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.

COVID-19 vaccination in patients with immune-mediated inflammatory diseases receiving rituximab: A personalized regimen should be formulated

To the Editor: We read with great interest the retrospective matched cohort study from Massachusetts by Pahalyants et al.[1] The authors presented the data of 7361 patients with immune-mediated inflammatory diseases (IMIDs) treated with immunosuppressive biologics and 74,910 matched controls and found that a diagnosis of the SARS-CoV-2 infection was less likely in the patients receiving tumor necrosis factor inhibitors than in the matched controls; whereas, overall, biologics did not increase the risk of a positive COVID-19 diagnosis, adjusting for demographics, comorbidity burden, and local infection rates. According to the patient baseline characteristics listed in Table I of the study by Pahalyants et al,[1] the proportions of the prescribed biologics were tumor necrosis factor inhibitors 55.9%, CD20-directed antibody (rituximab) 15.6%, and interleukin 4A inhibitor 8.6%. We hypothesize that Pahlyants et al1 underestimated the risk of COVID-19 among patients treated with rituximab given the lower proportion of rituximab usage reported and potential alterations in behavior among patients with IMIDs to decrease their risk of SARS-CoV-2 infection.

The accumulation of evidence from recent literature has emphasized that rituximab could largely blunt the humoral immune response to vaccines and confer an additional susceptibility to COVID-19 in patients with IMIDs. In recent clinical surveys from Europe, it was shown that only 39% of rituximab-treated patients develop antibodies against the SARS-CoV-2 receptor-binding domain after the second vaccination[2]; furthermore, rituximab was associated with a 2.28-fold increase in the risk of SARS-CoV-2 infection. However, because T-cell–mediated immune response after COVID-19 vaccination was detected in 58% of rituximab-treated patients even in the absence of circulating B cells (<1%),[2] the COVID-19 vaccine may also have sufficient efficacy in protecting rituximab-treated patients from SARS-CoV-2 infection.

Distinct from the general population, a personalized vaccination strategy should be formulated to augment the immunogenicity of COVID-19 vaccination in rituximab-treated patients. First, COVID-19 vaccine should be preferably administered prior to rituximab treatment; otherwise, the rationale for the timing of the initial COVID-19 vaccine may be at least 6 months after rituximab treatment, and a longer interval usually indicates a higher seropositivity rate. Fifty-six percent of patients with IMIDs vaccinated 1 year after rituximab treatment were seropositive.[3] Second, peripheral $CD19^+$ and $CD4^+$ lymphocyte counts serve as predictive markers for the immunogenicity of COVID-19 vaccination. The RituxiVac study by Moor et al[3] revealed that the optimal cutoffs, allowing a positive immune response to the COVID-19 vaccine, were more than 27 $CD19^+$ cells/μL and more than 653 $CD4^+$ cells/μL in rituximab-treated patients. Third, a booster dose of COVID-19 vaccine should be recommended to rituximab-treated patients to aid in the generation of an immune response. Kant et al[4] found that a third/booster dose could give a positive response in 7 of 15 patients at 1 month after rituximab treatment. Fourth, heterologous messenger RNA (mRNA)/vector vaccination regimens should be attempted in rituximab-treated patients because its better response has been confirmed by several recent studies in healthy individuals as compared with homologous mRNA/mRNA or vector/vector regimens. Simon et al[5] administered a third dose of vaccine to 66 patients with IMIDs who did not respond to 2 doses of COVID-19 vaccine and showed that patients receiving the heterologous mRNA/vector regimens exhibited a 15% increase in seropositivity rate, relative to those maintaining the homologous mRNA/mRNA regimens (55% vs 40%).

In addition, the latest vaccine recommendations and guidelines from the Centers for Disease Control and Prevention have recommended that the patients with IMIDs who were treated by the other immunosuppressive agents should receive the third dose at or more than 28 days after the completion of their 2-dose mRNA COVID-19 vaccine series (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#considerations-covid19-vax-immunocopromised).

Qian Yang, MD, Qi Jiang, MD, Man Man Niu, MD, Guo Zhen Fan, MD, and Peng Hu, MD, PhD

From the Department of Pediatrics, the First Affiliated Hospital of Anhui Medical University, Hefei, People's Republic of China.

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Correspondence to: Peng Hu, MD, PhD, Department of Pediatrics, the First Affiliated Hospital of Anhui

Medical University, No. 218 Ji-Xi Road, Hefei, Anhui Province, 230022, People's Republic of China

E-mail: hupeng28@aliyun.com

Conflicts of interest

None disclosed.

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