As dermatologists, we see many rosacea patients; most have some degree of facial redness, which is both an aesthetic and quality-of-life issue. My patients report to me that they feel like they look embarrassed all the time, or that some people may even presume that they have been drinking because they have so much flush to the face. The reality is that we see a fair amount of people who present with a spectrum of rosacea—from patients who have central facial redness to patients who have papulo-pustular lesions to those who have phymatous changes in their skin, and even ocular involvement. For papulo-pustular rosacea, topical therapies, including topical antibiotics or topical azelaic acid, and oral antibiotics help alleviate the symptoms associated with this subtype of rosacea but don’t reduce facial redness. Until now, we had been missing a really effective treatment for Type I rosacea—persistent redness to the central face, called Erythemato-Telangiectatic Rosacea.

**EFFECTIVE FOR FACIAL ERYTHEMA**

Brimonidine gel 0.33% (Mirvaso, Galderma) was recently FDA approved for the topical treatment of the facial erythema of rosacea in adults 18 years of age or older. Mirvaso is a first-in-class topical regimen for people who have persistent facial redness associated with rosacea. It is something that many of us are excited to incorporate into our practices that offers patients benefit and improvement. Mirvaso works by constricting the dilated facial blood vessels to reduce the redness of rosacea. Mirvaso should be applied in a pea-sized amount, once daily to each of the five regions of the face: the forehead, chin, nose, and each cheek. Mirvaso works quickly to reduce the redness of rosacea and lasts up to 12 hours, with benefit evident as early as 30 minutes after application.

Data from two identically designed, randomized, double-blind, vehicle controlled Phase III trials with more than 550 total patients showed that topical brimonidine gel applied once-daily was significantly more efficacious than vehicle gel throughout 12 hours on days 1, 15, and 29. The trials recruited subjects with moderate to severe erythema of rosacea, who were randomized to active treatment or vehicle control. Patients applied brimonidine topically once-daily. Evaluations included both the Clinician’s Erythema Assessment and Patient’s Self-Assessment. Because it’s a composite score, both physician and patient had to agree for the patient to be considered a responder. A long-term study in 276 patients who used Mirvaso for up to 12 months was also conducted.

In these clinical trials, the most common adverse reactions (≥1%) were cutaneous, including erythema, flushing, skin-burning sensation, and contact dermatitis—with slightly higher incidence of these in the active treatment group. Due to Alpha-2 adrenergic agents’ effects on blood pressure and other theoretical concerns, the labeling urges cautious use in some conditions. Refer to the full prescribing information for details.

**AN IN-DEPTH LOOK AT THE DATA**

From a data perspective, the pivotal, Phase III trial was designed so patients applied the medication once per day and then were evaluated on day 1, day 15, and day 29 throughout the course of the day—they had to stay at the clinical trial investigators’ office on the evaluation days. Patients applied Mirvaso at the office and the study showed that treatment started to work at 30 minutes, had its peak efficacy between three hours and about nine hours, and then started to trail off through 12 hours (though it was still better at 12 hours than at baseline). And by the next day, the effect had worn off.

**How Mirvaso fits into the current treatment armamentarium for rosacea.**

**JOEL L. COHEN, MD**
Although the progression of rosacea can vary substantially from one individual to another, flushing and persistent redness are the most common early signs of the disorder, according to a new survey conducted by the National Rosacea Society (NRS).

In the NRS survey of 1,072 rosacea patients on the order of appearance of rosacea signs and symptoms, 31 percent said that flushing was the first symptom they experienced, 63 percent said it was the second, and 24 percent reported that persistent redness was their first sign of rosacea, while it was named second by 34 percent and third by 39 percent.

Beyond flushing and redness, other signs and symptoms most commonly appeared in the following order: bumps (third, 30 percent or fourth, 24 percent), pimples (third, 28 percent or fourth, 20 percent), visible blood vessels (third, 17 percent or fourth, 28 percent), burning or stinging (third, 14 percent or fourth, 26 percent), dry appearance (fourth, 18 percent or fifth, 21 percent), raised red patches (fourth, 16 percent or fifth, 14 percent) and swelling (fifth, 15 percent, sixth, 12 percent, or seventh, 13 percent). Although eye irritation was rarely the first sign of rosacea, it was reported as second by 14 percent and as third by 10 percent of patients.

Twenty-five percent of respondents said they were in their 30s when their first sign of rosacea appeared, 22 percent were in their 40s, and 25 percent reported they were older than 50. Seventeen percent were in their 20s and 11 percent were under 20.

Based on the results of the study, we know the medication is a once-per-day treatment and that it offers some degree of improvement for 12 hours, and that patients return to baseline the next day. The study was designed to show that patients behaved very similarly over the course of the month—at day 1, day 15, and day 29 investigators saw the same degree of improvement. The medication continues to work with no waning of effect over the course of the month. It was a very nicely designed study, but in my personal opinion it should have looked at timepoints after 12 hours to study how patients look before the next morning—so that we could advise our patients on those expectations, as well. For the second part of the study, investigators had the patients discontinue the medication after four weeks of daily application and then present back for recheck at weeks two and four. This follow-up trial showed that patient’s central facial erythema did not look worse than when they started the medication. Thus, based on the first part of the study—four weeks of active application—there was no “waning effect” or “tachyphylaxis.” And, the second part of the trial showed that there was no “rebound” over the course of those four weeks.

An additional part of the Phase III study was an open label 52-week trial. The rationale for that was to account for seasonal variations and other situations that cause rosacea to flare, such as weather-related conditions, spicy foods, or stints of workouts. Similar to the initial findings, over the course of the year there was no evidence of any waning of effect or tachyphylaxis. And both the Phase III pivotal trial and the Phase III open label trial were conducted at various sites from East Coast to West Coast, and from Texas to Canada to account for any possible regional difference.

**A COMBINATION APPROACH**

The Phase III open label trial allowed patients to use concomitant medications, so if they needed to or wanted to, they could use other medications for rosacea or other medications in general. During the year, 85 percent of patients were on other medications, including for various medical conditions, and 23 percent were actually on other rosacea medications, in some cases topical azelaic acid or topical metronidazole or oral antibiotics. Thus, we know Mirvaso works well in concert with these other medications.

One legitimate question many physicians are asking is how Mirvaso is going to fit in to our practices in terms of the way we have up until now been treating facial erythema. Traditionally we’ve been treating central facial redness with lasers and light-based therapies, such as pulsed dye lasers (PDL) or intense pulsed light (IPL) devices specific for vessels. In my practice, I’ve been using a PDL or IPL (specifically Palomar’s Max G) for the overall redness as well as targeting the blood vessels and telangiectasias. I think patients will be able to benefit from a combination of treatment with Mirvaso and lasers. One thing to clarify is that the medication does not work on discrete vessels or telangiectasias. In fact, in some cases, a patient might use the topical medication and then those vessels that may have been “camouflaged” in the background of redness are going to be “unmasked” and become more apparent. Then those patients will probably present to our offices for laser treatment of specific vessels on the side of their nose, etc. I would recommend patients just not use Mirvaso on the days they come in for laser treatment, so that we can be most effective with the PDL or IPL device in treating some background redness as well as discrete vessels.

Dr. Cohen is a consultant for Galderma Laboratories.

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1. MIRVASO® Prescribing Information