Sorting Out New Systemic Therapies for Acne and Rosacea

Two recent FDA approvals may mark a change in the approach to acne and rosacea management. Here’s a look at new agents and their unique indications.

By Dina Anderson, MD

With its recent approval, sub-antimicrobial dose doxycycline (Oracea, CollaGenex) became the second tetracycline antibiotic formulation to reach the market this year with an indication for cutaneous disease management. However, physicians and patients must not confuse Oracea, the first oral agent approved for rosacea, with Solodyn (Medicis), the first oral minocycline formulation approved for once-daily use to manage inflammatory lesions in acne. Each agent is optimized to provide a different primary action in these unique dermatologic conditions.

Review of Antibiotic Therapy

Historically, tetracycline antibiotics have been used for the management of both acne and rosacea. Interestingly, while the pathogenesis of acne vulgaris clearly implicates *P. acnes*, there is no compelling evidence that bacteria play any role in the pathogenesis of rosacea. Attempts to identify in rosacea a role for causative organisms such as *H. pylori*, *P. acnes*, or even bacteria from *Demodex* mites have proven inconclusive or have failed.1,2

Inflammation, however, is widely accepted as a hallmark of rosacea and is also a feature of acne vulgaris.

The use of tetracycline antibiotics, which demonstrate activity against *P. acnes*, makes obvious sense for acne management. That antibiotics also confer anti-inflammatory effects has come to be viewed as an added benefit in acne management. However, in the case of rosacea, increasing evidence suggests that the benefit of antibacterial therapy is anti-inflammatory action alone; there is no target for antibacterial action.

Dermatologists in the clinic are well aware of potential problems associated with standard antibiotic formulations. Of primary concern is the growing issue of antibiotic resistance. In addition to resistant strains of *P. acnes*, researchers have cultured other resistant bacteria from acne patients treated with systemic antibiotics.3,4,5,6

Patients are increasingly savvy to issues of resistance. Furthermore, many patients are skeptical of oral antibiotics following wide publication of a questionable study suggesting a link between long-term antibiotic therapy and breast cancer risks.7

Finally, systemically administered tetracycline antibiotics at standard doses may be associated with GI upset. Minocycline is associated with CNS side effects and risk of bluish hyperpigmentation of the sclera, nails, teeth, mucous membranes, and skin. Clinicians and researchers have expressed interest in identifying therapeutic updates or alternatives that may minimize or obviate these concerns.

New Agents At-a-Glance

**Oracea.** Although Oracea is a formulation of doxycycline, a well-known antibiotic agent historically used for management of acne as well as rosacea, the new formulation confers no antimicrobial effect. Instead, Oracea delivers doxycycline in what is termed a sub-antimicrobial dose (SD)—a dosage below the minimal inhibitory concentration (MIC). Its primary method of action is its anti-inflammatory effect. The stated indication is the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients.

The 40mg once-daily dose is administered in a single capsule containing both immediate and delayed release beads. According to CollaGenex, in two phase III studies, patients receiving Oracea respectively experienced a 61 percent and 46 percent mean reduction in inflammatory lesions versus 29 percent and 20 percent mean reductions in patients receiving placebo.

Side effects of the drug were similar to placebo in these trials. One would anticipate that SD dosing would limit development of side effects associated with standard-dose doxycycline.
Furthermore, the SD dose, since it does not exert any effect on bacterial flora, is not expected to contribute to the development of antibiotic resistance.

**Solodyn.** Solodyn, by contrast, provides direct antimicrobial effects against *P. acnes*; the extended-release, low-dose formulation of minocycline is administered above the MIC. However, because oral tetracyclines are associated with anti-inflammatory effects, Solodyn confers anti-inflammatory action, as well. It is specifically indicated for management of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older.

The recommended once-daily dose of Solodyn is 1mg/kg, with tablets available in 45mg, 90mg, and 135mg doses. The company reports that clinical trials data showed a significant increase in inflammatory lesions associated with therapy; there were no additional therapeutic benefits with higher dosages of minocycline compared to the 1mg/kg dose of Solodyn. Of note, the company reports that CNS side effects were not significant in clinical trials of Solodyn. The lower dose is expected to decrease the risks or incidence of adverse effects.

It’s worth noting that combination therapy has been and will remain standard clinical practice in acne management. The use of benzoyl peroxide washes or topical retinoid formulations in addition to Solodyn will only improve the rate of clearance of inflammatory lesions.

**Implications**

The emergence of two new antibiotic formulations may have important implications for the care of patients with acne and rosacea. In light of growing disaffection with iPledge and subsequently declining numbers of prescriptions for isotretinoin, most dermatologists will welcome the emergence of convenient, effective oral therapies with favorable side-effect profiles. Oracea and Solodyn both feature once-daily dosing—which may contribute to enhanced patient compliance. However, despite their common class designation (both tetracyclines), the two agents differ in their indications* and actions. Oracea, the first oral agent approved for management of rosacea and the first SD agent approved in dermatology, may be considered an anti-inflammatory rather than an antimicrobial agent. It obviates concerns about antibiotic resistance associated with long-term tetracycline therapy.

Solodyn offers antimicrobial effects in a low-dose formulation while also conferring beneficial anti-inflammatory effects in acne management. Its low-dose coupled with delayed-release seem to minimize side effects commonly associated with tetracycline therapy.

* There have been small investigational studies of SD doxycycline in acne vulgaris. In one study, doxycycline 20mg BID produced significant reduction of inflammatory and non-inflammatory lesions over six months.