Response to: 'Neuroinflammatory events after anti-TNF α therapy' by Kaltsonoudis *et al*

First of all, we would like to thank Dr Kaltsonoudis *et al* for their interest in our study. Dr Kaltsonoudis *et al*¹ have raised an interesting suggestion in their correspondence based on their study from 2014.² They suggest that all patients who are candidates for tumour necrosis factor alpha inhibitor (TNFi) therapy should have a thorough neurological assessment (including brain MRI and neurophysiological tests) before commencing TNFi treatment. Moreover, they believe that the risk of neuroinflammatory events following treatment with TNFis is not disease-dependent, but agent-dependent, and that part of the observed risks following treatment may in fact be present already at treatment start.

In our large observational study,³ we excluded all patients recorded with a hospital contact with a neuroinflammatory diagnosis prior to study entry eliminating patients with existing neuroinflammatory disease that had reached clinical attention. However, as Dr Kaltsonoudis *et al* argue, we do not know whether some of the patients had a clinically asymptomatic neuroinflammatory disease at time of entry (that is, prior to TNFi treatment start) which may have been aggravated by TNFi use.

In clinical practice, patients with rheumatological disease starting on TNFi treatment are not currently examined for a possible asymptomatic inflammatory neurological disease. In order to do so, we think that additional studies are warranted to evaluate the costs and benefits of such an intervention.

With regards to the risk of neuroinflammatory events being disease- or drug-dependent, we believe that the results from our large study, similar in the two countries under study, are robust and point to the notion that the risk is disease-dependent, although we did not specifically investigate whether there is any interaction between the treated disease and the type of TNFi used to treat it. The hypothesis of disease-specific risks is further supported by studies finding opposite risks for multiple sclerosis among patients with psoriatic arthritis⁴ and rheumatoid arthritis.⁵

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