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Low Immunization Rate in Kidney Transplant Recipients Also After Dose 2 of the BNT162b2 Vaccine: Continue to Keep Your Guard up!

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We read with interest the report from Georgery et al[1] addressing the very low immunization rate of 3.8% in kidney transplant recipients (KTRs) 28 d after 1 dose of the BNT162b2 (Pfizer/BioNTech) vaccine. As addressed by the authors, this is markedly lower than what has been reported in other recent publications on mRNA vaccines (BNT162b2, Pfizer/BioNTech; mRNA-1273, Moderna) in this population.[2,3] Our findings after 2 doses of BNT162b2 are in line with their observations. We assessed the serological response 25–89 d after the second dose of the BNT162b2 vaccine in 141 KTRs without a known history of COVID-19 infection and negative SARS-CoV-2 anti-nucleocapsid IgG before vaccination. Antibodies to SARS-CoV-2 spike, the receptor-binding domain of spike and nucleocapsid were measured with a multiplexed bead-based flow cytometric assay as previously described.[4] The assay was calibrated to the World Health Organization international standard (National Institute for Biological Standards and Control code 20/136) to assess binding antibody units (BAU).

Table 1 summarizes the baseline characteristics and findings following the second dose of BNP162b2 vaccine in the 141 KTRs. The median age was 75 (range, 21–91) y, 56% were male individuals. The median time since transplantation was 9.6 y (range, 0.4–47.1), 72% were transplanted >5 y ago. The majority of the recipients were on a combination of calcineurin inhibitor (CNI), mycophenolate (MPA), and prednisolone (n = 105, 74%). On the day of measurement, only 25 patients (18%) had seroconverted with a mean SARS-CoV-2 spike IgG antibody titer of 21 ± 32 BAU/mL (threshold for positive response: 1.0 BAU/mL). Out of these 25 responders, 16 (64%) did not use MPA and only 6 (24%) were treated with triple maintenance immunosuppression with CNI, MPA, and prednisolone. Patients who seroconverted tended to be younger and had been living with a functioning kidney transplant for a longer time (Table 1). The impact of immunosuppression is obvious, but from the present data, it is not possible to differentiate the exact cause of the negative impact on seroconversion. However, treatment with MPA, especially in triple therapy, appears to lower seroconversion rates.

It is well known that KTRs are at increased risk of a severe outcome if infected with SARS-CoV-2, and there is a hope that vaccination will be protective. Short-term safety data on mRNA vaccines in KTRs seems similar to the general population, but the immunogenicity seems to be markedly reduced.[5] To date, it has not been proven that low levels of antibodies to spike predict a lack of protection against severe COVID-19. Although KTRs receiving MPA seem to have a reduced vaccine response rate, with the current knowledge, we do not promote reducing or withholding MPA during revaccination. Early results showing an increase in seroconversion after the second vaccine dose have prompted initiatives to administer a third jab. Whether or not this will enhance the immune response remains to be determined. In the meantime, KTRs should be informed to keep their guard up and behave as if they were not vaccinated!

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K.M. and A.Å. deigned the study, collected data, and wrote the article. T.T., E.B.V., and F.L.-J. performed the SARS-CoV-2 IgG analysis. A.Å. performed the statistical analysis. K.M., K.P., H.-P.M., A.-E.S., L.G.G., K.M.S., C.M., and J.S. included the patients. All authors revised and accepted the final version of the article.

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TABLE 1.

Baseline characteristics and findings following the second dose of BNP162b2 (Pfizer/BioNTech) vaccine in kidney transplant recipients

	All (N = 141)	POSitive IgG (N = 25)	NEGative IgG (N = 116)	Missing	*P* (POS vs NEG)
Demographics					
Age (y)	67.4 ± 17.2	59.1 ± 19.7	69.1 ± 16.2	0	**0.02**
Male sex	79 (56%)	12 (48%)	67 (58%)	0	0.50
Weight (kg)	74.9 ± 15.2	73.3 ± 12.9	75.3 ± 15.7	2	0.50
BMI (kg/m^2)	25.2 ± 4.3	25.6 ± 3.8	25.1 ± 4.4	2	0.52
Time since Tx (y)	11.7 ± 9.8	17.1 ± 13.5	10.4 ± 8.4	0	**0.01**
First Tx	122 (87%)	20 (80%)	102 (88%)	0	0.41
Living donor	55 (39%)	14 (56%)	41 (35%)	0	0.09
Years in RRT	14.1 ± 9.9	21.8 ± 12.5	12.4 ± 8.4	0	**0.001**
P-creatinine (µmol/L)	136 ± 78	141 ± 120	135 ± 66	1	0.80
Maintenance immunosuppression					
CNI + MPA + prednisolone[a]	105 (74%)	6 (24%)	99 (85%)		**<0.0001**
CNI + prednisolone	19 (13%)	12 (48%)	7 (6%)		**<0.0001**
Other combinations[b]	17 (12%)	7 (28%)	10 (9%)		**0.02**
MPA use	115 (82%)	9 (36%)	106 (91%)		**<0.0001**

Data presented as mean ± SD and number (%). Statistical comparison between groups with positive and negative SARS-CoV-2 IgG samples performed with Student's *T* test and chi-square tests. Bold values indicate statistical significance.

[a]CNI type; 35 cyclosporine and 70 tacrolimus.

[b]Everolimus + MPA + prednisolone (n = 7), azathioprine + prednisolone (n = 4), cyclosporine + azathioprine + prednisolone (n = 2), belatacept + MPA + prednisolone (n = 2), belatacept + everolimus + prednisolone (n = 1), tacrolimus + MPA (n = 1).

BMI, body mass index; CNI, calcineurin inhibitor; IgG, immunoglobulin G; MPA, mycophenolate; RRT, renal replacement therapy; Tx, transplantation.

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