

LETTER TO THE EDITOR

Humoral response to a fourth dose of mRNA vaccine in kidney transplant recipient responders to three doses of mRNA vaccine

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Kidney transplant recipients (KTRs) experience a low rate of seroconversion after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) messenger RNA (mRNA) vaccine, even after three or even four or five consecutive doses [1]. Furthermore, in KTR responders to vaccine, we recently reported a decline in both humoral and cellular immunity 6 months after a third mRNA vaccine dose [2]. Such a rapid decline is troubling because of the high probability of reduced vaccine effectiveness against variants of concern and breakthrough infection in KTRs.

Here, we report the extension of our previously published 80-KTR prospective cohort [2], evaluating whether the strategy of administering a fourth dose of mRNA vaccine 6 months after the third dose prevented the decline of humoral immunity in KTR responders to the initial vaccine schedule. The immune response to anti-SARS-Cov-2 mRNA vaccine was assessed by measuring anti-spike receptor-binding domain immunoglobulin G (IgG) antibodies (ARCHITECT IgG II Quant test; Abbott, Abbott Park, IL, USA) [positivity threshold = 8.5 binding antibody unit [BAU]/mL] [3]. A low response to vaccine was defined by an antibody titer less than 264 BAU/mL 1 month after injection [4]. This study was approved by the local ethics committee (CERNI No. E202137), and we obtained informed consent for all participants.

All KTRs had an initial vaccine schedule consisting of three doses of BNT162b2 mRNA vaccine. Among them, 49 of 80 (61.2%)

developed specific anti-SARS-Cov-2 antibodies, and 31 of 80 (38.8%) were seronegative. Notably, the repartition of an immunosuppressive regimen differed among these patients, with a higher proportion of belatacept-treated patients in the seronegative group after the third dose (Supplementary Table 1). Among KTR responders to the third dose, 40 of 49 (81.6%) received a fourth vaccine dose after a median time of 6.26 months after the third dose [interquartile range [IQR]: 5.82–6.94] (Figure 1). Characteristics of these 40 KTRs are summarized in Supplemental Table 2. No modification of immunosuppressive therapy was performed during the study period. No patient had a history of SARS-Cov-2 infection. Median antibody titer increased from 302 BAU/mL (IQR: 67–971) 1 month after the third dose to 1117 BAU/mL (IQR: 416–2554) 1 month after the fourth dose ($P < .0001$). The median increase in antibody titer was 204% (IQR: 85–671). The number of KTRs with a low antibody titer (<264 BAU/mL) decreased from 18 of 40 (45%) at 1 month after the third dose to 8 of 40 (20%) 1 month after the fourth dose of mRNA vaccine ($p = .0002$). Clinical and biological characteristics of KTRs with low or high antibody titer after the fourth dose are reported in Supplemental Table 3. Humoral response 1 month after the second, third, and fourth doses of vaccine is reported in Figure 2. During the median 5.1 (IQR: 4.1–5.5) months of follow-up after the fourth dose, 5 of 40 (12.5%) KTRs developed a SARS-Cov-2 infection, confirmed by polymerase chain reaction on

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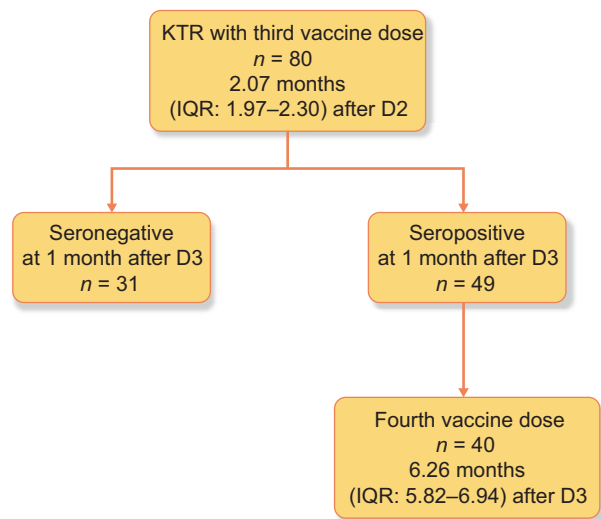


FIGURE 1: Humoral response was assessed by measuring anti-spike receptor-binding domain IgG antibodies (ARCHITECT IgG II Quant test; Abbott, Abbott Park, IL, USA) (positivity threshold = 8.5 binding antibody units/mL). D: dose; KTR: kidney transplant recipient; IQR: interquartile range.

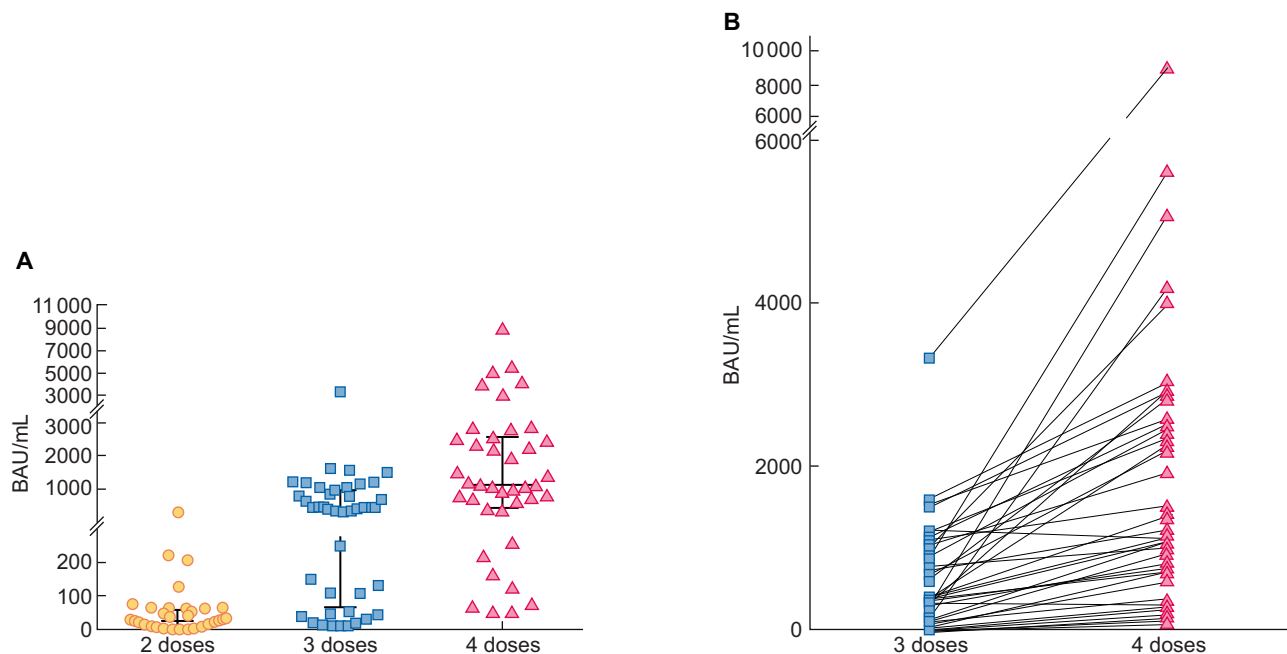


FIGURE 2: (A) Humoral response 1 month after the second, third, and fourth vaccine doses. (B) Detail of humoral response kinetics for each patient between the third and fourth vaccine doses ($P < .0001$). Humoral response was assessed by anti-spike receptor-binding domain IgG antibodies from the ARCHITECT IgG II Quant test (Abbott, Abbott Park, IL, USA). BAU: binding antibody unit.

nasopharyngeal swab, all with an omicron variant. None of them required hospitalization.

We highlight here that among KTR responders to mRNA SARS-CoV-2 vaccine, the administration of a fourth dose 6 months after the third dose to prevent immunity waning is associated with an increase in humoral response. In our study, and as demonstrated in the general population [5], this booster seems to be effective in protecting KTRs from SARS-CoV-2 infection and severe coronavirus disease 2019 (COVID-19). Our results should be interpreted while keeping in mind that this is a sample-limited study focused on the BNT162b2 mRNA vaccine. Moreover, the antibody titer does not define the full immune response, and the cellular immune response was not evaluated here. Nevertheless, it seems reasonable to propose a fourth dose to KTR responders to vaccine, in addition to the third dose, to improve the protection of KTRs against SARS-CoV-2 infection.

SUPPLEMENTARY DATA

Supplementary data are available at [ckj](#) online.

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The authors declare that no funding was received for this work.

CONFLICT OF INTEREST STATEMENT

None declared.

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