

# T-cell and Antibody Response After 2 Doses of the BNT162b2 Vaccine in a Belgian Cohort of Kidney Transplant Recipients

Arnaud Devresse, PhD,<sup>1</sup> Imane Saad Albichr, PharmD,<sup>2</sup> H el ene Georgery, MD,<sup>1</sup> Jean Cyr Yombi, MD,<sup>3</sup> Julien De Greef, MD,<sup>3</sup> Leila Belkhir, PhD,<sup>3</sup> Samy Mzougui,<sup>2</sup> Anais Scohy, PharmD,<sup>2</sup> Tom Darius, PhD,<sup>4</sup> Antoine Buemi, MD,<sup>4</sup> Eric Goffin, MD,<sup>1</sup> Benoit Kabamba, PhD,<sup>2</sup> and Nada Kanaan, MD<sup>1</sup>

Disappointing results in the humoral response after anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination in kidney transplant recipients (KTRs) have emerged from the literature.<sup>1,2</sup> 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 and upper limit of detection 250 U/mL]) and T-cell response (with a whole blood interferon-gamma [IFN- $\gamma$ ] 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, L ubeck, Germany—positive threshold >100 mIU/mL]) rates 1 mo after the second dose of the mRNA BNT162b2 vaccine (Pfizer-BioNTech), between April 17, 2021 and June 15, 2021, in a single-center cohort of KTRs. All patients signed informed consent and

the study received institutional review board approval (B4032021000056).

Ninety KTRs were included (median age: 60 [range, 38–79] y, 48% female individual, and median time since transplantation: 102 [range, 9–440] mo). Fifty-one percent of patients were treated with an association of tacrolimus, mycophenolate, and steroids, 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 [ $\pm$ SEM] anti-RBD Ab titer: 70.2 [ $\pm$ 11.9] U/mL) and 29 (32.2%) displayed a cellular response (positive IGRA test) (mean [ $\pm$ SEM] IFN- $\gamma$  value: 803.4 [ $\pm$ 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- $\gamma$  values were not significantly different between Ab responders and Ab nonresponders (Figure 1A). However, KTRs displaying high Ab response (anti-RBD Ab titer >150 U/mL) had significantly higher cellular response rate and IFN- $\gamma$  values compared with KTRs with a weaker-or no-Ab response (Figure 1A and B). Correlation between IFN- $\gamma$  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<sup>3</sup> found a 57.8% T-cell response rate in 26 KTRs after 2 doses of the BNT162b2 vaccine, using an ELISpot immunoassay. Cucchiari et al<sup>4</sup> reported a 54.7% rate after the second dose of the mRNA-1273 vaccine in 117 SARS-CoV-2 naive transplant patients, also using an ELISpot immunoassay. We found a lower rate (32%) that might be explained by the differences in sensitivity of the ELISpot test compared with IGRA ELISA as reported for the detection of latent tuberculosis infection.<sup>5</sup>

Interestingly, we found that 20% of Ab nonresponders have a T-cell response and 72% of KTRs showed either IFN- $\gamma$  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 responses. Larger studies are needed to characterize the cellular response and its clinical relevance.

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<sup>1</sup> Department of Nephrology, Saint Luc University Clinics, Brussels, Belgium.

<sup>2</sup> Department of Microbiology, Saint Luc University Clinics, Brussels, Belgium.

<sup>3</sup> Department of Internal Medicine and Infectious Disease, Saint Luc University Clinics, Brussels, Belgium.

<sup>4</sup> Department of Abdominal Surgery and Kidney Transplantation, Saint Luc University Clinics, Brussels, Belgium.

A.D., I.S.A., and H.G. are cofirst authors.

B.K. and N.K. are cosenior authors.

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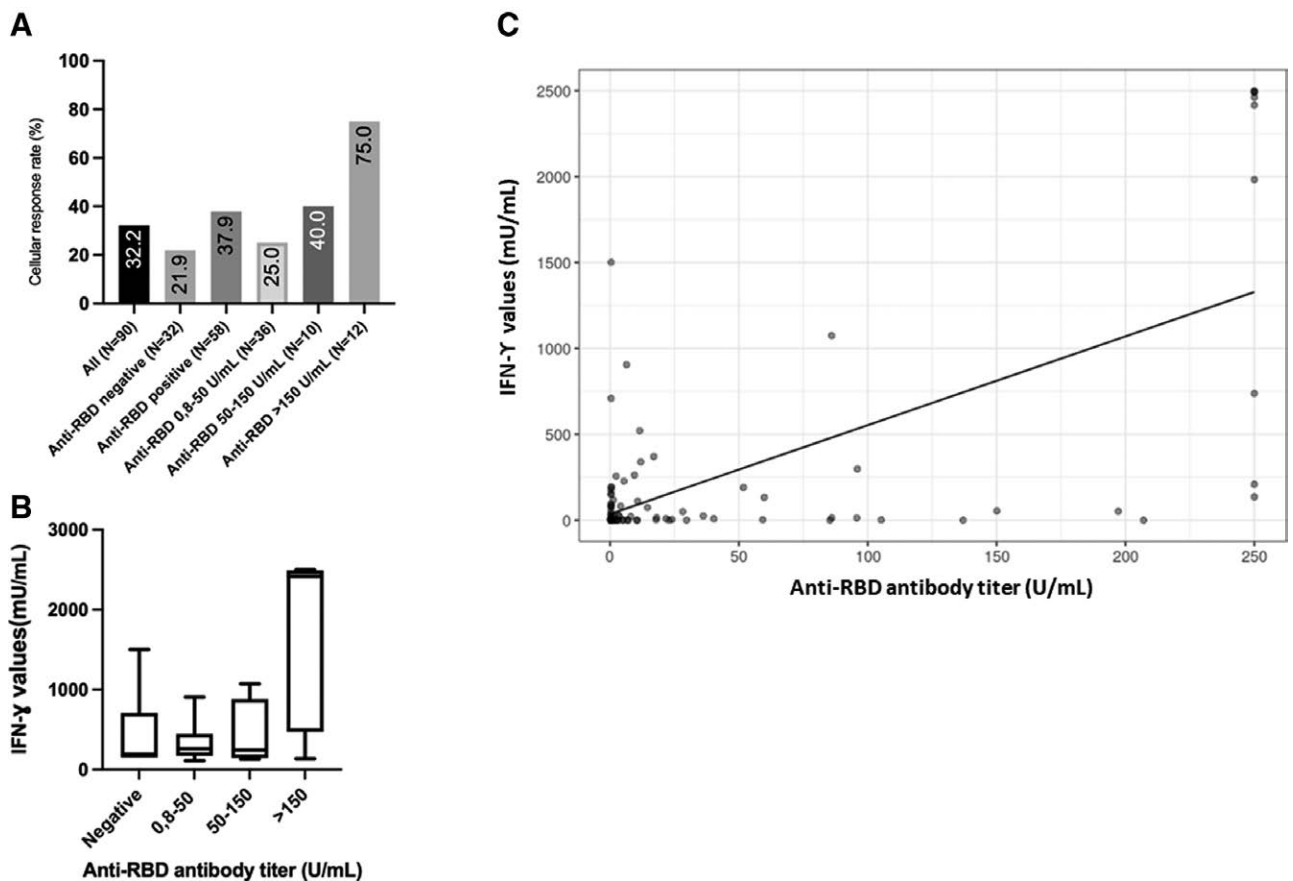
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Correspondence: Arnaud Devresse, PhD, Department of Nephrology, Cliniques Universitaires Saint-Luc, Avenue Hippocrate, 10, 1200 Brussels, Belgium. (arnaud.devresse@uclouvain.be).

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**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 ( $P=0.138$ ,  $\chi^2$  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 with others ( $P<0.001$ ,  $\chi^2$  test). B, IFN- $\gamma$  values (mIU/mL) and antibody titers. Patients with antibody titers  $>150$  U/mL had higher IFN- $\gamma$  values than others ( $P=0.049$ , Kruskal-Wallis test). C, Correlation between anti-RBD antibody titers and IFN- $\gamma$  values ( $r = 0.666$ ,  $P<0.001$ , Pearson correlation test). IFN- $\gamma$ , interferon-gamma; RBD, receptor-binding domain.

## REFERENCES

- Georgery H, Devresse A, Yombi JC, et al. Disappointing immunization rate after two doses of the BNT162b2 vaccine in a Belgian cohort of kidney transplant recipients. *Transplantation*. [Epub ahead of print. June 24, 2021]. doi:10.1097/TP.0000000000003861
- Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA*. 2021;325:2204–2206.
- Bertrand D, Hamzaoui M, Lemée V, et al. Antibody and T cell response to SARS-CoV-2 messenger RNA BNT162b2 vaccine in kidney transplant recipients and hemodialysis patients. *J Am Soc Nephrol*. 2021;32:2147–2152.
- Cucchiari D, Egri N, Bodro M, et al. Cellular and humoral response after mRNA-1273 SARS-CoV-2 vaccine in kidney transplant recipients. *Am J Transplant*. 2021;21:2727–2739.
- Lange C, Mori T. Advances in the diagnosis of tuberculosis. *Respirology*. 2010;15:220–240.