T cell and Antibody Response after two Doses of the BNT162b2 Vaccine in a Belgian Cohort of Kidney Transplant Recipients.

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Abbreviations:

Ab, antibody

Interferon-gamma (IFN-ϒ)

KTRs, kidney transplant recipients

Disappointing results in the humoral response after anti-SARS-CoV-2 vaccination in kidney transplant recipients (KTRs) have emerged from the literature.[1,2] In this context, exploring SARS-CoV-2-specific cellular response induced by vaccination is relevant.

We prospectively assessed the antibody (Ab) (with an immunoassay detecting Ab against the spike protein receptor-binding domain (RBD) [Elecsys anti-SARS-CoV-2, Roche Diagnostics GmbH, Mannheim, Germany - positive threshold >0.8 U/mL, upper limit of detection 250 U/mL]) and T cell response (with a whole blood interferon-gamma (IFN-ϒ) release assay (IGRA) using the antigens of the SARS-CoV-2 spike protein to activate T cells, following manufacturer's instructions [SARS-CoV-2 IGRA, Euroimmun, Lübeck, Germany- positive threshold >100 mIU/mL]) rates one month after the second dose of the mRNA BNT162b2 vaccine (Pfizer-BioNTech), between April 17th 2021 and June 15th 2021, in a single-center cohort of KTRs. All patients signed informed consent and the study received IRB approval (B4032021000056).

Ninety KTRs were included [median age: 60 (ranges 38-79) years, 48% female, and median time since transplantation: 102 (ranges 9-440) months]. Fifty-one percent of patients were treated with an association of tacrolimus (Tac), mycophenolate (MPA) and steroids (St), and 24% received an antimetabolite-free regimen. Seven had a previous history of documented SARS-CoV-2 infection before vaccination.

One month after the second vaccine dose, 58 (64.4%) KTRs mounted a humoral response [mean (±SEM) anti-RBD Ab titer: 70.2 (±11.9) U/mL], and 29 (32.2%) displayed a cellular response (positive IGRA test) [mean (±SEM) IFN-ϒ value: 803.4 (±165.1) mUI/mL]. Overall, 22 (24%) KTRs had both humoral and cellular responses, 7 (8%) had isolated cellular response, 36 (40%) had isolated humoral response, and 25 (28%) had no immune response.

The cellular response rate and IFN-ϒ values were not significantly different between Ab responders and Ab non-responders (Figure 1A). However, KTRs displaying high Ab response (anti-RBD Ab titer >150 U/mL) had significantly higher cellular response rate and IFN-ϒ values compared to KTRs with weaker-or no-Ab response (Figure 1A and 1B). Correlation between IFN-ϒ and Ab values (Figure 1C) was statistically significant ($r=0.666$, $p<0.001$, Pearson correlation test).

Reports on the T-cell response rate after anti-SARS-CoV-2 vaccination in KTRs are limited. Bertrand et al found a 57.8% T-cell response rate in 26 KTRs after two doses of the BNT162b2 vaccine, using an ELISpot immunoassay.[3] Cucchiari et al reported a 54.7% rate after the second dose of the mRNA-1273 vaccine in 117 SARS-CoV-2 naïve transplant patients, also using an ELISpot immunoassay.[4] We found a lower rate (32%) that might be explained by the differences in sensitivity of the ELISpot test compared to IGRA ELISA as reported for the detection of latent tuberculosis infection.[5]

Interestingly, we found that 20% of Ab non-responders have a T-cell response and 72% of KTRs showed either IFN-ϒ and/or Ab response. Moreover, KTRs with higher Ab response are more likely to develop a T-cell response. In that context, a third vaccine dose might help boost both cellular and serological response. Larger studies are needed to characterize the cellular response and its clinical relevance.

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Legend to Figure

Figure 1 : A. Cellular response rate in the cohort. The cellular response rate was not significantly different between patients with antibody response and without antibody response (p=0.138, Chi-squared test). However, among patients with humoral response, those with high antibody response (anti-RBD titers >150 U/mL) showed higher rates of cellular response compared to others (p<0.001, Chi-squared test). B. IFN-ϒ values (mIU/mL) and antibody titers. Patients with antibody titers >150 U/mL had higher IFN-ϒ values than others (p=0.049, Kruskal-Wallis test). C. Correlation between anti-RBD antibody titers and IFN-ϒ values (r=0.666, p<0.001, Pearson correlation test).

Abbreviations: IFN-ϒ, interferon-gamma; RBD, receptor-binding domain