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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Messenger RNA vaccines and neutralizing anti–severe acute respiratory syndrome coronavirus 2 antibodies in patients with immunodeficiency

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We would like to share our ideas on the article entitled "Detection of neutralizing anti–severe acute respiratory syndrome coronavirus 2 antibodies in patients with common variable immunodeficiency after immunization with messenger RNA vaccines."[1] Romano et al[1] concluded that "CVID patients must be included in COVID-19 vaccination programs because of the ability of mRNA vaccines to safely induce production of neutralizing antibodies in this category of patients." Given that Romano et al[1] noted that the production of neutralizing antibodies did not mean protection, it is, therefore, necessary to have further studies for confirmation on the advantage of vaccines. Whether the messenger RNA (mRNA) can result in unwanted immunologic problems in a common variable immunodeficiency (CVID) case is also another important question. An association between CVID and autoimmunity was proposed.[2,3] There are many reports on the possible association between mRNA COVID-19 vaccine and autoimmunity generation.[4] A careful risk and benefit evaluation is needed for making any recommendation on using the mRNA COVID-19 vaccine among CVID cases.

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Authors' response

We understand the concerns expressed by Drs Mungmunpuntipantip and Wiwanitkit regarding the efficacy and safety of messenger (m)RNA vaccines in patients with common variable immunodeficiency (CVID); however, we still strongly stick to the conclusions expressed in our report.[1] With regard to efficacy, the aim of our study was to evaluate whether patients with CVID could generate neutralizing antibodies against severe acute respiratory syndrome coronavirus 2, and all but 1 actually did.[1] Clearly, as already mentioned in the article, evaluation of the clinical significance of these antibodies (ie, protection against severe manifestations of coronavirus disease 2019 [COVID-19] and death) requires further studies.[1] Nevertheless, it should not be overlooked that vaccine-induced cell-mediated immunity may as well contribute to vaccination efficacy.[2] Therefore, prediction of vaccination efficacy should not be solely anticipated on the basis of antispike antibody titers. Long-term adverse effects of COVID-19 vaccination are unknown across all categories of subjects being immunized; conversely, short-term adverse effects are generally mild and easily managed.[3,4] Our patients with CVID have been followed up for more than 6 months since having completed the 2-dosage mRNA vaccine schedule, and none of them have developed or had flare-ups of autoimmune or other long-term inflammatory conditions; other studies have reported reassuring safety data as well.[2,5,6] Furthermore, patients with rheumatologic diseases who have a myriad of autoimmune conditions have been thus far safely vaccinated with mRNA vaccines, with no apparent impact on disease activity and no further safety concerns in the short term.[7,8] Severe adverse events, albeit rare, may nonetheless occur after vaccination, regardless of preexisting medical conditions. In any case, caution should be exercised in interpreting flare-ups of autoimmune diseases

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in patients with rheumatologic diseases and, likewise, development of denovo autoimmune conditions in patients with CVID several months after vaccination, as they may be because of the natural history of the specific disease rather than to delayed, unwanted adverse effects of mRNA vaccination.

Patients with primary immunodeficiency, including CVID, are at increased risk from acute and long-term sequelae of COVID-19. At the moment, accumulating evidence points to a favorable benefit to risk ratio for COVID-19 vaccination even in such frail subjects as patients with CVID, who must thus be given the opportunity to be protected against the most dreaded manifestations of severe acute respiratory syndrome coronavirus 2 infection.

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