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 comments¹ on our recently published work² 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 (TNF α), 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 TNF α 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.

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