Response to: 'Correspondence on 'SARS-CoV-2 vaccination in rituximab-treated patients: evidence for impaired humoral but inducible cellular immune response" by Westhoff *et al*

We have read the correspondence of Westhoff *et al* to our article[1] with great interest. The authors confirm our finding of an impaired humoral immune response in rituximab-treated patients by showing that also their rituximab treated patients did not develop antibodies to the SARS-CoV-2 spike protein after two doses of SARS-CoV-2 vaccinations with BNT162b2.[2] In line with our data, the authors provide evidence for a maintained cellular immune response in rituximab-treated patients. In addition, Westhoff *et al* could quantify the presence of a CD4 and CD8 T cell response in 78% and 43% of the rituximab-treated patients, respectively. The finding of a dissociated humoral and cellular immune response is adding an important piece to the understanding of the scope of secondary immunodeficiency induced by rituximab. Nevertheless, this specific scientific field is strongly driven by questions about clinical relevance, and it remains not sufficiently clear what leg of the immune system is essential for successfully fighting a SARS-CoV-2 infection. However, to date, the clinical relevance of these findings remain elusive, as large vaccination studies with clinical endpoints for this patient population are challenging and quite unlikely, even in the currently very active research field.

For now, given the uncertainty on these details, the conclusion for patients on rituximab treatment can only be that vaccination is not without potentially protective effects, even if antibodies cannot be detected. Future studies would need to investigate what level of B cell repopulation is necessary to also achieve a humoral immune response to vaccination, and whether such response may be elicited, even in the absence of such repopulation, through an additional boost vaccination.

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2 Bonelli MM, Mrak D, Perkmann T. SARS-CoV-2 vaccination in rituximab-treated patients: evidence for impaired humoral but inducible cellular immune response. *Ann Rheum Dis* 2021;80:1352–3.