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Comment on "An evidence-based guide to SARS-CoV-2 vaccination of patients on immunotherapies in dermatology"

To the Editor: We read with great interest the article by Gresham et al[1] summarizing the influence of immunotherapies used in dermatology on vaccine-induced immunity. We believe that a more in-depth discussion of rituximab and mycophenolate mofetil is crucial, as both drugs specifically act on B lymphocytes. The literature indicates that these treatments are associated with increased impairments of vaccine-induced responses compared to other immunomodulating/immunosuppressive therapies used in dermatology.[2]

The article by Gresham et al[1] cites a study conducted on patients with autoimmune blistering disorders as evidence that rituximab does not affect the humoral response to seasonal influenza vaccination.[3] However, this study recruited only patients who received their last rituximab dose more than 5 months before vaccination (median, 11 months). This time point was deliberately chosen as B lymphocytes start to recover after 5-6 months. In patients receiving rituximab, vaccination responses and the formation of neutralizing antibodies are blunted until naive B cells reappear. Decreased antibody titers for pneumococcal, tetanus, and influenza vaccines have been confirmed following rituximab administration. Therefore, this study cannot be used as evidence that vaccine-induced protection will be adequate in patients receiving rituximab for skin disorders, especially if the vaccine was given earlier than 5 months after the last rituximab dose. Substantial data have confirmed that vaccination should be administered preferably 6 months after the last rituximab dose. The authors reference another study that led to the conclusion that there is "no significant effect of rituximab on humoral response to yellow fever vaccination." However, this study included only 3 patients on rituximab (3/31) and one of them had the lowest antibody titer of all included patients.[4] Therefore, we believe that no conclusion can be made about the humoral response to yellow fever vaccination based on this study. For systemic immunotherapeutics, the evidence seems to point to a slightly different risk profile as mentioned in the conclusion of the paper since data indicate that rituximab and mycophenolate mofetil carry a higher propensity for reducing antibody levels compared to methotrexate, Janus kinase (JAK) inhibitors, and systemic corticoids (Fig 1).

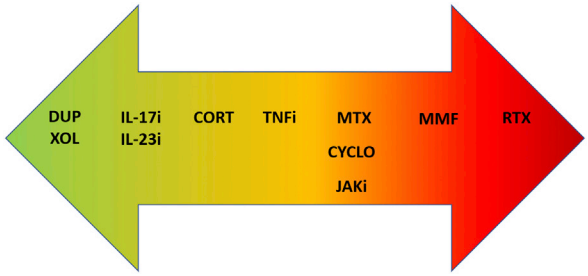

Fig 1. Ranking of the vaccine-induced immune responses from excellent (*green*) to impaired (*red*). *CORT*, Corticoids (prednisone <20 mg); *CYCLO*, cyclosporine; *DUP*, dupilumab; *IL-17i*, interleukin-17 inhibitor; *IL-23i*, interleukin-23 inhibitor; *JAKi*, janus kinase inhibitor; *MMF*, mycophenolate mofetil; *MTX*, methotrexate; *RTX*, rituximab; *TNFi*, tumor-necrosis factor-α inhibitor; *XOL*, Xolair.

The authors correctly mention that, although diminished, satisfactory immune responses to vaccination are reached in most JAK inhibitor-treated patients. The authors recommend temporarily withdrawing the drug 2-3 weeks before vaccination; however, it is unclear if this approach is effective. Only 1 cited paper mentions withdrawal of JAK inhibitors and temporary discontinuation did not improve vaccine-induced response rates to pneumococcal polysaccharide vaccine (continuous vs withdrawal; 75.0% vs 84.6%, respectively) or influenza (66.3% vs 63.7%, respectively).[5] As most patients were also receiving methotrexate and the subgroup of patients treated with JAK inhibitors alone was relatively small, there may be effects on T cell responses that were not captured by these data. Nonetheless, there is little evidence to recommend the temporary withdrawal of JAK inhibitors before SARS-CoV-2 vaccination.

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Conflicts of interest

None disclosed.

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