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### **Tapinarof cream 1% once daily and benvitimod 1% twice daily are 2 distinct topical medications**

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### Tapinarof cream 1% once daily and benvitimod 1% twice daily are 2 distinct topical medications

*To the Editor:* We thank Assaf et al for their review of the future of topical therapy for plaque psoriasis and share their conclusion that tapinarof, a therapeutic aryl hydrocarbon receptor-modulating agent, has the potential to be a much needed option for the treatment of psoriasis.

We would like to provide a clarification on the key points of difference between tapinarof cream 1% once daily and benvitimod 1% twice daily because Assaf et al inadvertently conflated the aspects of these distinct topical medications that contain the same active component (3,5-dihydroxy-4-isopropyl-trans-stilbene).

Tapinarof cream 1%, acquired by Dermavant Sciences, Inc, from GlaxoSmithKline, comprises a novel vehicle, with specific excipients to enhance efficacy, product delivery, and patient acceptability, resulting in a cosmetically elegant, once-daily, steroid-free cream, which is under clinical development. The benvitimod 1% formulation, which is not licensed to Dermavant Sciences, Inc, includes different excipients (eg, petrolatum) and requires twice-daily dosing, a potentially, clinically relevant adherence barrier. Furthermore, the tapinarof and benvitimod formulations are being investigated in separate clinical trials, with important differences in their designs.

Tapinarof cream 1% once daily has been evaluated in multiple North American centers in 2 phase 2b dose-ranging trials,<sup>1,2</sup> 2 phase 3 pivotal trials (PSOARING 1 and 2),<sup>3</sup> and a long-term extension trial (PSOARING 3).<sup>4</sup> As correctly reported by Assaf et al, tapinarof demonstrated a highly, statistically significant efficacy compared with the vehicle, reaching its primary endpoint ( $P < .0001$ ) in the pivotal phase 3 trials.<sup>3</sup> However, the primary endpoint in PSOARING 1 and 2 was the more stringent US Food and Drug Administration requirement of achieving a physician global assessment (PGA) score of 0 or 1 and at least a 2-grade improvement from baseline rather than a PGA score of 0 or 1 as stated by Assaf et al and as used in the Chinese benvitimod 1% trial.<sup>5</sup>

The pivotal tapinarof and benvitimod trials differ in other important respects. In PSOARING 1 and 2, 1025 patients with mild-to-severe plaque psoriasis were randomized to receive either tapinarof or the vehicle once daily; whereas, in the trial by Cai et al<sup>5</sup> in 2020, 344 patients with mild-to-moderate plaque

psoriasis were randomized to receive benvitimod twice daily.

Moreover, in an interim analysis of PSOARING 3, tapinarof cream 1% once daily demonstrated a remittive effect for approximately 4 months, defined as the maintenance of a PGA score of 0 or 1 (clear or almost clear) while off therapy after achieving complete disease clearance (PGA score of 0).<sup>4</sup> The duration of remittive benefit with tapinarof may actually be  $> 4$  months because the study's end truncated the window of observation. In the benvitimod trial, by contrast, 59 patients achieving a PGA score of 0 or 1 by week 12 were followed up, of whom 29 maintained the resolution at 52 weeks.<sup>5</sup>

In summary, tapinarof cream 1% once daily and benvitimod 1% twice daily are 2 distinct topical medications being assessed in separate clinical trial programs. While the benvitimod trial<sup>5</sup> provides additional confirmation of the clinical potential of the active principle, differences in the formulation and study design mean that direct comparisons between these investigational topical medications and between their clinical data should be made with caution.

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#### Conflicts of interest

Dr Stein Gold is a consultant with honorarium and an investigator for Dermavant Sciences, Inc. Dr Rubenstein is an employee of Dermavant Sciences, Inc, with stock options, and serves on the finance committee of the Society of Investigative Dermatology. Dr Peist is an employee of Dermavant Sciences, Inc, with stock options. Dr Jain is an employee of Dermavant Sciences, Inc, with

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#### REFERENCES

1. Robbins K, Bissonnette R, Maeda-Chubachi T, et al. Phase 2, randomized dose finding study of tapinarof (GSK2894512 cream) for the treatment of plaque psoriasis. *J Am Acad Dermatol*. 2019;80:714-721.
2. Peppers J, Paller AS, Maeda-Chubachi T, et al. A phase 2, randomized dose-finding study of tapinarof (GSK2894512 cream) for the treatment of atopic dermatitis. *J Am Acad Dermatol*. 2019;80:89-98.e3.
3. Lebwohl M, Stein Gold L, Strober B, et al. Tapinarof cream 1% once daily for the treatment of plaque psoriasis: efficacy and safety in two pivotal phase 3 trials. *EADV Virtual*. 2020: D3T03.3D.
4. Dermavant Sciences Inc. Positive data from PSOARING 3 support long-term use of tapinarof cream in adults with plaque psoriasis, with durable (on-therapy) and remittive (off-therapy) benefits. Accessed February 18, 2021. Businesswire.com
5. Cai L, Chen G, Lu Q, et al. A double-blind, randomized, placebo- and positive-controlled phase III trial of 1% benvitimod cream in mild-to-moderate plaque psoriasis. *Chin Med J (Engl)*. 2020;133:2905-2909.

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