Response to: 'Correspondence on 'A pilot study of tofacitinib for refractory Behçet's syndrome" by Zou *et al*

We thank Zou and colleagues for their interests and insightful comments[1] on our recently published work[2] and are impressed by the encouraging results of tofacitinib on patients with refractory Behçet's uveitis (BU).

In this study, 5 mg two times per day tofacitinib was given to active patients with BU with prednisone reduced from 50 to 60 mg per day to 30 mg per day and withdrawal of conventional immunosuppressants (cyclosporine A or tacrolimus), which lead to treatment 'success' and 'flare' in 10 (76.9%) and 3 (23.1%) of the 13 included patients, respectively. Moreover, all the 10 patients responded to tofacitinib discontinued corticosteroid during a follow-up period between 24 and 38 months. This study provides preliminary evidence that tofacitinib might be a promising treatment for refractory BU. A minor disadvantage is that the authors did not evaluate the fundus based on a standard scoring system.[3]

While there is evidence that Janus kinase (JAK)-mediated pathways are activated in active Behçet's syndrome (BS),[4] our study revealed that different phenotypes of BS responded variably to tofacitinib, which suggest that the role of tofacitinib in various BS phenotypes should be addressed individually due to the complexity and heterogeneity of BS.[2] Studies on intraocular inflammatory markers revealed significantly increased levels of interleukin (IL)-2, IL-8, IL-13, tumor necrosis factor α (TNFα), eotaxin and IL-1ra in aqueous humour samples from patients with BU.[5] Tofacitinib is a small molecule pan-JAK inhibitor, it is reasonable to infer that tofacitinib can cross the blood-ocular barriers easily to exert its anti-inflammatory effects in the eye by inhibiting multiple cytokine pathways.

Several studies have reported the effectiveness of JAK inhibitors in treating non-infectious uveitis. In a mouse model of experimental autoimmune uveitis, tofacitinib significantly suppressed secretion of IFN-γ and development of disease.[6] In a retrospective clinical study, juvenile idiopathic arthritis (JIA) cases refractory to at least two biological agents (including TNFα blockers, tocilizumab, rituximab and abatacept) responded to baricitinib 4 mg/day (n=3) and tofacitinib 10 mg/day (n=1).[7] Tofacitinib was also reported to be effective in an adult JIA patient with anterior uveitis and macular edema,[8] a patient with scleritis and a patient with anterior and intermediate uveitis.[9]

Currently, a few ongoing clinical trials are evaluating the role of JAK inhibitors for non-infectious uveitis (NCT03580343, NCT04088409 and NCT03207815) but none exclusively addresses BU. Thus, future studies are expected to delineate the efficacy and safety profiles of different JAK inhibitors for refractory BU, which is indeed a devastating condition for both patients and physicians.

Jinjing Liu ,[1] **Chan Zhao**,[2] **Wenjie Zheng** [1]

[1]Department of Rheumatology and Clinical Immunology, Key Laboratory of Rheumatology and Clinical Rheumatology, Ministry of Education, National Clinical Research Center for Dermatologic and Immunologic Diseases, State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
[2]Department of Ophthalmology, Peking Union Medical College Hospital, Key Laboratory of Ocular Fundus Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Correspondence to Professor Wenjie Zheng, Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing 100730, China; wenjzheng@gmail.com

Handling editor Josef S Smolen

Contributors All authors equally contributed to the writing of the manuscript. CZ and WZ are the corresponding authors.

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, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Liu J, Zhao C, Zheng W. *Ann Rheum Dis* 2023;**82**:e101.

Received 5 January 2021
Revised 8 January 2021
Accepted 8 January 2021
Published Online First 25 January 2021

Linked

► https://doi.org/10.1136/annrheumdis-2020-219810

Ann Rheum Dis 2023;**82**:e101. doi:10.1136/annrheumdis-2020-219828

ORCID iDs
Jinjing Liu http://orcid.org/0000-0003-2150-7540
Wenjie Zheng http://orcid.org/0000-0002-3165-8185

REFERENCES

1 Zou J, Lin C-H, Wang Y. Correspondence on 'A pilot study of tofacitinib for refractory Behçet's syndrome". *Ann Rheum Dis* 2023;82:e100.
2 Liu J, Hou Y, Sun L, *et al*. A pilot study of tofacitinib for refractory Behçet's syndrome. *Ann Rheum Dis* 2020;79:1517–20.
3 Tanaka R, Murata H, Takamoto M, *et al*. Behçet's disease ocular attack score 24 and visual outcome in patients with Behçet's disease. *Br J Ophthalmol* 2016;100:990–4.
4 Tulunay A, Dozmorov MG, Ture-Ozdemir F, *et al*. Activation of the JAK/STAT pathway in Behcet's disease. *Genes Immun* 2015;16:170–5.
5 Bonacini M, Soriano A, Cimino L, *et al*. Cytokine profiling in aqueous humor samples from patients with non-infectious uveitis associated with systemic inflammatory diseases. *Front Immunol* 2020;11:358.
6 Bing SJ, Lyu C, Xu B, *et al*. Tofacitinib inhibits the development of experimental autoimmune uveitis and reduces the proportions of Th1 but not of Th17 cells. *Mol Vis* 2020;26:641–51.
7 Miserocchi E, Giuffrè C, Cornalba M, *et al*. JAK inhibitors in refractory juvenile idiopathic arthritis-associated uveitis. *Clin Rheumatol* 2020;39:847–51.
8 Bauermann P, Heiligenhaus A, Heinz C. Effect of Janus kinase inhibitor treatment on anterior uveitis and associated macular edema in an adult patient with juvenile idiopathic arthritis. *Ocul Immunol Inflamm* 2019;27:1232–4.
9 Paley MA, Karacal H, Rao PK, *et al*. Tofacitinib for refractory uveitis and scleritis. *Am J Ophthalmol Case Rep* 2019;13:53–5.