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## Authors' reply to the comment "Treatment considerations for patients with pemphigus during the COVID-19 pandemic"



*To the Editor:* We read with interest the thoughtful reply by Schultz et al to our previous correspondence regarding treatment considerations for patients with pemphigus during the coronavirus disease 2019 (COVID-19) pandemic.<sup>1</sup> There is established agreement about the need to use caution when approaching iatrogenic immunosuppression, as is usually required in the management of pemphigus. Early in the pandemic, we had suggested postponing rituximab infusions when feasible, given the temporarily irreversible nature of B-cell depletion caused by rituximab, as well as the unknown effect of rituximab on susceptibility to and severity of infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Similar recommendations were made by Kasperkiewicz et al.<sup>2</sup> Given that rituximab administration generally requires patients to attend a medical center, avoidance of this setting, particularly at the peak of the pandemic, would lessen the burden on health care systems and minimize mutual potential SARS-CoV-2 exposures at health care settings. Similarly, Kasperkiewicz et al<sup>2</sup> speculated that rituximab could worsen severity of COVID-19, with this effect lasting for up to 1 year after administration.

It has since become clear that in some countries, such as the United States, the COVID-19 pandemic is unlikely to abate in the near future, thus raising concern about the feasibility of continuing to postpone rituximab infusions. Fortunately, recent evidence has demonstrated that B-cell depletion may not affect the outcome in patients who develop COVID-19, perhaps because T cells play a major role in immunity against SARS-CoV-2.<sup>3</sup> Published data from Italy showed that in a cohort of 371 patients with pemphigus, only 3 developed confirmed-positive COVID-19, and all recovered. Of the 12 patients in the study who had received rituximab, none had developed COVID-19.<sup>4</sup> Although this preliminary report offers some reassurance, additional prospective experience will be necessary to fully understand the effect of rituximab in patients with pemphigus who develop COVID-19.

Concern has been raised about rituximab potentially diminishing the immunologic response to the COVID-19 vaccine because it is known that patients receiving rituximab may have blunted immunoresponse to the vaccine that may persist for 6 to

12 months after rituximab infusions.<sup>3</sup> It remains to be seen how rituximab may affect immunoresponse to any future COVID-19 vaccine.

Given the well-demonstrated efficacy of rituximab in pemphigus, resuming this medication may be reasonable in patients without active COVID-19 infection, particularly if COVID-19 incidence is low in the patient's area. In patients with active pemphigus and COVID-19, systemic glucocorticoids at the lowest possible dose may be preferred, particularly given the promising results of dexamethasone in severe COVID-19 because of its anti-inflammatory effect against lung damage driven by the cytokine storm.<sup>5</sup> Screening for SARS-CoV-2 infection by polymerase chain reaction before infusion of rituximab may also be a prudent practice to adopt. Patients must be counseled on basic infection-prevention principles, such as mask wearing, hand washing, and social distancing.

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