More New Therapeutics for Psoriasis

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New treatments for psoriasis constitute an embarrassment of riches compared to any other area of dermatology. Despite the many advances over the last 25 years, additional topical and systemic treatments have recently become available. Gosh, it's great!

In May 2022, once-daily tapinarof cream 1% was approved for the topical treatment of plaque psoriasis in adults.[1] Tapinarof was identified as a metabolite made by bacteria symbiotic to a nematode, allowing the nematode to infect insects.[2] Tapinarof's anti-inflammatory effect extends to mammals. The drug works by activating the aryl hydrocarbon receptor, downregulating proinflammatory cytokines such as IL-17, and normalizing the expression of skin barrier proteins such as filaggrin.[2] In two 12-week, phase 3, randomized trials with 510 and 515 patients, respectively, 35% to 40% of tapinarof-treated psoriasis patients were clear or almost clear compared with only 6% of patients in the placebo group. The drug appears safe; common adverse events (AEs) included folliculitis, nasopharyngitis, contact dermatitis, headache, upper respiratory tract infection, and pruritus.[3]

A second new topical treatment for plaque psoriasis was approved in July 2022—once-daily roflumilast 0.3% cream—for patients 12 years and older.[4] Similar to apremilast, roflumilast is a phosphodiesterase 4 inhibitor that blocks the degradation of cAMP and reduces the downstream production of inflammatory molecules implicated in psoriasis.[5] In two 8-week, phase 3 clinical trials (ClinicalTrials.gov Identifiers NCT04211363 and NCT04211389)(N=881), approximately 40% of roflumilast-treated patients were clear or almost clear vs approximately 6% in the placebo group. Topical roflumilast was well-tolerated; the most common AEs included diarrhea, headache, insomnia, nausea, application-site pain, upper respiratory tract infection, and urinary tract infection.[6]

We have so many patients—and many more people with psoriasis who are not yet patients—with limited psoriasis who would be amenable to topical treatment but who are not responding to current treatments. There is considerable enthusiasm for the new topicals, but it is still questionable how much they will help our patients. The main reason the current topicals fail is poor adherence to the treatment. If we give these new treatments to patients who used existing topicals and failed, thereby inadvertently selecting patients with poor adherence to topicals, it will be surprising if the new treatments live up to expectations. Perhaps tapinarof and roflumilast will revolutionize the management of localized psoriasis; perhaps their impact will be similar to topical crisaborole—exciting in trials and less practical in real life. It may be

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that apremilast, which is now approved for psoriasis of any severity, will make a bigger difference for patients who can access it for limited psoriasis.

Deucravacitinib is a once-daily oral selective tyrosine kinase 2 inhibitor that blocks IL-23 and type I interferon signaling. It was approved for adults with moderate to severe plaque psoriasis in September 2021.[7] We know patients want oral treatment; they ask for apremilast even though injections may be much more potent. In a 16-week, phase 3 clinical trial comparing daily deucravacitinib (n=332), apremilast (n=168), and placebo (n=166), rates of clear or almost clear were approximately 55% in the deucravacitinib group, 32% in the apremilast group, and 7% with placebo. The most common AEs included nasopharyngitis, upper respiratory tract infection, headache, diarrhea, and nausea.[8] Although deucravacitinib is much more effective than apremilast, deucravacitinib will require monitoring and may have some risk for viral reactivation of herpes simplex and zoster (and hopefully not much else). Whether physicians view it as a replacement for apremilast, which requires no laboratory monitoring, remains to be seen.

Bimekizumab, a humanized monoclonal IgG1 antibody expected to receive US Food and Drug Administration approval in the coming months, inhibits both IL-17A and IL-17F and may become our most effective treatment of psoriasis. Although we are probably not hungering for a more effective psoriasis treatment (given our current embarrassment of riches), bimekizumab's remarkably high efficacy for psoriatic arthritis may be a quantum leap forward, especially if no new safety signals are identified; bimekizumab treatment is associated with a higher risk of oral candidiasis than other currently available IL-17 antagonists.[9] Biosimilars may reduce the cost of psoriasis management to the health system, but it seems unlikely that biosimilars will allow us to help patients who we cannot already help with the existing extensive psoriasis treatment armamentarium.

REFERENCES

1. Dermavant announces FDA approval for VTAMA® (Tapinarof) cream. International Psoriasis Council. Published May 26, 2022. Accessed January 10, 2023. https://www.psoriasiscouncil.org/treatment/dermavant-vtama/#:~:text=Dermavant%20Sciences%20announced%20that%20VTAMA,and%20Drug%20Administration%20(FDA)
2. Bissonnette R, Stein Gold L, Rubenstein DS, et al. Tapinarof in the treatment of psoriasis: a review of the unique mechanism of action of a novel therapeutic aryl hydrocarbon receptor-modulating agent [published online November 3, 2020]. *J Am Acad Dermatol*. 2021;84:1059-1067. doi:10.1016/j.jaad.2020.10.085
3. Lebwohl MG, Stein Gold L, Strober B, et al. Phase 3 trials of tapinarof cream for plaque psoriasis. *N Engl J Med*. 2021;385:2219-2229. doi:10.1056/NEJMoa2103629
4. FDA approves Arcutis' ZORYVE™ (Roflumilast) cream 0.3% for the treatment of plaque psoriasis in individuals age 12 and older. News release. Arcutis Biotherapeutics; July 29, 2022. Accessed January 10, 2023. https://www.arcutis.com/fda-approves-arcutis-zoryve-roflumilast-cream-0-3-for-the-treatment-of-plaque-psoriasis-in-individuals-age-12-and-older/
5. Milakovic M, Gooderham MJ. Phosphodiesterase-4 inhibition in psoriasis. *Psoriasis (Auckl)*. 2021;17:11:21-29. doi:10.2147/PTT.S303634
6. Zoryve. Package insert. Arcutis Biotherapeutics; 2022.
7. Hoy SM. Deucravacitinib: first approval. *Drugs*. 2022;82:1671-1679. doi:10.1007/s40265-022-01796-y
8. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88:29-39. doi:10.1016/j.jaad.2022.07.002
9. Freitas E, Blauvelt A, Torres T. Bimekizumab for the treatment of psoriasis [published online October 8, 2021]. *Drugs*. 2021;81:1751-1762. doi:10.1007/s40265-021-01612-z