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Waning humoral response 6 months after SARS-CoV-2 vaccination with the mRNA-BNT162b2 vaccine in hemodialysis patients: time for a boost

To the editor: We and others have found a high short-term seroconversion rate between 71% and 98% in hemodialysis patients following a complete 2-dose vaccination course with the mRNA-BNT162b2 vaccine (Pfizer–BioNTech).[1,2] After natural infection, 76% of hemodialysis patients remained seropositive after a median time period of 124 days after infection.[3] However, to our knowledge, there are no serial data available on the maintenance of the vaccine-induced severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) humoral response in hemodialysis patients. Herein, we are reporting on the antibody response over time during a follow-up of 6 months after SARS-CoV-2 vaccination in 41 chronic hemodialysis patients (mean [SD] age, 67.3 [15.5] years; 34.1% females). All patients had been vaccinated twice with the Pfizer–BioNTech mRNA-BNT162b2 coronavirus disease 2019 (COVID-19) vaccine (Comirnaty). Patient characteristics, safety, tolerability, and short-term immunogenicity data have been reported in detail elsewhere.[2] We assessed the antibody response again 6 months after vaccination by quantifying the anti–SARS-CoV-2–spike IgG antibody concentration using the LIAISON SARS-CoV-2-TrimericS IgG chemiluminescent immunoassay (Diasorin S.p.A.), which detects IgG antibodies against the trimeric spike glycoprotein, including the receptor-binding domain and the N-terminal domain sites from the S1 subunit. According to the manufacturer, a value of ≥33.8 binding antibody units (BAUs)/ml was considered as evidence of seroconversion. In addition, neutralizing antibodies were assessed via the cPass SARS-CoV-2 Surrogate Virus Neutralization Test assay (GenScript), according to the manufacturer's specifications. The assay was originally described by Tan *et al.*[4] and has received emergency use authorization from the US Food and Drug Administration. The assay provides the percentage neutralization, with <30% classified as negative; 30% to 100% represents a range of low-to-high neutralization ability. A patient flow diagram, further details of study methods and statistical analysis, and patients' characteristics are shown in Supplementary Figure S1, the Supplementary Methods, and Supplementary Table S1. Compared with the seroconversion rate of 97.9% and a median (quartile 1–quartile 3) anti–SARS-CoV-2–spike IgG concentration of 1110 (293.5–1720) BAUs/ml 4 weeks after the second vaccine dose, 6 months later the seroconversion rate decreased to 65.8% with a median anti–SARS-CoV-2–spike IgG concentration of 85.6 (24.5–192.5) BAUs/ml (Figure 1). To further analyze the neutralizing capacity of seropositive patients after 6 months, we additionally assessed neutralizing antibodies. The median (quartile 1–quartile 3) percentage virus neutralization was 40.7% (32.9%–46.7%), and the percentage of patients above the 30% threshold for neutralizing antibody positivity was 56.1% of all patients and 85.2% of seropositive patients. Patients with maintained seroconversion after 6 months had a higher seroconversion rate after the first vaccine dose (63.0% vs. 7.1%; $P = 0.001$), had a significantly higher absolute anti–SARS-CoV-2–spike IgG concentration after the first (47.6 vs. 12.0 BAUs/ml; $P < 0.001$) and second (1440 vs. 136.5 BAUs/ml; $P < 0.001$) vaccine dose, had a higher hepatitis B vaccination seroconversion rate (80% vs. 40%; $P = 0.045$), and were less often treated with glucocorticoids (7.4% vs. 35.7%; $P = 0.035$). During the 6 months of follow-up, no patient acquired COVID-19. As a limitation, our study lacks cellular immune response data, including vaccine-induced T-cell response, which was found in 62%–78% of hemodialysis patients 3 to 8 weeks after vaccination with BNT162b2.[5–7]

Further studies are necessary to clarify whether the rapid antibody loss is caused by the impaired immune system in hemodialysis patients or due to the new RNA-based vaccine platform. Nevertheless, a third booster dose after 6 months may be necessary to sustain a protective humoral immunity in this vulnerable patient cohort.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Figure S1. Patient flow diagram.

Table S1. Patients' characteristics.

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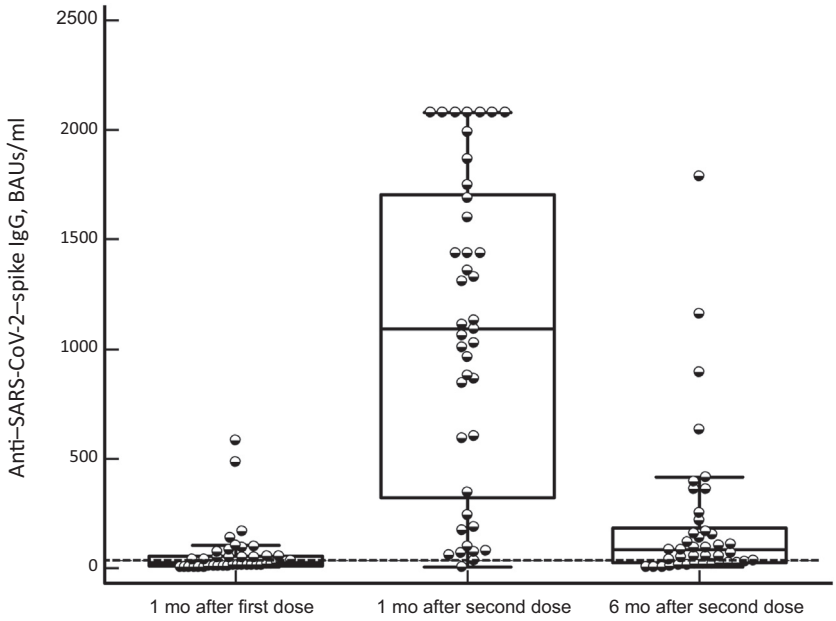

Figure 1 | Anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–spike IgG concentration after vaccination with the mRNA-BNT162b2 vaccine (Pfizer–BioNTech) in hemodialyis patients. Box-and-whisker plots including individual data points are displayed. The threshold for seropositivity (≥33.8 binding antibody units [BAUs]/ml) is represented by the dashed line.

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Improved cellular and humoral immunity upon a second BNT162b2 and mRNA-1273 boost in prime-boost vaccination no/low responders with end-stage renal disease

To the editor: Patients with end-stage renal disease (ESRD) develop inefficient immune responses upon vaccination and have a high risk of developing severe coronavirus disease 2019 (COVID-19). The globally expanding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of concern (VOC), B.1.6.17.2/Delta, evades immune responses and might constitute a particular threat to these patients.[1–3]

Herein, we evaluated the efficacy of a third dose (second boost) by BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) mRNA vaccines (Supplementary Table S1 and Supplementary Figure S1) in ESRD patients with no response/low response (NR/LR) after prime-boost BNT162b2 vaccination and compared with ESRD with high response (HR) following the regular prime-boost vaccination. Enzyme-linked immunosorbent assay, pseudovirus neutralization assay, and flow cytometry were applied to assess humoral and cellular immunity against the spike (S) protein of SARS-CoV-2 wild type (WT-S) and the Delta-VOC (Delta-VOC-S) before and 3 to 5 weeks following the last booster vaccination.

In NR/LR, 20 of 23 patients developed high-binding WT-S antibody titers (Figure 1a and Supplementary Figure S2A), with neutralizing capacity in 19 of 22 patients. The third vaccination led to an increase in WT-S protein-reactive $CD4^+$ T cells (Figure 1b) without differences between the applied vaccines (Supplementary Figure S2B and C). The higher frequency of S-reactive T follicular helper (Tfh) cells was the only difference observed in mRNA-1273–boosted patients (Supplementary Figure S2D).

Cellular immunity against WT-S and Delta-VOC-S was comparable irrespectively of helper or cytotoxic T cells or vaccine type (Figure 1e and f and Supplementary Figure S2E and F). In contrast, only 8 had neutralizing antibodies against Delta-VOC-S (Figure 1g). A clear association between cellular and humoral immunity was observed for each patient (Figure 1h). More important, when comparing the data