Vehicles Matter!

Leon H. Kircik MD

Cutibacterium acnes (*C. acnes*, formerly *Propionibacterium acnes*), the bacterium that lends its name to one of the most common dermatologic conditions, has been studied for decades. Yet science continues to uncover discoveries about this ubiquitous, commensal organism and the pathogenesis of acne vulgaris.

A Gram-positive lipophilic bacterium that is dominant in sebaceous glands, *C. acnes* has been classified into three phylotypes.[1] Although *C. acnes* is not infectious, proliferation of the bacterium in the anaerobic milieu of the sebum-rich, blocked follicle helps to promote the development of acne vulgaris by driving pro-inflammatory processes.[2] Treatment targeted at reducing *C. acnes* populations and their associated local inflammation is foundational to acne management. Antibiotic treatment for acne using tetracycline class antibiotics or clindamycin, which targets the bacterium, is rational and well-established. However, the risk of developing antibiotic resistance requires a cautious approach to the use of both topical and oral antibiotics.

Relatively recently, sarecycline, a next-generation oral tetracycline, has come to market for the treatment of acne. It has been shown to bind simultaneously to two different subunits of *C. acnes*, which accounts for its narrow-spectrum activity.[3] While the risk for antibiotic resistance associated with sarecycline may be reduced relative to other antibiotics used to treat acne, prescribers, and patients are nonetheless cautioned to use the agent responsibly and to continue to employ strategies to mitigate resistance risk. That means that patients require concomitant topical treatment with benzoyl peroxide, an antimicrobial agent that is effective against gram-positive bacteria but not associated with promoting antibiotic resistance.[4] Benzoyl peroxide works via oxidation, which renders it effective against certain microorganisms but also potentially incompatible with other topical drugs.

A combination topical formulation currently under investigation for the treatment of acne is a novel first-in-class fixed-dose triple combination topical gel that contains clindamycin phosphate 1.2%, benzoyl peroxide 3.1%, and adapalene 0.15% in a polymeric mesh gel. This formulation is yet another example that "vehicles matter." The polymeric mesh allows for benzoyl peroxide and adapalene microparticles to be homogeneously dispersed in the gel, thus overcoming the issue of adapalene and benzoyl peroxide being unstable together in the same topical formulation.

In a 12-week phase 2 double-blind, randomized, vehicle-controlled clinical trial including subjects aged 9 years or older with moderate-to-severe acne, once daily topical application of triple combo achieved treatment success in more than 50% of participants over the vehicle at week 12. Reductions in inflammatory and noninflammatory lesions were greater than 70%.[5]

These impressive trial results suggest that a triple combination may be a versatile treatment option for a significant proportion of patients with acne. The three-agent formulation may be a suitable treatment for patients with mild to moderate acne vulgaris, allowing for the concomitant use of three different drugs in a single application.

Trial data suggest that the triple-combination topical formulation may exhibit synergistic efficacy by simultaneously affecting multiple pathophysiologic factors associated with acne vulgaris, including targeting *C. acnes* to reduce its proliferation and inflammation.

Once again, "VEHICLES MATTER" !!!

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