Dr. Li et al reply

To the Editor:

We appreciate Wang et al¹ for their interest in our article² and for highlighting the pathogenic role of cytokine dysregulation in SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome. The authors also address the possible mechanism of secukinumab in the treatment of SAPHO syndrome: blocking the expression of Th17 cell-related cytokines.

There is currently no standardized treatment for SAPHO syndrome.³ Current treatment strategies are not effective for all patients, especially those who do not respond to tumor necrosis factor inhibitor (TNFi) treatment. Studies also reported some SAPHO, psoriasis (PsO), and paradoxical PsO cases with abnormal rashes that occurred during the treatment of TNFi.^{4,5}

Further, Th17 cells and its pathways were considered to be the key pathway in SAPHO syndrome. This mechanism was also supported by our previous findings: the expression of interleukin (IL)-17 in serum and of Th17 cell-related cytokines (IL-17 and IL-23) in bone biopsy was elevated in patients with SAPHO syndrome.^{6,7} Accordingly, IL-17 antagonists have been recognized as a treatment for PsO and psoriatic arthritis (PsA), and have also shown efficacy in palmoplantar pustulosis (PPP). At present, among patients with ankylosing spondylitis, those who were anti-TNF-naïve and who were inadequate responders to anti-TNF can be treated efficiently with anti-IL-17A monoclonal antibody,⁸ and a similar situation has been reported in patients with PsA.⁹ Moreover, Terui et al reported that patients with PPP were efficiently treated by an anti-IL-23 monoclonal antibody.¹⁰ To some extent, SAPHO syndrome can also be regarded as a special subtype of PsA. IL-17 or IL-23 inhibitors can be used to treat SAPHO syndrome, thus suggesting a potential relationship between SAPHO and PsA.

To our knowledge, our study was the first to use magnetic resonance imaging to evaluate the efficiency of secukinumab in the treatment of SAPHO syndrome. Nevertheless, as suggested by Wang et al,¹ this study has some limitations such as the retrospective design, limited sample size, and follow-up period. Further controlled prospective studies with larger sample sizes and extended follow-up periods are needed to confirm the efficacy and safety of IL-17 inhibitors in SAPHO syndrome. A head-to-head comparative trial with TNFi therapy is also required.

Chen Li^{1,2} , MD, PhD
Shaohui Geng³ , MBBS
Shufeng Wei¹, MBBS
Shuwen Guo¹, MD, PhD

¹Department of Rheumatology, Fangshan Hospital, Beijing University of Chinese Medicine;

²Department of Traditional Chinese Medicine, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences;

³School of Life Sciences, Beijing University of Chinese Medicine, Beijing, China.

C. Li and S. Geng contributed equally to this work.

This study was supported by the National Natural Science Foundation of China (81822030), Beijing Natural Science Foundation (7172175), the CAMS Initiative for Innovation Fund for Medical Sciences (CIFMS; 2017-I2M-3-001, 2017-I2M-3-003), the Central Level Public Interest Program for Scientific Research Institute (2018RC31003), the Capital Medical Research and Development Fund (2016-4-40112), and the National Key Research and Development Program of China (2016YFC0901500).

The authors declare no conflicts of interest relevant to this article.

Address correspondence to Dr. C. Li, Department of Rheumatology, Fangshan Hospital, Beijing University of Chinese Medicine, No.4, Chengguan Health Care Road, Fangshan District, Beijing, China; Department of Traditional Chinese Medicine, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, No. 1 Shuaifuyuan, 100730 Beijing, China. Email: casio1981@163.com.

REFERENCES

1. Wang G, Zhuo N, Li Y. Off-label use of secukinumab: a potential therapeutic option for SAPHO syndrome. *J Rheumatol* xxxxxx.
2. Wang L, Sun B, Li C. Clinical and radiological remission of osteoarticular and cutaneous lesions in SAPHO patients treated with secukinumab: a case series. *J Rheumatol* 2021;48:953-5.
3. Liu S, Tang M, Cao Y, Li C. Synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome: review and update. *Ther Adv Musculoskelet Dis* 2020;12:1759720X20912865.
4. Li C, Wu X, Cao Y, et al. Paradoxical skin lesions induced by anti-TNF-alpha agents in SAPHO syndrome. *Clin Rheumatol* 2019;38:53-61.
5. Fania L, Morelli M, Scarponi C, et al. Paradoxical psoriasis induced by TNF-α blockade shows immunological features typical of the early phase of psoriasis development. *J Pathol Clin Res* 2020; 6:55-68.
6. Zhang S, Li C, Zhang SY, et al. Serum levels of proinflammatory, anti-inflammatory cytokines, and RANKL/OPG in synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome. *Mod Rheumatol* 2019;29:523-30.
7. Guo CL, Li C, Han FF, Gao JE, Ma X. Association analysis of interleukin-23 receptor SNPs and SAPHO syndrome in Chinese people. *Int J Rheum Dis* 2019;22:2178-84.
8. Sieper J, Deodhar A, Marzo-Ortega H, et al; MEASURE 2 Study Group. Secukinumab efficacy in anti-TNF-naïve and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the MEASURE 2 study. *Ann Rheum Dis* 2017;76:571-92.
9. McInnes IB, Behrens F, Mease PJ, et al. Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial. *Lancet* 2020;395:1496-505.
10. Terui T, Kobayashi S, Okubo Y, Murakami M, Hirose K, Kubo H. Efficacy and safety of guselkumab, an anti-interleukin 23 monoclonal antibody, for palmoplantar pustulosis a randomized clinical trial. *JAMA Dermatol* 2018;154:309-16.