

Clinical course and outcome of COVID-19 in patients with rheumatic diseases: are all biological disease-modifying antirheumatic drugs alike? Response to: 'Increased risk for severe COVID-19 in patients with inflammatory rheumatic diseases treated with rituximab' by Schulze-Koops *et al*

We appreciated the comment from Schulze-Koops *et al*¹ in response to our paper on the clinical course and outcome of COVID-19 in a cohort of patients treated with biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).² The authors stated that the message conveyed by our report or other similar observational data or clinical studies is potentially harmful for patients with rheumatic diseases who might think they are protected against complications of COVID-19 by their immunomodulatory drug. Nevertheless, in our publication, we clearly stated that our findings did not allow any conclusions on the overall outcome of immunocompromised patients affected by COVID-19 and that a high level of vigilance and strict follow-up should be maintained on these susceptible patients. Moreover, our findings supported the observation that patients with chronic arthritis treated with the reported b/tsDMARDs described in our cohort (therefore excluding rituximab) did not seem to be at increased risk of severe complications compared with the general population, which does not imply that they would be protected against the virus and that patients should reduce hygiene precautions and social distancing in a highly lethal condition even in the general population.

According to our report and further evidence accumulating since the pandemic outbreak confirming similar risks of incidence and complications between immunocompromised patients with rheumatic diseases and the general population, it seems reasonable to suggest that preventive withdrawal of bDMARDs in the absence of ongoing infections should be avoided as this would expose our patients to the risk of disease relapses.^{3,4}

Nevertheless, we agree with Schulze-Koops that the available evidence should be interpreted critically and that evidence supporting the relative safety of one class of bDMARDs should not be inferred to all types of biologics or to different diseases treated with the same drug. Particularly, rituximab, by its long-term action on the humoral response might indeed impair the ability of the subject to effectively recover from COVID-19. The evidence regarding outcomes of patients with rheumatic diseases contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection while receiving treatment with rituximab is controversial.^{5,6} We had previously commented on a correspondence supporting the favourable outcome of COVID-19 in a patient with granulomatosis with polyangiitis treated with rituximab by discussing the uncertainty existing around the effects that immunosuppressive agents with different mechanisms of action might play on SARS-CoV-2 infection.⁶ While it is hypothesised that some bDMARDs might not contribute to a worsening of the clinical course of these patients, or might even attenuate its severity in the context of an aberrant inflammatory cytokine production triggered by SARS-CoV-2, other treatments, especially those acting on B-cells and antibody production might turn out to be particularly detrimental.

In conclusion, despite some reassuring observational evidence, until data from large cohorts and controlled studies become available, high vigilance and caution should always be applied when managing our patients with chronic rheumatic conditions.

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