Tapinarof and the future of topical treatments in plaque psoriasis

To the Editor: With more than 8 million patients affected in the United States, psoriasis represents a serious public health issue with a significant physical, psychological, and economic burden.[1] Super-potent topical steroids are the mainstay treatment of mild to moderate and localized disease; however, they come with a restriction of use limited to 2 to 4 weeks and are not supposed to be applied to facial or intertriginous sites. Other topical treatments, including calcineurin inhibitors, tazarotene, vitamin D_3 analogs or anthralin, are used as alternatives in clinical practice, but with moderate evidence.[1,2] Therefore, an unmet need exists for efficacious topical therapies without restrictions on treatment duration or application sites, including sensitive skin areas.

In the latest issue of the *Journal of the American Academy of Dermatology*, Bissonnette et al[2] tackled this exact problem by presenting the mechanism of action of tapinarof, a novel therapeutic aryl hydrocarbon receptor modulating agent. As stated by the authors, this promising drug has shown positive results in phase 2 studies, leading to the progression to phase 3 clinical trial programs.

During the European Academy of Dermatology and Venereology Congress 2020, the results of both phase 3 trials PSOARING 1 (A Phase 3 Efficacy and Safety Study of Tapinarof for the Treatment of Plaque Psoriasis in Adults; NCT03956355) and PSOARING 2 (NCT03983980) were reported.[3] These 2 identical double-blind and vehicle-controlled randomized studies are designed to assess the efficacy and safety of tapinarof cream, 1% once daily, in patients with mild to severe plaque psoriasis.

On a combined population of 1025 patients, tapinarof cream demonstrated clinical efficacy compared with vehicle, reaching its primary end point of clear to almost clear on the physician global assessment with a $P < .0001$. Psoriasis Area and Severity Index (PASI) improvement superior to 75% was also reached in a statistically significant proportion of patients. Most adverse events were well tolerated, with low rates of treatment discontinuation. Folliculitis and contact dermatitis were most commonly reported.

Another recent phase 3 trial[4] adds more evidence to the issue. In this placebo-controlled trial of 686 patients with mild to moderate plaque psoriasis, twice-daily applied 1% tapinarof was superior to placebo in physician global assessment and PASI improvement. This study also compared tapinarof to calcipotriol. At 12 weeks of treatment, PASI 75 was achieved in 50.4% of patients in the tapinarof group compared with only 38.5% in the calcipotriol group ($P < .05$).

So where do we go from these results? Tapinarof application seems to be effective and well tolerated in mild to severe plaque psoriasis. Next, it would be interesting to see how this new drug will compare to other nonsteroid topical treatments in psoriasis, such as calcineurin inhibitors and tazarotene, to place it in the topical hierarchy. It will also be interesting to see where it will fit next to roflumilast, a potent selective phosphodiesterase-4 inhibitor also emerging in plaque psoriasis treatment, with already positive results from phase 2b trials.[5] But what is certain is that tapinarof can potentially provide physicians with a novel nonsteroidal topical treatment that is highly effective and well tolerated, a much needed therapeutic option for patients with plaque psoriasis.

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Conflicts of interest

None disclosed.

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