Response to 'Correspondence on 'Comparative effectiveness of first-line tumour necrosis factor inhibitor versus non-tumour necrosis factor inhibitor biologics and targeted synthetic agents in patients with rheumatoid arthritis: results from a large US registry study' by Zheng *et al*

We thank Zheng *et al*¹ for their interest in our study² and for providing constructive comments. They mention that even though the baseline mean Clinical Disease Activity Index (CDAI) was not statistically different, the proportion of patients with moderate or high disease at baseline was different and this could have been a key effect modifier.¹

We used standardised differences to evaluate variables at baseline. Calculation of the standardised difference not only accounts for the means of the two cohorts, but also the SD. We noticed that continuous CDAI was balanced across the two therapy classes (as listed in the manuscript table 1, SD=−0.015)² and similarly observed for categorical CDAI (low/moderate/high; SD=0.0515; results not shown in the manuscript). Furthermore, in the postmatched population, continuous CDAI remained well balanced (manuscript table 1: SD=−0.0256)² as did the categorical CDAI measure (SD=0.0658; results not shown). Thus, we do not believe that baseline CDAI distribution could have influenced the observed results.

Zheng *et al* further point out that the proportions of patients receiving conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) as monotherapy, dual therapy or triple therapy in the two groups during the 1-year follow-up visit were not specified and that residual confounders, such as smoking status, baseline haemoglobin levels and dosage of csDMARDs used, could exist.¹

In our study, coexisting csDMARD use was considered only at baseline, but not during follow-up.² Prior csDMARD use was also evaluated. Changes in concurrent DMARD therapy over the follow-up period were not evaluated. This is a limitation of the study, but the findings of a non-significant difference could be interpreted in the context that rheumatologists could modify concurrent therapy in real-life study settings. The study allows for changes in therapy and does not claim that final results were not statistically different with stable concurrent therapy. Smoking and baseline anaemia were considered as effect modifiers and were not found to be significantly associated with the outcome as described in the 'Determination of effect modifiers' section of the Methods.²

Although uncommon, some rheumatologists prescribe anakinra. We believe that the small number of patients on anakinra (14 patients among thousands in the 2 cohorts) did not affect the findings and would not alter the results if removed from the analysis.

Thank you for pointing out the mistakes and typos, we will work with the journal to proceed with a correction.

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