

# Doxycycline, Metronidazole Effective for Rosacea

BY DAMIAN McNAMARA

SINT MAARTEN, NETHERLANDS ANTILLES — A combination of doxycycline and metronidazole cleared more inflammatory rosacea lesions and worked faster than metronidazole alone in a randomized controlled trial.

This combination should be considered a first-line treatment for rosacea, according to the efficacy and safety findings that were presented by Dr. Joseph F. Fowler Jr. at the Caribbean Dermatology Symposium.

Previous research suggested that agents with anti-inflammatory activity, including doxycycline or tetracycline and topical metronidazole, are effective for management of rosacea symptoms (*Cutis* 2004;73:15-18; *Skinmed* 2003;2:43-47).

Dr. Fowler assessed the safety and efficacy of using 40-mg delayed-release doxycycline capsules (Oracea, Galderma), which is the anti-inflammatory dose of the antibiotic, in combination with

metronidazole topical gel 1%.

"I chose metronidazole 1% because it is one of the more established products. ... I was able to show both drugs had an effect. But when combining the two, you get much faster and greater improvement," said Dr. Fowler, clinical pro-



**By week 4, lesion count decreased by 10 among combination patients and by 3 in those on monotherapy.**

DR. FOWLER

fessor in the dermatology division, University of Louisville (Ky.).

A total of 36 patients were randomized to combination treatment, and another 36 to an oral placebo and metronidazole gel 1% (monotherapy group). Following baseline assessment, patients

were evaluated at weeks 4, 8, and 12, at which time metronidazole therapy was stopped. Patients continued to take oral doxycycline or placebo for another 4 weeks.

The 56 women and 16 men enrolled in the study had a mean age of 48 years. Baseline mean total inflammatory lesion count (papules, pustules, and nodules) was similar between groups—21 in the combination group and 19 in the monotherapy group.

A total of 64 participants completed the study—30 in the combination group and 34 in the monotherapy arm. In all, 4 people withdrew because of adverse events (including 3 in the combination group), 2 people withdrew consent, 1 was removed for a protocol violation, and 1 was lost to follow-up.

The primary outcome, mean change in total inflammatory lesion count, was significantly improved in the combination group. For example, from baseline to week 4, the count decreased by 10 le-

sions among combination patients versus 3 among monotherapy patients. "The quick onset [of the oral drug] is a critical take-home message," Dr. Fowler said.

By week 16, the mean reduction in total inflammatory lesions was 13 in the combination group, compared with 7 for the monotherapy group.

Patients in the combination therapy group had greater improvements on investigator global assessment at all time points, including significant differences at weeks 12 and 16.

Between weeks 12 and 16, patients who received doxycycline monotherapy maintained the benefits of decreased inflammatory lesion counts and improvements on global assessment.

Dr. Fowler was a consultant and clinical research investigator for CollaGenex Pharmaceuticals Inc. at the time of the study.

Galderma has since acquired CollaGenex, and Dr. Fowler receives research support from Galderma. ■

## Minimize Side Effects From Treatment of Acne, Rosacea

BY MARY ELLEN SCHNEIDER

When treating rosacea and acne, pay close attention to the potential for adverse effects ranging from skin irritation to drug resistance, according to Dr. Joseph F. Fowler Jr.

Irritation is especially common in rosacea patients, and there can be significant adverse effects from systemic treatments of both rosacea and acne. Fortunately, newer formulations of both topical and systemic drugs have been created to reduce the adverse effects and increase the efficacy of these treatments, said Dr. Fowler of the University of Louisville (Ky.).

At the Caribbean Dermatology Symposium, he outlined a treatment plan for acne and rosacea patients with sensitive skin and reviewed the adverse effects of current treatments. Dr. Fowler disclosed being a consultant and conducting clinical studies for a number of pharmaceutical companies that produce rosacea and acne treatments.

Rosacea patients tend to have more sensitive skin, Dr. Fowler said in an interview, so topical medications need to be carefully chosen. Data suggest that metronidazole 1% (MetroGel, Galderma) is the least irritating. Another topical option is azelaic acid gel 15% (Finacea), which has been shown to be somewhat more irritating, but slightly more efficacious. Both of these options cause less irritation than do many of the generic products on the market.

"From a topical standpoint, it is fairly difficult to find products that are both highly effective and nonirritating," Dr. Fowler said. "We probably

don't have a topical agent that is tremendously efficacious, especially in more severe rosacea."

When a topical therapy is efficacious but is causing irritation, Dr. Fowler recommends using an adjunctive therapy such as calcineurin inhibitors, antifungal treatments, and moisturizers. The treatments may not do much alone, but they can be added to the regimen to allow tolerance of the first topical agent.

For patients with moderate to severe rosacea or even mild cases where an oral agent is preferred, systemic treatment may be appropriate. However, Dr. Fowler tries to use the lowest doses possible because of concerns about oral antibiotics' adverse effects, such as gastrointestinal symptoms, vertigo, photosensitivity, autoimmune disease, and antibiotic resistance.

For example, he tries to avoid using higher doses (the levels used in acne treatment) when treating chronic rosacea. Dr. Fowler recommends using sub-antimicrobial-dose doxycycline generic 20 mg/twice a day or Oracea delayed release. He said that he prefers to use Oracea delayed release because the once-a-day formulation is better for patient compliance. In addition, the delayed release probably gives more of an anti-inflammatory effect, he noted.

In acne, watch out for irritation from topical retinoids, he said. Generally, the irritation tends to increase as the efficacy increases. When using a topical retinoid, Dr. Fowler recommends slowly stepping up treatment from a mild retinoid such as low-dose adapalene to one with a higher strength. ■

## Each Beach Vacation Raises Risk of Small Nevi in Kids

BY DENISE NAPOLI

Each beach vacation from birth to age 6 by white Colorado children was associated with a 5% increase in small nevi when the children were examined at age 7, but not with large nevi development.

In addition, the total estimated UV dose received on waterside vacations and the number of days spent on vacation were not significantly related to nevi count, suggesting that a threshold dose of UV exposure is received relatively early during each waterside vacation, such that 3-day-long getaways may have the same effect on nevi development as 10-day trips, according to the authors.

Although it is the larger nevi (greater than or equal to 2 mm) that are most commonly associated with skin cancer, increased numbers of small nevi in childhood also confer melanoma risk.

"Parents should be aware of the effect that vacations may have on their children's risk for developing melanoma as adults, and they should be cautious about selection of vacation locations," wrote Dr. Kelly J. Pettijohn, from the department of community and behavioral health at the Colorado School of Public Health, Denver, and associates.

A total of 681 children born in 1998 who were lifetime residents of Colorado were studied. Patients' parents were asked in 20- to 30-minute phone interviews about

the child's vacation history, sunburn history, and demographic data. Skin exams were also conducted in 2005, when the patients were 7 years old (*Cancer Epidemiol. Biomarkers Prev.* 2009;18:454-63).

A history of severe sunburn, of sunscreen use, of hat use, or of sun sensitivity failed to predict the development of nevi. "The only significant linear relationship between vacations and nevi less than 2 mm was for number of waterside vacations before age 6," wrote the authors.

Each vacation was associated with a 5% increase in these small nevi after controlling for other factors.

In addition, the authors found that waterside vacations taken within 1 year of the skin exam did not affect small nevi counts. This finding suggests a time lag of at least 1 year may be necessary for the effects of sun exposure during waterside vacations to result in new nevi, they noted. The authors reported no potential conflicts of interest. ■



Parents should be made aware of the effect that vacations have on their children's risk of melanoma.