

**Disappointing Immunization Rate After 2 Doses of the BNT162b2 Vaccine in a Belgian Cohort of Kidney Transplant Recipients**

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**Authorship page**

Authorship: HG, AD, NK, research idea, study design, data analysis; HG, data acquisition; AS and BK performed serologic analysis, HG, AD, AS, BK, TD, AB, JDG, LB, JCY, EG and NK took care of the patients. All authors discussed and reviewed the manuscript.

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**Abbreviations:** KTRs, kidney transplant recipients

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Vaccination against SARS-CoV-2 is actively ongoing around the world to prevent COVID-19 infection that may be associated with dramatic outcomes, particularly in kidney transplant recipients (KTRs). We recently published a very low humoral response rate at 3.8% (n=3/78), 28 days after a single dose of the BNT162b2 vaccine (Pfizer-BioNTech).<sup>1</sup>

This paper reports the serological response rate 28 days after the second dose of vaccine using an immunoassay detecting antibodies against the spike protein receptor-binding domain (Elecsys anti-SARS-CoV-2, Roche Diagnostics GmbH, Mannheim, Germany - positive threshold >0.8 U/mL). All patients had no history of COVID-19 infection and tested negative for anti-SARS-CoV-2 antibody before vaccination. Seventy-nine patients were included. The median age was 61 (range 18-88) years; 48% were male. The median time since transplantation was 105 (range 5-609) months and 63% were transplanted more than 6 years ago. Forty-seven percent were treated with an association of tacrolimus, mycophenolate and steroids, and 29% received an antimetabolite-free immunosuppressive therapy. At day 28 after the second vaccine injection, 39 patients (49%) mounted a serological response. Among responders (Figure 1), only 4 (10%) had high antibody titers (>250 U/mL- the upper detection limit of our assay) while 35 (90%) had intermediate response with a median antibody titer of 11.9 U/mL (range 0.93-207). From the 3 patients who seroconverted after the first dose,<sup>1</sup> 2 had antibody titer >250 U/mL after the second injection and 1 had intermediate value (59.8 U/mL). No patient developed COVID-19 infection after the second vaccine injection.

These results are in line with those previously published.<sup>2-4</sup> Cucchiari et al<sup>2</sup> showed a 29.9% immunization rate 2 weeks after the second dose of the mRNA-1273 (Moderna) vaccine in 133 SARS-CoV-2-naïve kidney or kidney-pancreas transplant recipients. Benotmane et al<sup>3</sup> reported an immunization rate of 48% 1 month after the second dose of the mRNA-1273 vaccine in 205 KTRs. They also found that patients with a first KT, a longer time from transplantation, better kidney function, and less immunosuppression were more likely to seroconvert. Boyarski et al<sup>4</sup> showed a seroconversion rate of 54% in 658 solid organ

transplanted patients 29 days after the second injection of a mRNA vaccine (47% and 53% of patients were vaccinated with the mRNA-1273 and the BNT162b2 vaccine, respectively). The use of antimetabolites was associated with poor antibody response.

Interestingly, all these reports indicate that even among responders, a large number of patients has intermediate levels of antibody titers after the second dose. Although no threshold has been clearly established for protective immunity, antibody levels in our study and in others<sup>2-5</sup> seem lower than in immunocompetent individuals.<sup>5</sup> Consequently, it is not excluded that “weak” responders might actually remain unprotected against severe infection.

Overall, there is a growing evidence that KTRs show weak response after anti-SARS-CoV-2 vaccination and consequently remain at risk of severe COVID-19 infection. Thus, investigating alternatives, such as increasing the number-or the dose- of vaccine in nonresponders or weak responders or modulating immunosuppression during vaccination is needed.

This work received IRB approval.

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Figure Legend

**Figure 1. Antibody titer in patients who seroconverted 28 days after 2 doses of the BNT162b2 vaccine.** Four patients had antibody titers >250 U/mL (the upper detection limit of our assay)

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Figure 1

