Response to: 'Aortic ulceratio in a tocilizumab-treated patient with Takayasu arteritis' by Liebling *et al*

I thank Liebling and colleagues for their interest in our manuscript[1] and for sharing their experience with a patient with refractory Takayasu arteritis who developed aortic ulceration while on tocilizumab therapy.[2] Our first multicentre, randomised, double-blind, placebo-controlled study (the TAKT study) showed a favourable effect for tocilizumab over placebo in patients with refractory Takayasu arteritis. As shown in online supplementary figure S1 of our manuscript,[1] the study included patients who did not respond to conventional or biologic disease-modifying antirheumatic drugs, similar to the patient reported by Liebling *et al*. The data from an open-label extension of this study, the largest prospective clinical trial in patients with Takayasu arteritis, showed the steroid-sparing effect of tocilizumab when the glucocorticoid dose was tapered based on the disease activity of the patient.[3] The difference in the exposure-adjusted relapse rate between the double-blind period in which glucocorticoid was mandatorily tapered (203.1 events per 100 patient-years in the placebo group and 101.1 events per 100 patient-years in the tocilizumab group) and the open-label extension period (23.6 events per 100 patient-years) highlights the importance of the glucocorticoid dose reduction rate for the management of this disease, as was previously reported by Ohigashi *et al*.[4] While it is not clearly described in their recent letter, the difference in the speed of glucocorticoid dose tapering while this patient was receiving tocilizumab and other biologics might have influenced her clinical course.

Several reports have indicated that progression of aortic structural damage in patients with Takayasu arteritis may occur without clinical symptoms or elevated inflammatory markers.[5 6] Both clinical assessment and serial imaging tests are important for monitoring patients with Takayasu arteritis, especially when receiving tocilizumab as it suppresses the clinical symptoms and normalises acute-phase reactants. In our TAKT study, radiographic progression was observed in some patients while they were receiving tocilizumab with glucocorticoid tapering. It should be noted, therefore, that once radiographic progression is detected, then therapy modification including an increase in glucocorticoid dose or addition of immunosuppressant therapy should be considered in order to prevent further structural remodelling even if there are no signs of relapse.

Finally, the treatment options remain uncertain for patients with Takayasu arteritis who have inadequate responses to the current therapies. Needless to say, some patients with Takayasu arteritis may have an inadequate response to tocilizumab and may benefit from switching to other biologics. As the evidence for the efficacy and safety of the treatments for Takayasu arteritis is currently limited, the evidence-based treatment algorithm for patients with Takayasu arteritis will need to be further explored in the future.

Yoshikazu Nakaoka

Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute, Suita, Osaka, Japan

Correspondence to Yoshikazu Nakaoka, Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute, Suita, Osaka 565-8565, Japan; ynakaoka@ncvc.go.jp

Handling editor Josef S Smolen

Contributors YN wrote the response to the eLetter.

Competing interests YN reports personal fees from Chugai as a consultant for the sponsor-initiated clinical trial (Chugai Pharmaceutical Co., Ltd.) using tocilizumab for Takayasu arteritis; grants and personal fees from Chugai; grants and personal fees from Astellas, Pfizer, AbbVie and MSD outside the submitted work; grants from Takeda, Otsuka and Bayer; and personal fees from Daiichi Sankyo and Kowa Pharmaceutical Co. outside the submitted work.

Patient consent Obtained.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Nakaoka Y. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2018-214239

Received 7 September 2018
Accepted 7 September 2018

Linked

► http://dx.doi.org/10.1136/annrheumdis-2018-214191

Ann Rheum Dis 2018;**0**:1. doi:10.1136/annrheumdis-2018-214239

REFERENCES

1 Nakaoka Y, Isobe M, Takei S, *et al*. Efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis: results from a randomised, double-blind, placebo-controlled, phase 3 trial in Japan (the TAKT study). *Ann Rheum Dis* 2018;77:348–54.
2 Liebling EJ, Peterson R, Victoria T, *et al*. Aortic ulceration in a tocilizumab-treated patient with Takayasu arteritis. *Ann Rheum Dis* 2018. doi: 10.1136/annrheumdis-2018-214191. [Epub ahead of print: 27 Aug 2018].
3 Nakaoka Y, Isobe M, Takei S. Long-term efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis treated continuously over 52 weeks: results from phase 3, randomized, double-blind, placebo-controlled trial and open-label extension in Japan. *Arthritis Rheumatol* 2017;69(Suppl 10).
4 Ohigashi H, Haraguchi G, Konishi M, *et al*. Improved prognosis of Takayasu arteritis over the past decade—comprehensive analysis of 106 patients. *Circ J* 2012;76:1004–11.
5 Paul JF, Fiessinger JN, Sapoval M, *et al*. Follow-up electron beam CT for the management of early phase Takayasu arteritis. *J Comput Assist Tomogr* 2001;25:924–31.
6 Freitas DS, Camargo CZ, Mariz HA, *et al*. Takayasu arteritis: assessment of response to medical therapy based on clinical activity criteria and imaging techniques. *Rheumatol Int* 2012;32:703–9.