Clinical Kidney Journal, 2022, vol. 15, no. 4, 820–821

https://doi.org/10.1093/ckj/sfac010
Advance Access Publication Date: 13 January 2022
Letter to the Editor

LETTER TO THE EDITOR

Humoral and T-cell response to SARS-CoV-2 mRNA BNT162b2 vaccination in a cohort of kidney transplant recipients and their cohabitant living kidney donor partners

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with a high rate of mortality in kidney transplant recipients (KTRs) [1]. The current vaccine strategy for KTRs appears not to provide effective protection against coronavirus disease 2019 (COVID-19) [2] and the occurrence of severe COVID-19 in some vaccinated KTRs may suggest a lack of immunity [3].

At this time, one way to protect KTRs might be to vaccinate their immediate family members, especially their spouses. However, it is not known how effective the SARS-CoV-2 vaccine is in the cohabitants of KTRs.

We prospectively investigated KTRs and their respective cohabitant living kidney donor partners (LKDPs) who were vaccinated with two doses of the Pfizer-BioNTech messenger RNA (mRNA) BNT162b2 (Comirnaty) vaccine. Criteria for exclusion were as follows: divorced or not closely cohabiting couples and anti-SARS-CoV-2 immunoglobulin G (IgG) titer above the positivity threshold (>15 AU/mL) at administration of the first dose of vaccine.

This study was approved by the local ethics committee. After written informed consent, between 22 March and 16 April 2021, on the same days, KTRs and their cohabitant LKDPs were vaccinated with two doses of Pfizer-BioNTech mRNA BNT162b2 SARS-CoV-2 vaccine 21 days apart.

The humoral immune response was assessed at the time of administration of the first and second vaccine dose and then 1 and 3 months after the administration of the second vaccine dose. Cellular immunity was assessed 3 months after administration of the second vaccine dose.

Sera of all KTRs and LKDPs were tested using the Liaison® assay (DiaSorin, Saluggia, Italy), detecting IgG against two spike glycoprotein (S1 and S2) antigens. A concentration of SARS-CoV-2 S1/S2 IgG <12 AU/mL is considered negative, a concentration between 12 and 15 AU/mL is considered uncertain and a concentration >15 AU/mL is considered positive.

As far as cellular immunity response is concerned, spike-specific $CD4^+$ and $CD8^+$ T-cell responses were quantified in the circulation of the KTRs and LKDPs using the QuantiFERON SARS-CoV2 test (Qiagen, Venlo, The Netherlands), a commercially available interferon γ (INF-$_\gamma$) releasing assay (IGRA); according to the manufacturer, a concentration of INF-$_\gamma$ ≥0.15–0.20 IU/mL is considered positive.

A total of 18 KTRs (females 44%, age 59 ± 8 years) and their respective cohabitant LKDPs (females 56%, age 59 ± 8 years) were included in the study (Table 1).

At administration of the first vaccine dose, all KTRs {3.8 AU/mL [interquartile range (IQR) 3.8–4.2]} and all LKDPs [3.8 AU/mL (IQR 3.8–4.0)] had an anti-SARS-CoV-2 IgG titer below the threshold for positivity (15 AU/mL).

At the administration of the second dose of vaccine, only one KTR had an anti-SARS-Cov-2 IgG titer (55.8 AU/mL) above the

Received: 29.12.2021; Editorial decision: 10.1.2022

Table 1. Characteristics and humoral and cellular response after mRNA BNT162b2 vaccination of KTRs and their respective cohabitant LKDPs

Characteristics	KTRs	LKDPs	*p*
Male:female	11:8	8:11	0.3
Age (years), mean ± SD	59 ± 8	59 ± 8	0.9
Primitive kidney disease, *n* (%)			
ADPKD	8 (45)	-	-
Glomerulonephritis	4 (22)	-	-
Other	6 (33)	-	-
Time from transplantation (months), mean ± SD	68 ± 33	-	-
Immunosuppressive therapy, *n* (%)			
Steroids	16 (89)	-	-
CNI	18 (100)	-	-
MMF	16 (89)	-	-
MTORi	2 (11)	-	-
IgG anti-SARS-CoV-2 (S1 and S2) (AU/mL), median (IQR)			
At first vaccine dose administration	3.8 (3.8–4.2)	3.8 (3.8–4.0)	0.6
At second vaccine dose administration	3.8 (3.8–5.2)	56.7 (40.1–71.4)	<0.005
1 month after second vaccine dose	4.5 (3.8–29.3)	226.5 (146.3–302.3)	<0.0001
3 months after second vaccine dose	3.8 (3.8–16.2)	156.0 (93.0–318.3)	<0.0001
$CD4^+$ T-cell INF-$_\gamma$ (IU/mL)	0.01 (0–0.04)	0.31 (0.14–0.64)	<0.0005
$CD4^+/CD8^+$ T-cell INF-$_\gamma$ (IU/mL)	0.01 (0–0.03)	0.66 (0.21–1.57)	<0.0001
Cumulative T-cell positivity, *n* (%)	2 (11)	16 (89)	<0.0001
Cumulative humoral or cellular positivity, *n* (%)	5 (28)	18 (100)	<0.0001

ADPKD: autosomal dominant polycystic kidney disease; CNI: calcineurin inhibitors; MMF: mycophenolate mofetil; mTORi: mammalian target of rapamycin inhibitors.

threshold of positivity. One LKDP had an anti-SARS-CoV-2 IgG titer (10.2 AU/mL) below the threshold for positivity, while all the other LKDPs had an anti-SARS-CoV-2 IgG titer above the threshold (Table 1).

One month after administration of the second vaccine dose, five KTRs had an anti-SARS-CoV-2 IgG titer [48.0 AU/mL (IQR 33.5–72.2)] above the threshold of positivity, whereas seroconversion was observed in all LKDPs [226.5 AU/mL (IQR 146.3–302.3)].

About 3 months after administration of the second vaccine dose, only five KTRs had an anti-SARS-CoV-2 IgG titer [38.5 AU/mL (IQR 16.3–75.1)] above the threshold of positivity, while seroconversion persisted in all LKDPs [156.0 AU/mL (IQR 93.0–318.3)].

As far as cellular immunity response is concerned, 2 (11%) KTRs showed a specific T-cell response 3 months after the second dose of vaccine, while 16 (89%) LKDPs showed a specific T-cell response.

The current vaccine strategy, even after a third booster dose [4], appears not to provide effective protection against COVID-19 for KTRs, while it provides full protection in LKDPs, indicating that vaccination should be highly recommended in immediate family members of KTRs.

ACKNOWLEDGEMENTS

We are grateful to all patients participating in the study and to all nurses of hemodialysis centers.

CONFLICT OF INTEREST STATEMENT

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. The authors declare that they have no relevant financial interests.

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