Dermatol Ther (Heidelb)
https://doi.org/10.1007/s13555-024-01137-9

LETTER

Letter to the Editor Regarding: Spesolimab Efficacy and Safety in Patients with Moderate-to-Severe Palmoplantar Pustulosis: A Multicentre, Double-Blind, Randomised, Placebo-Controlled, Phase IIb, Dose-Finding Study

Ruiyao Hu · Yue Wang · Fanzhang Meng · Zhimin Lin · Naigang Chen · Chen Li

Received: January 2, 2024 / Accepted: March 1, 2024

DEAR EDITOR

We read with interest the article by Burden et al. [1] in which these authors report their evaluation of the efficacy of spesolimab in patients with moderate-to-severe palmoplantar pustulosis (PPP). In this study, 152 patients were randomized into five groups, with the patients in four groups receiving different doses of the drug and the patients in one group receiving placebo. The primary efficacy endpoint was the percentage change from baseline in the Palmoplantar Pustule Area and Severity Index (PPP ASI) at 16 weeks. After 16 weeks of treatment, there was no significant change from baseline in this efficacy endpoint between the spesolimab and placebo groups. In addition, compared to the Asian patient population, more people in the non-Asian patient population experienced disease improvement with spesolimab treatment than their counterparts in the placebo group. However, we have a few points that should be discussed.

First, in our opinion, the disease progression of PPP may be somewhat self-limiting, and there may be a tendency for spontaneous improvement of the disease. The results of a few recent efficacy studies of PPP have shown no significant difference in the efficacy assessment between the drug and placebo groups [2]. Could this help to explain the lack of a significant difference in the primary efficacy endpoint in the present study?

Second, infections play a role in influencing the disease progression of PPP. The occurrence and symptoms of PPP are affected by focal infection. A study of 132 patients with PPP found that skin symptoms acutely worsened after patients developed focal infections [3]. The

Ruiyao Hu and Yue Wang contributed equally to this article.

This comment refers to the article available online at https://doi.org/10.1007/s13555-023-01002-1.

R. Hu · C. Li (✉)
Department of Rheumatology, Fangshan Hospital Beijing University of Chinese Medicine, Beijing, China
e-mail: casio1981@163.com

Y. Wang
Beijing University of Chinese Medicine Third Affiliated Hospital, Beijing, China

F. Meng
School of Clinical Medicine, Beijing University of Chinese Medicine, Beijing, China

Z. Lin
Beijing University of Chinese Medicine, Beijing, China

N. Chen
Department of Radiology, Fangshan Hospital Beijing University of Chinese Medicine, Beijing, China

Published online: 09 April 2024

authors of other studies have reported that tonsil infections and dental infections are more common in focal infections [4], and in most patients, the symptoms of PPP improve after the infections are controlled [5]. In their study, Burden et al. [1] did not specify the presence or absence of acute infections in patients when assessing the primary efficacy endpoint, which may have influenced the results.

Third, we know that smoking affects PPP. In a 51-patient study reported by Putra-Szczepaniak et al., the severity of PPP was higher in patients who were addicted to smoking and who smoked pack-years [6]. Thus, it is known that smoking is a factor that can influence the efficacy of the drug, but Burden et al. [1] did not specify the smoking status of the patients.

Finally, Burden et al. [1] mention racial differences in efficacy of drug treatment. The heterogeneity of the clinical features of PPP is dependent on ethnicity and genetics. Mutations in *IL36RN* underlie the genetics of PPP treatment with spesolimab, and there is significant variation in the incidence of *IL36RN* mutations in different regions of the world (range: 5%-70%), and a lower incidence of the *IL36RN* mutation has been observed in patients with PPP [7]. We believe that genetic testing of patients should be prioritized when evaluating the efficacy of spesolimab. Patients with *IL36RN* mutations should be selected for enrolment or be evaluated in subgroups based on the presence of *IL36RN* mutations.

We thank the authors for contributing to the evaluation of the efficacy and safety of spesolimab in patients with moderate to severe PPP through a multicenter, randomized, controlled, double-blind study. We believe that the self-limiting nature of PPP, infection, and smoking are all factors that limit this disease and that their influence should be considered in this clinical trial. Selection of appropriate ethnicity or prioritization of genetic testing at the time of patient enrolment may benefit the efficacy evaluation of spesolimab.

Author Contributions. Ruiyao Hu and Yue Wang prepared the manuscript. All authors critically revised and approved the final manuscript.

Funding. This work was supported by the National Natural Science Foundation of China (No.82074246) for CL and construction project of clinical key specialty in fengtai district of Beijing. No funding or sponsorship was received for this study or publication of this article.

Declarations

Conflict of Interest. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical Approval. None of the full or partial content of the paper has been submitted or published elsewhere.

REFERENCES

1. Burden AD, Bissonnette R, Navarini AA, et al. Spesolimab efficacy and safety in patients with moderate-to-severe palmoplantar pustulosis: a multicentre, double-blind, randomised, placebo-controlled, phase IIb. Dose-Finding Study Dermatol Ther (Heidelb). 2023;13(10):2279–97.

2. Obeid G, Do G, Kirby L, et al. Interventions for chronic palmoplantar pustulosis. Cochrane Database Syst Rev. 2020;1(1):CD011628.

3. Ishibashi A, Nishiyama Y, Endo M, Kawaji W, Kato T. Orthopedic symptoms in pustular bacterid (pustulosis palmaris et plantaris): Tietze's syndrome and arthritis of manubriosternal joint due to focal infection. J Dermatol. 1977;4(2):53–9.

4. Yamamoto T, Hiraiwa T, Tobita R, et al. Characteristics of Japanese patients with pustulotic arthro-osteitis associated with palmoplantar pustulosis: a multicenter study. Int J Dermatol. 2020;59(4):441–4.

5. Misiak-Galazka M, Zozula J, Rudnicka L. Palmoplantar pustulosis: recent advances in etiopathogenesis and emerging treatments. Am J Clin Dermatol. 2020;21(3):355–70.

6. Putra-Szczepaniak M, Reich A, Jankowska-Konsur A, et al. Pack-year cigarette smoking affects the course of palmoplantar pustulosis. Adv Clin Exp Med. 2021;30(2):189–95.

7. Bachelez H. Pustular psoriasis: the dawn of a New Era. Acta Derm Venereol. 2020;100(3):adv00034.