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Kidney International (2021) **99,** 1496–1498; https://doi.org/10.1016/j.kint.2021.04.006

Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine

see commentary on page 1275

To the editor: The efficacy rates of vaccines to prevent infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have not been specifically investigated in kidney transplant recipient (KTRs). Preliminary results suggest that among KTRs who received the first injection of an mRNA-based vaccine, the antibody response is weak.[1,2] This study reports on the immunization rates of KTRs who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine (Moderna).[3]

All participants had a negative history for coronavirus disease 2019 (COVID-19) and tested negative for anti–SARS-CoV-2 antibodies on the day of first injection. Serologic response was assessed on the day of the second injection and 1 month thereafter using the ARCHITECT IgG II Quant test (Abbott). Titers >50 arbitrary units (AUs)/ml were considered positive (detection range, 6.8–80,000 AUs/ml). This assay is reported to correlate with *in vitro* virus neutralization.[4]

The study sample consisted of 205 KTRs (Table 1). Only 98 patients displayed a positive serology 28 days after the second dose. The median antibody titer was 803.2 AUs/ml (interquartile range, 142.6−4609.6 AUs/ml). Compared with patients who did not respond after the first injection, patients with a positive serology after the first dose (n = 24 [11.7%]) displayed a higher antibody titer after the second injection (104 vs. 9415 AUs/ml, respectively; $P = 7.3^{-11}$). Antibody titers measured 1 month after the first and second

Table 1 | Characteristics of kidney transplant recipients stratified according to the serologic response after 2 doses of the mRNA-1273 SARS-CoV-2 vaccine

Characteristics	Entire cohort (n = 204)[a]	SARS-CoV-2–seronegative patients (n = 106)	SARS-CoV-2–seropositive patients (n = 98)	*P*	Missing data
Age, yr	57.7 (49.4–67.5)	58 (51–67.7)	57.3 (46.9–66.2)	0.45	0
Male sex	130 (63.8)	66 (62.3)	64 (65.3)	0.66	0
BMI, kg/m^2	25.6 (22.4–28.5)	25.4 (22.3–27.6)	25.9 (22.6–29.9)	0.3	2
Time from kidney transplantation, yr	6.2 (3–12.8)	5.4 (2.4–12)	7.1 (3.8–14.7)	0.04	1
First transplantation	170 (83.3)	80 (75.5)	90 (91.8)	0.002	0
Deceased donor	163 (79.9)	84 (79.3)	79 (80.6)	0.86	0
ABO group				0.1	2
O	84 (41.6)	38 (36.5)	46 (46.9)		
A	86 (42.6)	48 (46.2)	38 (38.8)		
B	11 (10.9)	15 (14.4)	7 (7.1)		
AB	10 (5)	3 (2.9)	7 (7.1)		
Induction treatment				0.5	9
Anti-thymocyte globulin	118 (60.5)	63 (61.8)	55 (59.1)		
Anti-CD25	70 (35.9)	37 (36.3)	33 (35.5)		
No induction	7 (3.6)	2 (2)	5 (5.4)		
CNI				0.13	0
Tacrolimus	115 (56.4)	67 (63.2)	48 (49)		
Cyclosporine	73 (35.8)	32 (30.2)	41 (41.8)		
No CNI	16 (7.8)	7 (6.6)	9 (9.2)		
MMF/MPA	161 (78.9)	91 (85.9)	70 (71.4)	0.02	0
Azathioprine	6 (2.9)	0	6 (6.12)	0.01	0
mTOR inhibitors	27 (13.2)	9 (8.5)	18 (18.4)	0.04	0
Steroids	122 (59.8)	69 (65.1)	53 (54.1)	0.12	0
Tacrolimus + MMF/MPA	98 (48)	60 (56.6)	38 (38.8)	0.001	0
Tacrolimus + MMF/MPA + steroids	64 (31.3)	46 (43.4)	18 (18.4)	0.0001	0
Belatacept	5 (2.5)	4 (3.8)	1 (1)	0.37	0
eGFR, ml/min per 1.73 m^2	57.1 (42.4–70.6)	54.4 (38.1–67.5)	62.5 (47.8–72.5)	0.004	1
Serum creatinine, μmol/L	120 (100–161)	137 (109–173)	110 (96–141)	0.0003	1

BMI, body mass index; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; MMF, mycophenolate mofetil; MPA, mycophenolic acid; mTOR, mammalian target of rapamycin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
Continuous variables are presented as medians (interquartile ranges), whereas categorical variables are given as n (%).
[a]The patient who developed COVID-19 was excluded from the analysis.

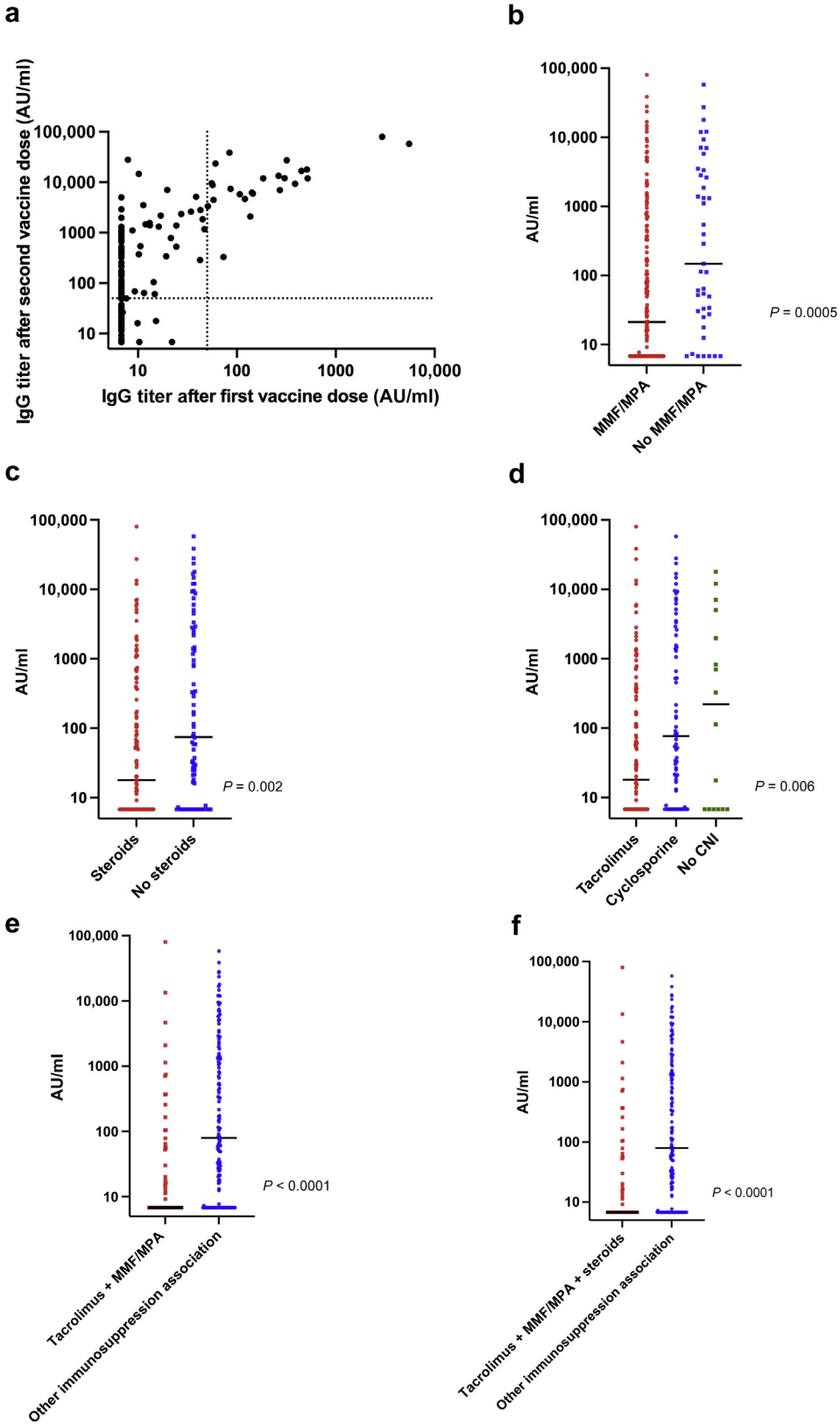

Figure 1 | Anti-spike IgG antibody titers (arbitrary unit [AU]/ml) measured after the second injection of the mRNA-1273 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine in 204 kidney transplant recipients without a history of coronavirus disease 2019 (COVID-19). Patients with titers >50 AU/ml were considered as seropositive. Bars represent median values. (**a**) Scattergram showing a significant positive correlation between anti-spike IgG antibody titers (AU/ml) after the first and second vaccine injections (Spearman $\rho = 0.68$; $P < 0.0001$). (**b**) Kidney transplant recipients being treated with antimetabolites (mycophenolate mofetil [MMF]/mycophenolic acid [MPA]) had lower median antibody titers compared with those who did not receive antimetabolites (continued)

injections were significantly correlated to each other (Figure 1a). Patients with a first kidney transplantation, a longer time from transplantation, better kidney function, and less immunosuppression were more likely to seroconvert (Table 1). Patients treated with calcineurin inhibitors, mycophenolate mofetil, or steroids showed significantly lower anti–SARS-CoV-2 antibody titers (Figure 1b–f). One patient developed a severe form of COVID-19 five days after the second injection.

In summary, the immunization rate among KTRs who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine can be as low as 48%. The issue of a third vaccine dose in nonresponsive KTRs is an intriguing one that could be usefully explored in further research.

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Kidney International (2021) **99,** 1498–1500; https://doi.org/10.1016/j.kint.2021.04.005

Outcome of diacylglycerol kinase epsilon–mediated hemolytic uremic syndrome in an infant

To the editor: We read with great interest the article by Brocklebank *et al.* entitled "Long-Term Outcomes and Response to Treatment in Diacylglycerol Kinase Epsilon Nephropathy" in the June 2020 issue of *Kidney International*.[1] We also had a patient with diacylglycerol kinase epsilon (DGKE) nephropathy who presented with hemolytic uremic syndrome (HUS). He was admitted with decreased urine output for 2 days when he was 70 days old. He also had nonbloody diarrhea without fever. He had hemolytic anemia, thrombocytopenia, and kidney failure. Plasma complement C3 and a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13 activity was normal. Eculizumab was given on the third day of admission. On the 10th day, he was discharged with normal kidney functions; eculizumab therapy was continued with 2-week intervals. Three months later, he presented with an HUS relapse after upper respiratory system infection under eculizumab therapy. Afterwards, genetic analysis results were obtained; a compound heterozygous mutation (i.e., p.Gln143* on exon 1 and p.Pro378Arg on exon 7) of *DGKE* was identified. Eculizumab was stopped at the age of 3 years. No relapse has been observed since then. Now he is 6 years old, with normal renal functions; he is receiving enalapril, 0.5 mg/kg per day, and losartan, 0.6 mg/kg per day, because of ongoing proteinuria, which was 160 mg/d (10.5 mg/m^2 per hour) at his last visit. In summary, he had a severe HUS relapse under eculizumab therapy, whereas he is without relapse during 3 years after stopping eculizumab. We agree with the fact that eculizumab is useless in DGKE-mediated atypical HUS and that it can be safely withdrawn in these individuals to avoid adverse effects, including severe infections.

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Figure 1 | (continued) (21.2 [interquartile range {IQR}, 6.8−401.9] AU/ml vs. 147.4 [IQR, 27.5−3352.5] AU/ml, respectively; $P = 0.0005$). (**c**) Kidney transplant recipients being treated with steroids had lower median antibody titers compared with those who did not receive steroids (17.9 [IQR, 6.8−378.9] AU/ml vs. 74.8 [IQR, 7.2−2417.9] AU/ml; $P = 0.002$). (**d**) Kidney transplant recipients being treated with calcineurin inhibitors (CNIs) had lower median antibody titers compared with those who did not receive CNIs (18.1 [IQR, 6.8−330] AU/ml for patients under tacrolimus and 76.6 [IQR, 10.1−2392.2] AU/ml for patients under cyclosporine vs. 220 [IQR, 6.8−4269] AU/ml for patients who did not receive CNIs). (**e**) Kidney transplant recipients being treated with tacrolimus + antimetabolites (MMF/MPA) had lower median antibody titers compared with those did not (9.2 [IQR, 6.8−110.2] AU/ml vs. 90.9 [IQR, 7.7−1976] AU/ml, respectively; $P < 0.0001$). (**f**) Kidney transplant recipients being treated with tacrolimus + antimetabolites (MMF/MPA) + steroids had lower median antibody titers compared with those who did not (6.8 [IQR, 6.8−57.4] AU/ml vs. 79.4 [IQR, 6.9−1393.5] AU/ml, respectively; $P < 0.0001$).