Response to: 'Off-label use of tofacitinib: a potential treatment option for SAPHO syndrome' by Xie *et al*

We would like to thank Xie *et al*¹ for their interest in our paper² and for their insights into the possible mechanism of action of tofacitinib in synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome and the trend of stratified medicine.

As Xie *et al* highlighted, tofacitinib presented clinical and radiological efficacy in patients with SAPHO syndrome who had an inadequate response to tumour necrosis factor (TNF) inhibitors or bisphosphonates. Similarly, a clinical trial proved that tofacitinib was effective in patients with TNF inhibitor-resistant psoriatic arthritis (PsA).³ By inhibiting the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway, tofacitinib modulates the network of a wide range of inflammatory cytokines, including interleukin-6 (IL-6), IL-17 and TNF- α , which were potentially involved in the pathogenesis of SAPHO syndrome.^{4–10} We speculated that the multipathway inhibitory effect of tofacitinib might contribute to its efficacy in refractory SAPHO syndrome.

The heterogeneity of treatment response also raises the issue of stratified treatment approach in SAPHO syndrome. Clinical and genetic markers have been identified using machine learning to enable prediction of treatment responses to anti-TNF agents in rheumatoid arthritis.¹¹ Furthermore, Miyagawa *et al* proved that strategic treatment based on immunological phenotypes of the individual patient yielded a significant decrease in disease activity compared with routine treatment in PsA.¹² Given the high heterogeneity of SAPHO syndrome, we believe that further efforts in precision medicine may facilitate the understanding and management of the disease.

As mentioned by Xie *et al*, our retrospective study had a limited sample size and follow-up time. It was the first step to demonstrate a new potential treatment for SAPHO syndrome. Future controlled perspective study with a larger sample size and longer follow-up duration is required to establish the efficacy and safety of tofacitinib in SAPHO syndrome.

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Handling editor Josef S Smolen

Contributors YL and YC prepared the manuscript and contributed equally to this article. All the authors have critically revised and approved the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

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To cite Li Y, Cao Y, Li C, *et al*. *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2020-217956

Received 20 May 2020

Accepted 21 May 2020

► <https://doi.org/10.1136/annrheumdis-2020-217956>

Ann Rheum Dis 2020;**0**:1. doi:10.1136/annrheumdis-2020-217956

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REFERENCES

- 1 Wenhui Xie HH, Zhang Z. Off-Label use of tofacitinib: a potential treatment option for SAPHO syndrome. *Ann Rheum Dis* 2020;10.1136/annrheumdis-2020-217854.
- 2 Li Y, Huo J, Cao Y, *et al*. Efficacy of tofacitinib in synovitis, acne, pustulosis, hyperostosis and osteitis syndrome: a pilot study with clinical and MRI evaluation. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217250
- 3 Gladman D, Rigby W, Azevedo VF, *et al*. Tofacitinib for psoriatic arthritis in patients with an inadequate response to TNF inhibitors. *N Engl J Med* 2017;377:1525–36.
- 4 Gao W, McGarry T, Orr C, *et al*. Tofacitinib regulates synovial inflammation in psoriatic arthritis, inhibiting STAT activation and induction of negative feedback inhibitors. *Ann Rheum Dis* 2016;75:311–5.
- 5 Rosengren S, Corr M, Firestein GS, *et al*. The JAK inhibitor CP-690,550 (tofacitinib) inhibits TNF-induced chemokine expression in fibroblast-like synoviocytes: autocrine role of type I interferon. *Ann Rheum Dis* 2012;71:440–7.
- 6 Maeshima K, Yamaoka K, Kubo S, *et al*. The JAK inhibitor tofacitinib regulates synovitis through inhibition of interferon- γ and interleukin-17 production by human CD4+ T cells. *Arthritis Rheum* 2012;64:1790–8.
- 7 Daoussis D, Konstantopoulou G, Kraniotis P, *et al*. Biologics in SAPHO syndrome: a systematic review. *Semin Arthritis Rheum* 2019;48:618–25.
- 8 Firinu D, Barca MP, Lorrain MM, *et al*. TH17 cells are increased in the peripheral blood of patients with SAPHO syndrome. *Autoimmunity* 2014;47:389–94.
- 9 Hurtado-Nedelec M, Chollet-Martin S, Nicaise-Roland P, *et al*. Characterization of the immune response in the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome. *Rheumatology* 2008;47:1160–7.
- 10 Zhang S, Li C, Zhang S, *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.
- 11 Guan Y, Zhang H, Quang D, *et al*. Machine learning to predict anti-tumor necrosis factor drug responses of rheumatoid arthritis patients by integrating clinical and genetic markers. *Arthritis Rheumatol* 2019;71:1987–96.
- 12 Miyagawa I, Nakayama S, Nakano K, *et al*. Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in psoriatic arthritis. *Rheumatology* 2019;58:336–44.