The therapeutic landscape for acne is continuing to grow with two recent approvals for topical acne drugs and several in the pipeline. Excitingly, many of these new drugs are novel molecules that treat acne by different mechanisms compared to traditional therapies. This article will review the newest topical therapies on the market and what can expect to come in the next several years.

NEW TO THE MARKET

Benzoyl peroxide 3.75%/clindamycin phosphate 1.2% gel. A fixed-dose benzoyl peroxide 3.75%/clindamycin phosphate 1.2% (Onexton, Valeant Pharmaceuticals) gel recently received FDA approval for the treatment of acne. It is a micronized and microdispersed gel with an aqueous, non-alcohol base that’s free of surfactants and preservatives. In a 12-week multi-center, double-blind, vehicle-controlled study, 498 patients with moderate to severe acne were randomized to receive either the BP/clindamycin combination or vehicle once daily.¹ The mean reduction in comedonal lesions was 51.8 percent in patients receiving active drug, as compared to 27.7 percent receiving vehicle. Additionally, reductions in inflammatory lesions were 60.4 percent and 31.3 percent in patients receiving the BP/clindamycin product and vehicle, respectively.

Treatment success in the study was defined as patients who were clear or almost clear at 12 weeks along with an at least two-grade improvement in the Evaluators Global Severity Scores (EGSS). In the study, 35 percent were considered a treatment success, compared to 17 percent in the vehicle arm. Moreover, 29 percent of patients experienced even greater than two-grade improvement in severity and were clear or almost clear, as compared to 15 percent of those in the vehicle group. These patients started the study as severe (EGSS=4) and improved three grades to a mild (EGSS=1) score and were included in this more stringent endpoint. Finally, a subset analysis of adult women at least 25 years old revealed 50.7 percent treatment success with the active drug versus 30.4 percent in the vehicle treated women.

Adapalene 0.3%/benzoyl peroxide 2.5%. Fixed dose combination adapalene 0.3%/benzoyl peroxide 2.5% (Epiduo Forte, Galderma) gel was FDA approved for the treatment of acne in July 2015. In the pivotal phase 3 study, 503 patients were enrolled across 31 sites in the US and Canada. Patients had moderate to severe acne and were treated with once-daily ADA 0.3%/BPO 2.5% gel, ADA 0.1%/BPO 2.5%, or vehicle gel.² The ADA 0.1%/BPO 2.5% gel was included for safety comparisons only as compared to ADA 0.3%/BPO 2.5%. Of note over, half of the patients were severe, with an Investigator’s Global Assessment score (IGA) of 4. The IGA success rate was defined as clear or almost clear score (IGA=0 or 1) along with a two-grade improvement. In the ITT population, 33.5 percent of patients on active drug achieved treatment success, as compared to 11.5 percent in the vehicle gel group. Subgroup analysis of severe cases revealed a success rate of 31.2 percent in the ADA 0.3%/BPO 2.5% gel group, as compared to 13.3 percent in the vehicle group.

In evaluating individual parameters of lesions counts, there was a 66.4 percent reduction in inflammatory lesions in the active drug group compared to 35.3 percent in the vehicle group. As for comedonal lesions, there was 66.2 percent and 33 percent reduction in the active and vehicle arms, respectively.

Overall, ADA 0.3%/BPO 2.5% gel was well tolerated. Irritation was comparable between the ADA 0.3%/BPO 2.5% and ADA 0.1%/BPO 2.5% groups.
WHAT’S ON THE HORIZON

In addition to the two recently approved topical medications, there are several new chemical entities and different drugs currently being developed for the treatment of acne. Following is a brief preview of several of these investigational products.

**DRM01.** DRM01 is a novel anti-acne drug. A topical sebum inhibitor, it affects the first and rate-limiting step in fatty acid synthesis. In sebocyte cultures, it has been shown to inhibit sebum production, and in a hamster ear model it has been shown to reduce sebaceous gland size. In a phase 2a, randomized, vehicle-controlled study recently presented at the recent World Congress of Dermatology 2015 meeting, DRM01 demonstrated safety and efficacy in treating acne patients. 108 patients with a mean age of 25.2 years were enrolled into the 12-week study. Baseline mean lesion counts were 29.7 inflammatory and 40.9 noninflammatory in the active group, as compared to 28.6 inflammatory and 38.8 noninflammatory lesions in the vehicle group. At week 12, there was a 64 percent reduction in inflammatory lesions versus a 46 percent reduction in the vehicle group. Comedonal lesions were decreased by 48 percent in the active group versus 29 percent in the vehicle group. Finally, 24.5% of patients in the active group achieved a greater than two-grade improvement in IGA scores, as compared to 7.3 percent in the vehicle group. The agent was well tolerated, with most adverse events being mild or moderate. The most common were application site dryness, burning, and stinging.

**FMX101.** FMX101 is a topical minocycline in development for moderate to severe acne. In a phase 2, multicenter, randomized, double-blinded trial at three study centers in Israel, 150 patients were randomized to receive either FMX101 1%, FMX101 4%, or vehicle. After 12 weeks, there was a 72 percent and 73 percent reduction in inflammatory and comedonal lesions, respectively, in the FMX101 4%, which was statistically better than vehicle. Fifty-three percent of patients on the 4% drug achieved an IGA score of clear or almost clear, as compared to 19.6 percent of patients on vehicle. Moreover, 36.2 percent of patients on the 4% drug achieved an IGA of clear or almost clear in addition to greater than two grades of improvement, versus 15.2% in the vehicle arm. There were no adverse events related to the study drug during the study.

**SB204.** SB204 is a topical nitric oxide releasing gel from Novan Therapeutics. Nitric oxide is found naturally in the body and has anti-microbial and anti-inflammatory activity. The active ingredient in the gel, NVN1000, is active against *P. acnes*, has anti-inflammatory effects, and has been shown to inhibit lipogenesis in vitro.

A Phase 2 multi-center, randomized, double-blinded, vehicle-controlled study across four sites in Latin America evaluated acne patients with the drug. Patients had between 20 and 40 inflammatory lesions, 25 to 70 non-inflammatory lesions, and no greater than two nodules on the face. Patients were randomized to receive either SB204 1%, SB204 4%, or vehicle for 12 weeks.

Patients in the 4% group saw approximately a 57 percent reduction in inflammatory lesions and 25 percent reduction in comedonal lesions at week 12. In addition, at the end of the study, 80 percent less sebum was measured from the skin using sebutapes. Patients in both the SB204 groups had less than 80 percent sebum than those in the vehicle group. Moreover, dose dependent decrease in squalene and free fatty acids was observed. The agent was well tolerated, with only mild cutaneous tolerability adverse events.

**SEB002.** SEB002 is a proprietary topical agent from Sebacia that delivers light-absorbing gold-coated silica microparticles to enhance photodynamic treatment. It is applied to the skin, where it is absorbed into the pilosebaceous unit. A 755nm–1064nm diode, alexandrite, or ND:Yag device is used to deliver heat, which is selectively absorbed by the gold particles in the sebaceous glands. This results in a selective photothermal effect that destroys the glands.

In a European Study, 48 patients were randomized to receive immediate treatment (three treatments at two-week intervals) or an over-the-counter face wash for 12 weeks followed by a crossover to the active treatment. Patients reported mild to moderate pain during the procedure (no anesthetic was used).

While some patients experienced mild erythema, it subsided within 30-60 minutes. There were no restrictions on sun exposure and no downtime for patients. At 28 weeks, patients in the active group saw a 61 percent reduction in inflammatory lesions and the crossover group achieved 50 percent reduction.

**CONCLUSION**

With advances in formulation technology along with a pipeline of new drugs, including new chemical entities, the armamentarium of acne treatments is expanding. With new options available, the bar is being raised in terms of both efficacy and safety for our acne patients.

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2. Data on file, Galderma Laboratories.