Clinical Kidney Journal, 2022, vol. 15, no. 5, 1012–1014

https://doi.org/10.1093/ckj/sfac047
Advance Access Publication Date: 16 February 2022
Letter to the Editor

LETTER TO THE EDITOR

Sustained humoral response 6 months after the anti-SARS-CoV-2 mRNA-BNT162b2 vaccine in haemodialysis patients: should booster vaccine doses be given to all patients at the same time?

Vincenzo La Milia [1], Silvia Tonolo [2], Francesco Luzzaro [2], Claudio Bonato [3], Monica Limardo [1], Selena Longhi [1], Chiara Ravasi [1], Sara Viganò [1] and Andrea Cavalli [1]

[1]Nephrology and Dialysis Unit, A. Manzoni Hospital, Lecco, Italy, [2]Microbiology Unit, A. Manzoni Hospital, Lecco, Italy and [3]Department of Clinical Services, A. Manzoni Hospital, Lecco, Italy

Correspondence to: Vincenzo La Milia; E-mail: v.lamilia@asst-lecco.it

In haemodialysis (HD) patients persistent seroconversion (PSC) was found 6 months after natural severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1] and in 71–98% of patients after complete vaccination [2].

Some authors [3] demonstrated a marked reduction of PSC in HD patients and suggested a booster third vaccine dose (booster) in HD patients 6 months after the administration of second vaccine dose (2nd VD).

This prospective study reports the anti-SARS-CoV-2 IgG titres evaluated before vaccination, at the administration of first vaccine dose (1st VD), at the administration of 2nd VD and then every month until 6 months after the 2nd VD.

After written informed consent, between February and April 2021, 192 HD patients in our department were vaccinated with two doses of Pfizer-BioNTech mRNA-BNT162b2 SARS-CoV-2 vaccine (Comirnaty) administered 21 days apart. Of these, 174 HD patients [61% males, age 72 years, interquartile range (IQR): 62–81 years; HD vintage 40 months, IQR: 21–71 months] had a 6-month follow-up after administration of 2nd VD.

The anti-SARS-CoV-2 IgG titre was evaluated using the Liaison® assay (DiaSorin S.p.A.). The dosing interval is between <3.8 and >400 Apparent Unit (AU)/mL. According to the manufacturer, a concentration >15 AU/mL was considered as evidence of seroconversion.

In a subgroup of HD patients, we evaluated also cellular immunity response (CIR) 6 months after the administration of the 2nd VD. Spike-specific $CD4^+$ and $CD8^+$ T-cell response was quantified using the QuantiFERON SARS-CoV-2 test (Qiagen S.p.A.), a commercially available interferon-γ releasing assay.

The study protocol was approved by the institutional review board and by the local ethics committee.

Six months after the administration of 2nd VD, 135 HD patients (78%) still had PSC; of these patients, 37 (21%) had had symptomatic or asymptomatic coronavirus disease 2019 (COVID-19) infection and had high anti-SARS-CoV-2 IgG titre (85.3 AU/mL, IQR: 37.1–144.5 AU/mL) on the day of 1st VD, while 98 HD patients (56%) had a titre <12 AU/mL (3.8 AU/mL, IQR: 3.8–3.8 AU/mL) on the day of 1st VD. Only 39 (22%) HD patients did not have PSC 6 months after the administration of 2nd VD: these patients also had anti-SARS-CoV-2 IgG titre <12 AU/mL (3.8 AU/mL, IQR: 3.8–3.8 AU/mL) on the day of 1st VD.

Figure 1 shows the trend in anti-SARS-CoV-2 IgG titre in the three groups of patients.

Among the 39 HD patients, 12 patients (31%) never had anti-SARS-CoV-2 IgG levels >15 AU/mL after vaccination, whereas 27 patients (69%) had anti-SARS-CoV-2 IgG levels >15 AU/mL transiently after vaccination and titres then progressively decreased over time. None of 39 patients without PSC had anti-SARS-CoV-2

Received: 24.1.2022; Editorial decision: 2.2.2022

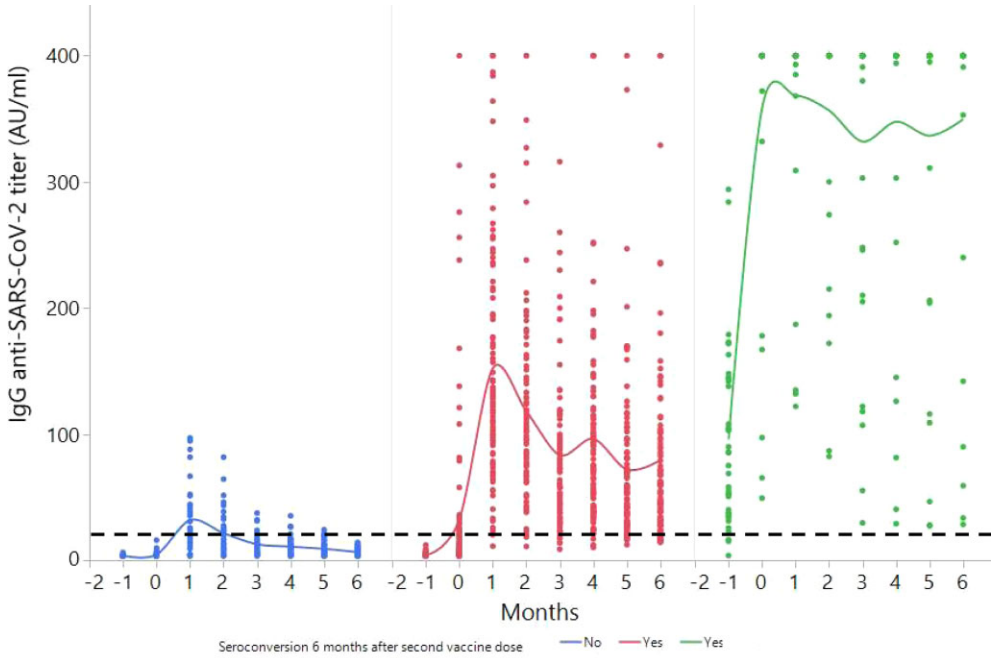

FIGURE 1: Follow-up of IgG anti-SARS-CoV-2 (anti-spike S1 and S2) in patients who received a first vaccine dose (Month 1) and a second vaccine dose (Month 0). Blue indicates patients without seroconversion, red indicates patients with seroconversion and green indicates patients with seroconversion 6 months after the second dose vaccine administration and IgG anti-SARS-CoV-2 positive at administration of first vaccine dose. The curves are smooth cubic spline curves through the media of data. The dotted black line represents the threshold of positivity for IgG anti-SARS-CoV-2.

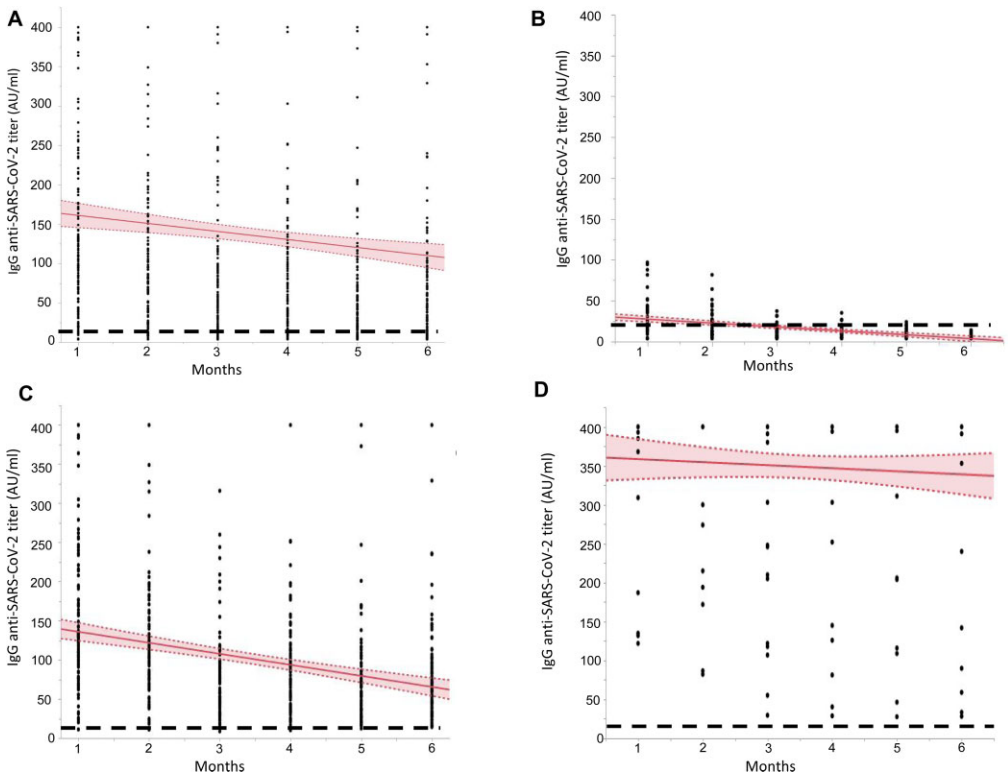

FIGURE 2: Trend of anti-SARS-CoV-2 IgG titre after the second vaccine dose administration. Linear regression and 95% confidence interval (shaded band). (**A**) All patients ($r^2 = 0.01$); (**B**) patients without seroconversion 6 months after the second dose vaccine administration ($r^2 = 0.25$); (**C**) patients with seroconversion 6 months after the second dose vaccine administration ($r^2 = 0.09$); (**D**) patients with seroconversion 6 months after the second dose vaccine administration and IgG anti-SARS-CoV-2 positive at administration of first vaccine dose ($r^2 = 0.004$). The dotted black line represents the threshold of positivity for IgG anti-SARS-CoV-2.

IgG titre >100 AU/mL 1 month after administration of 2nd VD, and in these HD patients the decrease of anti-SARS-CoV-2 IgG titre had a much steeper slope curve than in the other two groups of patients (Figure 2).

CIR ($CD4^+/CD8^+$) positivity against SARS-CoV-2 was found in 93% of patients with PSC and anti-SARS-CoV-2 IgG positivity before vaccination, in 70% of patients with PSC who had anti-SARS-CoV-2 IgG titre <12 AU/mL on the day of 1st VD and in 17% of patients without PSC.

In other studies [4, 5] vaccine-induced T-cell response was found in 62–78% of HD patients 3–8 weeks after vaccination with mRNA-BNT162b2; however, there are few published data about long-term CIR.

During the 6 months of follow-up, no patient had COVID-19 infection.

In conclusion, only 23% of HD patients did not develop or lost PSC against SARS-CoV-2 6 months after complete vaccination with two doses of Comirnaty vaccine; of these patients, 17% had CIR against SARS-CoV-2.

It is probable that the booster is indicated in approximately 20% of HD patients at Month 6 or earlier after administration of 2nd VD. Only other prospective studies will be able to show us the best timing of booster in HD patients with PSC against SARS-CoV-2.

ACKNOWLEDGEMENTS

We are grateful to all patients participating in the study and to all nurses of haemodialysis centres.

CONFLICT OF INTEREST STATEMENT

None declared. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. The authors declare that they have no relevant financial interests.

REFERENCES

1. La Milia V, Tonolo S, Luzzaro F *et al*. The humoral immune response to SARS-CoV-2 mounts and is durable in symptomatic haemodialysis patients. *Nephrol Dial Transplant* 2021; 36: 1132–1134
2. Carr EJ, Kronbichler A, Graham-Brown M *et al*. Review of early immune response to SARS-CoV-2 vaccination among patients with CKD. *Kidney Int Rep* 2021; 6: 2292–2304
3. Davidovic T, Schimpf J, Abbassi-Nik A *et al*. Waning humoral response 6 months after SARS-CoV-2 vaccination with the mRNA-BNT162b2 vaccine in hemodialysis patients: time for a boost. *Kidney Int* 2021; 100: 1334–1335
4. Van Praet J, Reynders M, De Bacquer D *et al*. Predictors and dynamics of the humoral and cellular immune response to SARS-CoV-2 mRNA vaccines in hemodialysis patients: a multicenter observational study. *J Am Soc Nephrol* 2021; 32: 3208–3220
5. Strengert M, Becker M, Ramos GM *et al*. Cellular and humoral immunogenicity of a SARS-CoV-2 mRNA vaccine in patients on haemodialysis. *eBioMedicine* 2021; 70: 103524