Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Comment on: "SARS CoV-2 vaccine AND rituximab, timing is probably a key for a better vaccine response" by Verhoeven et al. *Joint Bone Spine* 2021;88:105258

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Verhoeven et al. contributed to the open issue of the COVID-19 vaccine response in patients receiving rituximab by describing the first case of infection occurring after vaccination [1]. In that case, the course of COVID-19 was benign even the humoral response was weak.

Indeed, the level of protection by vaccination due to T-cell response in the absence of antispike antibody response is the main issue for patients undergoing B-cell depleting therapies [2]. However, it is still unknown whether SARS-CoV-2 vaccination provides protection against severe COVID-19 in patients undergoing persistent B-cell depletion.

In this context, recently, we have followed a patient who was infected by SARS-CoV-2 two months after exposure to rituximab and five months after the second dose of mRNA BNT162b2 vaccine.

She was a 69-year-old woman suffering from dermatomyositis. She was treated with rituximab 1 gram two weeks apart in June 2019, and then in January 2020 and in July 2020 for recurrent cutaneous manifestations. Patient was given BNT162b2 vaccine doses on April 1 and 28, 2021. At the time of vaccination, CD19+ B-cells were still undetectable and serum levels of IgG were 641 mg/dL. Both at four weeks and 12 weeks after the second dose of vaccine, antibodies (IgG + IgM + IgA) against the receptor-binding domain of the Spike glycoprotein were absent (Elecsys anti-SARS-CoV-2 S ECLIA, total anti-SARS-CoV-2 antibodies < 0.4 U/mL; positivity cut off > 0.79 U/mL).

In July 2021, she received a single dose of 500 mg of rituximab. The CD19+ B-cell count before rituximab was 25/uL and the total IgG levels 659 mg/dL. On 9th September the patient resulted positive for COVID-19 on the nasopharyngeal molecular test PCR.. The patient complained of only mild symptoms, such as anosmia, ageusia and rhinitis. The molecular test resulted negative fourteen days from the first one.

Five weeks after COVID-19 infection, both humoral and cell-mediated responses were evaluated, the latter by measuring interferon-gamma (IFN-gamma) released upon SARS-CoV-2 Spike 1 antigen stimulation (IGRA test, Euroimmun). Anti-SARS-CoV-2 antibodies were still absent (< 0–4 U/mL), while cell-mediated response was detectable (IFN-gamma cellular response 259.0 pg/mL, IFN-gamma mitogen control 499 pg/mL, IFN-gamma negative control 4–6 pg/mL).

Therefore, our report increases the knowledge regarding the SARS-CoV-2 infection in fully vaccinated patients with a rheumatic condition, since in the present case B-cell depletion persisted at the time of vaccination, even if the last infusion of rituximab had been administered eight months before, and the humoral response was absent. Though the observed cell-mediated response could be only due to the infection, mRNA vaccine for SARS-CoV-2 could similarly elicit cell-mediated response which might protect patients against severe COVID-19, independently from B-cell recovery [3–5]. Anyway, vaccination for SARS-CoV-2 infection in rituximab recipients should be encouraged at any time, if rituximab cannot be delayed for clinical reason.

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Disclosure of interest

The authors declare that they have no competing interest.

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