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SARS-CoV-2 immune responses in B cell depleted patients with autoimmune disease

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We thank Dr. Niu and colleagues for the remark that chronic glucocorticoid treatment increases the susceptibility for COVID-19 and decreases the response to vaccination (1). The authors therefore asked for a potential effect of concomitant glucocorticoid therapy on blunted vaccination responses in rituximab-treated patients with autoimmune disease. It is known since the 1970s that glucocorticoids reduce T cell (2,3) and B cell (4,5) activation and thereby inhibit mounting of adaptive immune responses against infections.

When interrogating whether background glucocorticoid treatment could have added to reduced immune responses to vaccinations or infection with the severe acute respiratory syndrome coronavirus- 2 (SARS-CoV-2), we found no major exposure to glucocorticoid treatment in this cohort. Thus, only three patients (one vaccinated and two infected) were on concomitant glucocorticoid treatment. Furthermore, doses of glucocorticoids were low (mean ±SD dose: 4.6 ±3.8 mg prednisolone/day). Hence, it is unlikely the background glucocorticoids were responsible for the impaired immune response to vaccination for and infection with SARS-CoV-2.

Another potential source of glucocorticoids in this context is their administration in combination with the rituximab infusion. This attributes to a single shot of 25 mg prednisolone together with the rituximab infusion. Previous data from patients with shock (6) and asthma attacks (7,8), in which short-term systemic bolus glucocorticoids are also frequently used, have not shown any effect of such treatment on vaccination responses to tetanus (6) and influenza (7,8). Short-term glucocorticoid treatment also does not seem to reveal any effect on the immune response to the SARS-CoV-2 vaccine (9). Therefore, one

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cannot assume that such single dose of glucocorticoids significantly contributes to the observed blunted humoral immune responses to SARS-CoV-2 in rituximab-treated patients.

The observation that T cell responses are maintained, while B cell responses are severely suppressed in rituximab-treated patients with autoimmune diseases, supports a specific effect of B cell depleting agents rather than an effect of glucocorticoids that would also impair T cell activation. These findings and the comments raised by Dr. Niu and colleagues, however, also suggest that continuous higher doses of glucocorticoids may be problematic in B cell depleted patients, as immune responses to infection and avccinations largely depend on intact T cell responses if B cell are absent.

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