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## Reply to “Treatment considerations for patients with pemphigus during the COVID-19 pandemic”



*To the Editor:* We read with interest the letter by Shakshouk et al, “Treatment Considerations for Patients With Pemphigus During the COVID-19 Pandemic.”<sup>1</sup> We agree with careful consideration of treatment for patients with pemphigus during this unprecedented pandemic. Rather than delaying all rituximab infusions, however, we advocate that rituximab be discussed and considered individually through shared decision making. In particular, rituximab should be considered for patients with severe disease and without active coronavirus disease 2019 (COVID-19) illness after discussion of specific individual-level risks (age, comorbidities, and occupation) and benefits of rituximab. We would also consider rituximab for younger patients without comorbidities and with less severe disease.

First, rituximab is an effective and targeted therapy for pemphigus. We have limited data directly comparing adverse events in patients treated with rituximab versus other therapies, but compared with prednisone alone, rituximab plus short-term prednisone resulted in decreased cumulative exposure to prednisone and fewer adverse effects,<sup>2</sup> including known risk factors for COVID-19<sup>3</sup>: diabetes mellitus requiring insulin and major weight gain. Because of its superior efficacy, as well as uncertainty about pandemic length and time to develop an effective vaccine, rituximab has the potential to result in better patient outcomes while reducing cumulative immunosuppression throughout the pandemic.

Second, the risk of COVID-19 infection and its associated outcomes after rituximab treatment is concerning but unknown. Although this represents only a single case, 1 patient with granulomatosis with polyangiitis who developed COVID-19 1 month after rituximab treatment and while receiving low-dose prednisone and methotrexate had a full recovery.<sup>4</sup> Furthermore, rituximab may be protective against severe COVID-19 infection because antiviral IgG has been shown to induce severe lung injury in COVID-19 illness and patients treated with rituximab may be less able to develop antiviral IgG, as in the above-mentioned case.<sup>4</sup> Additionally, T-cell response to viral antigens can still occur after rituximab treatment.<sup>4</sup>

Conversely, physicians should discuss that rituximab may reduce immunoresponse to vaccination,<sup>5</sup> which may decrease the ability of patients to effectively receive a COVID-19 vaccine. The

response to vaccination appears to improve when given 6 months or more after rituximab dosing.<sup>5</sup> Immunoresponse to infection itself may similarly be blunted, theoretically leading to risk of reinfection.

In summary, we agree with careful consideration of rituximab for patients during the COVID-19 pandemic. However, with an unknown peak of COVID-19, it may not be feasible or beneficial to delay rituximab. On an individualized basis through shared decision making, dermatologists should consider rituximab for select patients. Our approach is to discuss rituximab for patients with severe disease who might otherwise require high doses of prednisone or more broadly immunosuppressive agents over an extended period, and for those with less severe disease but fewer comorbidities and younger age. Rheumatologic dosing of rituximab, rather than hematologic, can be considered to decrease health care exposures, and we would recommend against maintenance dosing in stable patients for whom the risk of disease flare is deemed low.<sup>2</sup> Before rituximab is used, we recommend discussing vaccination concerns and general infection control guidance, including social distancing, frequent hand washing, and use of masks.

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