RESPONSE TO COMMENT ON D'ADDIO ET AL.

Immunogenicity and Safety of SARS-CoV-2 mRNA Vaccines in a Cohort of Patients With Type 1 Diabetes. Diabetes 2022;71:1800–1806

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We would like to thank Dr. Sookaromdee and Dr. Wiwanitkit for their interest in our article (1) that was recently published in *Diabetes* and for their important comment (2). In our study we demonstrated that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccines are safe for patients with type 1 diabetes (T1D) and that these patients develop a humoral response to vaccination comparable to that observed in a group of control subjects without diabetes. Conversely, we showed that T-cell immune response, particularly cytotoxic response, is altered in patients with T1D after vaccination, with the release of cytotoxic factors perforin and granzyme A being reduced when cells were rechallenged in vitro with SARS-CoV-2 peptides. In their comment, Sookaromdee and Wiwanitkit pointed out that asymptomatic coronavirus disease 2019 (COVID-19) infection may have occurred during vaccination and potentially represents a confounding factor for immunological analysis (2). We agree that it is important to rule out the presence of asymptomatic COVID-19 infection in our study population. Indeed, in our first screening, patients who tested positive for COVID-19 within the previous 3 months or had active COVID-19, with symptoms of or positive swab test for SARS-CoV-2, were excluded from the study. More importantly, patients who tested seropositive at baseline before receiving the first dose of SARS-CoV-2 mRNA vaccine due to an asymptomatic SARS-CoV-2 infection or showed baseline IgG value of $\geq$1.0 were grouped separately, as reported in Supplementary Fig. 3 in our article (1), and were excluded from the immunological studies. This applied to patients with T1D and to control subjects without diabetes, who were also interrogated at baseline about any recent swab test result when the health safety report was completed. Therefore, patients with or without T1D and included in the immune T-cell studies were all seronegative for SARS-CoV-2 at baseline, so the chance of asymptomatic COVID-19 in this group was significantly low, although we cannot exclude the development of the disease during the immunization period. We can thus conclude that although asymptomatic infection with SARS-CoV-2 may occur in the context of vaccination and could represent a limitation, our study design allowed us to demonstrate an altered immune response toward SARS-CoV2 mRNA vaccines in patients with T1D.

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References

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