

# Very Low Immunization Rate in Kidney Transplant Recipients After One Dose of the BNT162b2 Vaccine: Beware not to Lower the Guard!

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Vaccination campaigns to protect kidney transplant recipients (KTRs) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have massively started in most countries. Although the safety of RNA vaccines in KTRs seems similar to the general population,<sup>1</sup> the emerging results about efficacy show a lower response rate.<sup>2-5</sup>

We assessed the serological response 28 d after a first dose of the BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine (Pfizer-BioNTech) in 78 KTRs without a history of COVID-19 infection and who tested negative for anti-SARS-CoV-2 antibody the day of the vaccine injection. The serological response was measured using an immunoassay detecting antibodies against the spike protein receptor-binding domain (Elecsys anti-SARS-CoV-2, Roche Diagnostics GmbH, Mannheim, Germany).

Table 1 summarizes the baseline characteristics of the 78 KTRs. The median age was 62 (ranges 18–84) y and 62% were women. The median time since transplantation was 116 mo (ranges 4–608) and 69% were transplanted >6 y ago. Half of the patients were treated with an association of tacrolimus (Tac), mycophenolate (MPA), and steroids (St). At day 28, only 3 patients (3.8%) seroconverted with antibody titers at 1.83, 1.97, and 26.4 U/mL (positive threshold >1 U/mL), respectively. Out of these

three responders, 2 were receiving an anti-metabolite-free immunosuppressive regimen.

Two patients immunosuppressed with Tac/MPA/St developed a severe form of COVID-19 infection requiring mechanical ventilation 9 and 15 d after the vaccine injection and both eventually died. The first patient was a 59-y-old man, with a history of diabetes, transplanted 26 mo ago. The second was a 60-y-old man, transplanted 30 y ago, with a history of monoclonal gammopathy, who was reaching kidney failure secondary to chronic allograft nephropathy.

Low serological response in KTRs to vaccine was recently reported. Benotmane et al.<sup>2</sup> reported 11.7% and 48% rates of positive serology after the first and second dose of mRNA-1273 SARS-CoV-2 vaccine (Moderna), respectively, in 205 KTRs without a history of COVID-19 infection and who tested negative for anti-SARS-CoV-2 antibody before the first dose. Husain et al.<sup>3</sup> reported a positive serology rate after two doses of RNA vaccine (mRNA-1273 and BNT162b2) of 25% in a case series of 28 KTRs of whom 3 had a history of COVID-19 infection. Boyarsky et al.<sup>4</sup> reported a positive serology rate 20 d after one dose of RNA vaccine (mRNA-1273 and BNT162b2) at 17% in their study including 436 KTRs without a history of COVID-19 infection. Interestingly, they showed that KTRs receiving anti-metabolite maintenance immunosuppression therapy, older patients, and those who received BNT162b2 mRNA vaccine were less likely susceptible to develop an antibody response. In our

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**TABLE 1.**

**Baseline characteristics of the 78 patients at the time of vaccination**

|                                               |             |
|-----------------------------------------------|-------------|
| Age, y (ranges)                               | 62 (18–84)  |
| Women, n (%)                                  | 36 (46%)    |
| Time from kidney transplantation, mo (ranges) | 116 (4–608) |
| Time from kidney transplantation ≥6 y, n (%)  | 54 (69%)    |
| Immunosuppressive regimen                     |             |
| Tac/MPA/St, n (%)                             | 39 (50%)    |
| Tac/St, n (%)                                 | 19 (24%)    |
| Others, n (%) <sup>a</sup>                    | 20 (26%)    |
| Anti-metabolite free regimen, n (%)           | 24 (31%)    |

<sup>a</sup>Tac/Aza/St, n = 4; Tac/Aza, n = 1; mTORinh/St, n = 3; Tac/MPA, n = 4; MPA/St, n = 1; Csa/St, n = 2; MPA/St, n = 1; Csa/St, n = 2; Csa/Aza/St, n = 1; Aza/St, n = 1; Csa/MPA/St, n = 1; Csa/MPA, n = 1.

Aza, azathioprine; Csa, cyclosporine; MPA, mycophenolate; mTORinh, mTOR inhibitor; St, steroids; Tac, tacrolimus.

study, the response to the first BNT162b2 mRNA vaccine dose is even more disappointing—only 3.8% of positive serology. Moreover, 2 patients contracted a fatal COVID-19 infection after their first vaccine dose.

Given these poor results, KTRs must be strongly advised to remain vigilant and keep on applying strict precautionary measures even after vaccination. In addition, there is an urgent need to evaluate the efficacy of the third dose of vaccine in KTRs<sup>5</sup> and to assess which anti-SARS-CoV-2 vaccine might be the most efficient in KTRs.

This work received Institutional Review Board approval.

## REFERENCES

1. Ou MT, Boyarsky BJ, Motter JD, et al. Safety and reactogenicity of 2 doses of SARS-CoV-2 vaccination in solid organ transplant recipients. *Transplantation*. [Epub online ahead of print April 9, 2021]. doi: 10.1097/TP.0000000000003780
2. Benotmane I, Gautier -Vargas G, Cognard N, et al. Low immunization rates among kidney transplant recipients who received two doses of the mRNA-1273 SARS-CoV-2 vaccine. *Kidney Int*. [Epub online Ahead of print April 20, 2021]. S0085-2538(21)00389-6. doi: 10.1016/j.kint.2021.04.00
3. Husain SA, Tsapepas D, Paget KF, et al. Post-vaccine anti-SARS-CoV-2 spike protein antibody development in kidney transplant recipients. *Kidney Int Reports*. [Epub online ahead of print April 22, 2021]. doi:10.1016/j.ekir.2021.04.017SARS
4. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. *JAMA*. [Epub online ahead of print March 15, 2021]. e214385. doi:10.1001/jama.2021.4385
5. Ikizler TA, Coates PT, Rovin B, et al. Immune response to SARS-CoV2 infection and vaccination in patients receiving kidney replacement therapy. *Kidney Int*. 2021;99:1275–1279.