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Letter

Oral ponesimod for psoriasis compared to other investigational therapies

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Abstract

Oral ponesimod is a new therapy for the treatment of moderate-to-severe plaque psoriasis. Vaclavkova et al conducted a phase 2 trial that demonstrated moderate efficacy of ponesimod in the treatment of psoriasis. Here we discuss various biologic agents with alternative mechanisms of action, that have demonstrated superior efficacy in psoriasis, and call into question the risks versus benefits of ponesimod therapy.

Keywords: ponesimod, psoriasis

Vaclavkova et al reported the results of a randomized, double-blind, placebo-controlled phase 2 trial of oral ponesimod in psoriasis patients [1]. Of those on ponesimod 20 mg and 40 mg, PASI75 was achieved in 46.0% and 48.1% at week 16, and both were significant compared to placebo ($p < 0.0001$). Ryan et al noted that ponesimod demonstrated lower efficacy than current biologics [2]. It also compared modestly with the biologics on the horizon targeting IL-17. In a phase 3 trial, of those on secukinumab 300 mg and 150 mg, 81.6% and 71.6%, respectively, reached PASI75 at week 12, which was significantly higher compared to placebo ($P < 0.001$ for both groups) [3]. In two phase 3 trials, PASI 75 response rates for those on brodalumab 210 mg and 140 mg were higher than with placebo (86% and 67%, respectively, vs. 8% [AMAGINE-2] and 85% and 69%, respectively, vs. 6% [AMAGINE-3]; $P < 0.001$) [4]. In another set of two phase 3 trials, those on ixekizumab showed similarly high PASI 75 response rates [5].

Investigational biologics targeting IL-23 (guselkumab, tildrakizumab, and BI 655066) showed similarly high efficacy in psoriasis [6-8]. The oral Janus kinase inhibitor tofacitinib had similarly modest efficacy as with ponesimod [9]. While we welcome new therapies with novel mechanisms of action for our psoriatic patients, I wonder how much of an impact a therapy with relatively moderate efficacy but with somewhat worrisome adverse events such as dyspnea (demonstrated to be dose-dependent) [1] may have in patient management.

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