wide variety of treatment options exist and that the regimen may change as needed in order to enhance therapeutic results. Patients must understand early on that rosacea is a chronic, often progressive, disease with no cure. Complete clearance may not be possible; the treatment goal is control.

During the initial exam and at subsequent visits, "Ask patients if they have eye symptoms," Dr. Crawford urges, "because that's often overlooked." Ocular involvement may manifest as dryness or a sensation of grittiness or a foreign body in the eye. Any patient with ocular symptoms requires an ophthalmology consult.

Finally, dermatologists should take some time to discuss skin care and cosmetics with patients. In addition to camouflage make-ups and techniques, a growing number of cosmeceutical products claim to offer benefit in managing the signs and symptoms of rosacea. "They are certainly worthwhile and can help," Dr. Crawford says of these products. He notes, however, that patients may need to try several different products until they find one they like that provides the benefits they seek.

Those who doubt the need to specifically address camouflage techniques with patients may consider a relatively recent report[1] suggesting that provision of cosmetic camouflage advice actually improved the quality of life for patients with certain skin diseases. Among 56 participating patients from three centers, there was a signigicant difference in mean scores on the Dermatology Quality of Life Index (DQLI) before and one month after the first visit to a cosmetic camouflage clinic. The mean duration of the skin condition for these patients was 15 years. Although most practices may not be equipped with a camouflage clinic, practices may consider appointing a medical aesthetician or other staff member to handle patient education regarding selection and use of appropriate camouflaging make-ups and skin care products.

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New Directions

Recently, interest has grown in the use of topical calcineurin inhibitors or TCIs to manage rosacea. As yet there are no data from large-scale clinical trials, but a few smaller trials, published case reports, and anecdotal reports support the use of either pimecrolimus (Elidel, Novartis) or tacrolimus (Protopic, Astellas) to manage symptoms of rosacea.[2,3]

Dr. Crawford published a study of pimecrolimus in rosacea. He and his colleagues evaluated 12 patients with erythrotelangiectatic or papulopustular rosacea treated with topical pimecrolimus cream twice daily for 12 to 18 weeks.[2] The most notable effect of therapy was improvement of erythema, with 10 of 12 patients showing significant improvement. Five of six patients with a papulopustular component noted a decrease in lesions of at least 80 percent. Based on these results and additional experience with the agent, Dr. Crawford says he has expanded the use of pimecrolimus for rosacea in his practice.



Don't Be Fooled by Demodex Folliculitis

It seems that any discussion of rosacea invariably leads to mention of the Demodex mite, which has been historically linked with rosacea, even though no studies have proven a role for the mite in its pathogenesis. I do not believe that Demodex causes rosacea. However, I (along with a growing number of colleagues) believe there is a distinct entity called Demodex folliculitis that may mimic rosacea and/or co-exist with it. Demodex folliculitis may also be mistaken for seborrheic dermatitis.

Patients with Demodex folliculitis present with centro-facial erythema accompanied by scale. Telangiectases and papules/pustules typically do not occur with Demodex folliculitis alone. Consider Demodex folliculitis whenever there is doubt regarding the diagnosis of rosacea or SD. Maintain some degree of suspicion whenever patients initially diagnosed with rosacea or SD do not respond to appropriate therapies aimed at these diseases.

If there is suspicion of Demodex involvement, observe the old directive, "if it scales, scrape it." Though Demodex reside normally on the skin, identification of numerous mites on KOH examination will confirm Demodex infestation that warrants treatment. Treatment options include topical permethrin, crotamiton 10%, or a single oral dose of ivermectin 6mg.

– Joseph Bikowski, MD

Within the context of the current rosacea grading scale, where Type I is erythematotelangiectatic (characterized by erythema, flushing, telangiectases, and edema) and Type II is papulopustular (erythema accompanied by papules and pustules), Dr. Crawford observes that numerous available therapies are effective for Type II but not as effective for Type I. TCIs appear to improve the erythematous portion of both presentations. Still, Dr. Crawford says, it isn't necessarily a first-line treatment option. "Generally, I will try topical antibiotics or azelaic acid first before going on to Elidel," Dr. Crawford says, but he adds, "I am not apprehensive to use it." He says topical pimecrolimus is "pretty close to as effective" as standard topical therapies for rosacea.

Currently, he advises patients to apply topical pimecrolimus twice a day for six to eight weeks. If they respond well to therapy, he tapers to a once-daily maintenance application that he has had patients use indefinitely. In light of the recent black box warnings applied to both tacrolimus and pimecrolimus, Dr. Crawford recognizes that some physicians may question the safety of using these agents indefinitely. He notes that data used to support the black box warning came from studies of systemic TCI formulations provided at doses far higher than would ever be used in humans and certainly not attainable via topical application

A panel of five independent oncologists found no definitive link between pimecrolimus or tacrolimus and increased risk of lymphoma.[4] To date, there isn't strong evidence of attributable cancer associated with topically applied tacrolimus or pimecrolimus, Dr. Crawford says. "If you look at the number of reported cases of lymphoma, it is actually lower than would be expected in the background population. In terms of the post-marketing nonhuman primate study that showed lymphoma development in monkeys, that study used an oral formulation of pimecrolimus that was 30-times the highest dose ever recorded in a human with topical use," he remarks.

Of note, researchers last year published results of a study of pharmacokinetics of topical TCIs in adult patients with extensive moderate to severe atopic dermatitis.[5] Even in this population of patients with known barrier dysfunction and extensive disease, tacrolimus was detectable in just 36 percent of blood samples of treated patients and pimecrolimus was detectable in just 12 percent of samples. Blood levels were higher for tacrolimus 0.1% ointment (mean area under the curve <9.7ng.h/mL) than for pimecrolimus 1% cream (mean area under the curve <2.5ng.h/mL).

Dr. Crawford has seen no adverse events in his patients who have used topical pimecrolimus for extended periods of times. "With any medication you try to get people to use it

for as little time as possible in order to get the results they desire," he says.

Because the primary benefit of TCIs in rosacea seems to be reduction of erythema (whereas topical metronidazole or azelaic acid effectively targets papules and pustules via their anti-inflammatory and anti-microbial properties), TCIs are often used in combination with traditional rosacea therapies. Although his study protocol involved application of topical pimecrolimus alone, Dr. Crawford now commonly uses combinations, usually instructing patients to apply one agent each morning and the other at night. Building the regimen requires consideration of the patient's presentation as well as physician preference. "There is no strict regimen, and you have to tailor the regimen on a patient by patient basis," Dr. Crawford says.

Topical TCIs may represent an alternative to certain rosacea therapies. With the exception of very severe rosacea, Dr. Crawford says he is more likely to initiate a trial of topical pimecrolimus before prescribing a standard oral antibiotic. If the TCI alone does not produce sufficient clearing, a systemic antibiotic can be added on, he says. Plus, he says. "I think pimecrolimus is a far superior and safer product than a topical steroid." Patients who use topical corticosteroids risk tachyphylaxis, steroid "acne," and telengiectases, but no such side effects are associated with topical TCI therapy.

Topical TCIs may actually represent a treatment option for steroid-aggravated rosacea, reports suggest.[6] When rosacea has been inappropriately treated with topical corticosteroids either at too high a potency or for too long a period, withdrawal of the steroid may lead to aggravation of facial symptoms. Case reports show that twice-daily application of pimecrolimus quickly controls flaring when an aggravating steroid is withdrawn.

There are contraindications to the use of TCIs, including any active viral, fungal, or bacterial infections, including active HSV or HPV, in the treatment area. "If there is any suspicion of infectious process, it may not be the best to use," Dr Crawford says.

An Open Mind

Effectively managing rosacea requires that dermatologists weigh a number of treatment options in order to devise a regimen that meets the patient's needs and achieves his or her treatment goals. Adjunctive agents, such as cosmeceutical and skin care products, warrant discussion and trials if patients are interested. Don't overlook the potential benefit of targeted advice regarding camouflaging make-up.

Dermatologists and patients should have realistic expectations and be flexible, willing to adapt the regimen as needed. Because rosacea is by nature a chronic and progressive disease with no cure, dermatologists should inform patients that over time, with the natural course of the disease, redness, papules, pustules, and other symptoms have a tendency to worsen, Dr. Crawford reminds. "It may not be reasonable to promise a patient you can make his/her face look perfectly clear or normal. A more plausible approach would be to inform the patient that a reduction in papules/pustules, redness, or halting in the progression of the disease is actually a good treatment outcome," he says. Avoid overplaying the potential effectiveness of treatment options to avoid patient dissatisfaction and exceedingly high expectations.

However, it's equally important that dermatologists try various treatments in order to achieve optimal results. "Keep an open mind and don't box yourself in," Dr. Crawford urges.

Popular Ingredients for OTC Topical Rosacea Products

Green tea extracts (such as EGCG):
Reduce erythema and provide "calming" effects.*

Dimethicone:
"Calming" properties and protecting against irritants.*

Xanthine (caffeine):
Reduce erythema and prevent flares.*

Quadrinone:
Anti-inflammatory.*

Vitamin C:
Reduce erythema and stabilize tone.*

Nicotinamide:
Anti-inflammatory; lesion reduction.*
Also available in oral form.

**** Actions attributed to ingredient.***

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