

Response to: 'Tofacitinib for the treatment of polyarteritis nodosa: a literature review' by Akiyama *et al*

We appreciate the interest of Akiyama *et al* in our report and thank them for the data presented in their letter.^{1,2} Akiyama *et al* have presented a thorough literature review and have described a positive and efficacious effect of tocilizumab in 11 cases of refractory polyarteritis nodosa (PAN) described in 6 case series. Indeed, the use of tocilizumab, an interleukin (IL)-6 inhibitor, in vasculitis is gaining evidence in the literature, specifically in large vessel vasculitis including giant cell arteritis and Takayasu arteritis.^{3,4} Nevertheless, it should be noted that although the IL-6 pathway is the major inducer of STAT 3, and therefore was used by us *in vitro* to stimulate this pathway in order to evaluate STAT 3 activation, clinically blocking the IL-6 pathway in our patient, using tocilizumab, was not beneficial, contrasting with our positive result with tofacitinib. We hypothesised that redundancy or other stimulators of the STAT 3 pathway like IL-23 may explain this discrepancy. Furthermore, we did not find tocilizumab clinically or radiologically beneficial in another patient with severe refractory PAN involving skin and coronary arteries—evidenced by positron emission tomography-CT scan revealing active inflammation in an aneurism within a coronary artery and by MRI demonstrating active deep skin involvement while under treatment with tocilizumab (unpublished data).

Thus, in considering the review by Akiyama *et al*, publication bias should always be considered when evaluating case reports, as we all tend to prefer publishing our positive experience.

Recently, we have also reported our positive experience with another agent, infliximab, for refractory PAN and reviewed the literature.⁵ The ever-expanding spectrum of biological treatments is confusing for the practitioner and although case reports and case series are important to guide us in rare refractory patients, we should still follow guidelines and use evidence-based treatments that were evaluated in large randomised controlled clinical trials as first-line therapy.

New technologies may help us diagnose and treat refractory patients. Whole-exome sequencing studies may reveal novel mimickers, the monogenic vasculitides, as deficiency of adenosine deaminase 2, stimulator of interferon genes-associated vasculopathy with onset in infancy, and haploinsufficiency of A20 that should be considered in refractory cases. Finally, precision medicine, as we suggested in our report, may guide us in the future, helping us to find the right fit for each patient.^{6,7}

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