

## Response to: 'COVID-19 in patients with rheumatological diseases treated with Anti-TNF' by Brito *et al* and 'Clinical characteristics and outcomes of patients with COVID-19 and rheumatic disease in China 'hot spot' versus in US 'hot spot': similarities and differences' by Zhao *et al*

We appreciate the comments by Brito *et al*,<sup>1</sup> and Zhao *et al*,<sup>2</sup> in response to our manuscript evaluating outcomes among a cohort of patients with rheumatic diseases and COVID-19.<sup>3</sup> We were interested to read the reports of their patients during the COVID-19 pandemic and would like to reply to some of their queries.

Brito *et al* raised the important point that the risk of severe infections may vary with therapeutic class of immunosuppressive therapy. We agree that further studies are needed to assess this important question, and we plan to investigate this by therapeutic class for our cohort in future studies as our sample size grows. We agree that studies of therapeutic class will have to account for potential confounding factors, including glucocorticoid exposure, in their design. A recent report performed among patients with rheumatic diseases suggested lower odds of hospitalised infection for biological/targeted disease-modifying anti-rheumatic drugs (DMARDs) and higher odds for glucocorticoid use.<sup>4</sup> However, adjustment for immunosuppressive medication use is not possible when comparing patients with rheumatic disease to those without rheumatic disease who would not be expected to use these medications. While we await additional studies, we support the American College of Rheumatology's recommendations for management of rheumatic diseases during the pandemic, which do not recommend preemptively discontinuing immunosuppression.<sup>5</sup>

Brito *et al* also reported on three patients who did well clinically after developing COVID-19 while maintaining treatment with tumour necrosis factor (TNF) inhibitors for rheumatic disease. It is unclear how these cases of COVID-19 were identified. Given the small sample size, high variability in COVID-19 presentations (ie, many patients in a general population experience only mild illness), possibility of reporting bias (ie, clinicians may have been more likely to see patients with more mild symptoms in clinic) and lack of a comparison group, further studies will be needed to determine the relationship of TNF inhibitors to severe outcomes in COVID-19.

Zhao *et al* described a cohort of 29 patients with rheumatic diseases from Wuhan, China, the first epicentre of the COVID-19 pandemic. Compared with findings in our study, they observed a lower rate of mechanical ventilation (2/29 (7%) in theirs vs 7/52 (14%) in ours). As they suggest, these differences may be related to differences between the two cohorts, including the distribution of age, rheumatic diseases, comorbidities, race/ethnicity and regional variations in the management of rheumatic disease and COVID-19. However, another recent investigation from Wuhan, China showed that the rate of mechanical ventilation was 38% in patients with rheumatic disease versus 10% in patients with non-rheumatic disease, a statistically significant difference and similar to our findings.<sup>6</sup>

As investigators report their experience with COVID-19 in patients with rheumatic diseases from around the world, we believe it is important for all to report the proportions of patients on conventional, biological and targeted synthetic DMARD,

prior to the development of COVID-19. This information will help readers understand the generalisability of each study's observations to their patients. In the context of a growing body of literature suggesting that hydroxychloroquine may not have efficacy in COVID-19,<sup>7-9</sup> we would urge caution with regards to interpreting a protective effect from hydroxychloroquine based on the favourable outcomes of five patients with unknown COVID-19 disease severity. We await final data from ongoing randomised controlled trials evaluating the safety and efficacy of hydroxychloroquine in COVID-19.

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**Correction notice** This article has been corrected since it published Online First. The title and reference 2 have both been corrected.

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