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Letter to the Editor

LETTER TO THE EDITOR

Immunogenicity, reactogenicity and breakthrough infections after two doses of the inactivated CoronaVac vaccine among patients on dialysis: phase 4 study

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Coronavirus disease 2019 (COVID-19)-associated lethality among patients with end-stage renal disease on dialysis is higher than in the general population [1]. Reported seroconversion rates after messenger RNA and viral-vector vaccines range between 77 and 97% [2–5]. Recently we demonstrated a seroconversion rate of 44% after the first dose of the World Health Organization–validated CoronaVac inactivated virus vaccine (Sinovac Biotech) [6, 7]. Here we report antibody response, breakthrough infections and 28-day lethality after the second dose.

Patients, on dialysis, ages 20–75 years, were asked to receive the two-dose schedule of CoronaVac between 29 April 2021 and 1 June 2021. The characteristics of the global cohort were described previously [7]. The humoral response was assessed 28 days after the first dose (D1) and 28 days after the second dose (D2) using the AdviseDx SARS-CoV-2 IgG II assay [Abbott Laboratories, Abbott Park, IL, USA; lower limit for positivity 50 arbitrary units (AUs)/mL]. A value ≥840 AU/mL was used to define 'high-responders', based on the US Food and Drug Administration guideline criterion for the therapeutic use convalescent plasma [8]. For this analysis, the final follow-up date for the occurrence of new confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 18 September 2021. The study was approved by the local ethics committee and registered at ClinicalTrials.gov (NCT04801667); all patients signed an informed consent form.

There were 198 patients vaccinated with one dose and 195 fully vaccinated. Two patients died from COVID-19 and one patient was vaccinated against hepatitis B before the second dose. The most common adverse reactions after the second dose were local pain and tenderness (11%). Fever, myalgia, headache or diarrhea occurred in ≤5% of the patients and no severe adverse reactions were observed.

From the 198 initial subjects, 138 were included in the immunogenicity cohort (56 individuals had been previously exposed to SARS-CoV-2 and 4 had no sequential serological tests available). The seroconversion rate 28 days after the first dose was 44% ($n = 62$), increasing to 91% ($n = 126$) 28 days after the second dose. The median immunoglobulin G (IgG) value among patients with a positive test showed a 6-fold increase, from 103 AU/mL [interquartile range (IQR) 82–202)] after the first dose to 626 AU/mL (IQR 389–1751) after the second dose. A similar trend was observed in the proportion of high responders, increasing from 3 to 40%. Of 76 patients with a negative test after the first dose, 64 (84%) developed antibody response [17 high responders (22%)] after the second dose, showing a median IgG value of 411 AU/mL (IQR 216–907) (Figure 1). The 12

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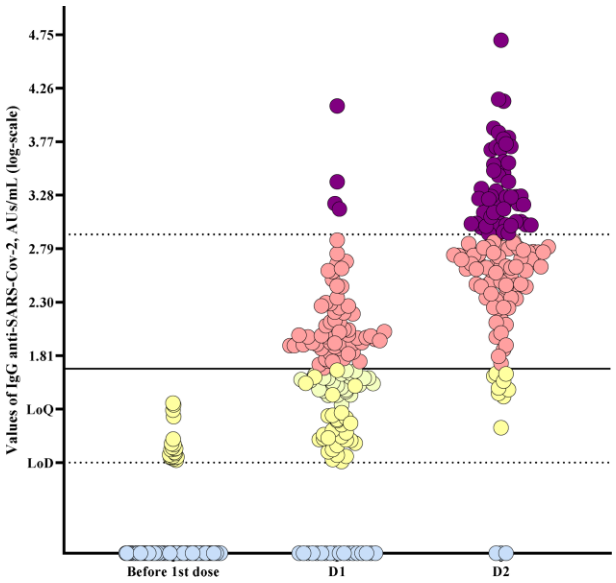

FIGURE 1: Abbott AdviseDx SARS-CoV-2 IgG II immunoassay for total IgG antibodies against the receptor binding domain of the S1 subunit of the SARS-CoV-2 spike protein, in logarithmic scale. The lowest limit of detection by the manufacturer is 6.8 AU/mL (0.83 log) and the analytical measuring interval is 21 [1.32 log, limit of quantification (LoQ)] to 40 000 AU/mL (4.60 log). The threshold for considering the test as positive is 50 AU/mL, or 1.69 log (black line). The value considered in this analysis for classifying the patient as a high responder is 840 AU/mL (2.92 log). Before the first dose of the vaccine, all 138 patients had negative serology; 117 (85%) had undetectable values (blue dots) and 21 (15%) had detectable values below the lowest analytical level (yellow dots). At D1 (28 days after the first dose), 18 (13%) patients remained with undetectable titers, 58 (43%) had detectable but lower than LoQ values and 62 (44%) seroconverted, with 4 (3%) considered as high responders. Twenty-eight days after the second dose of the vaccine (D2), 3 (2%) patients remained with undetectable titers, 9 (7%) had detectable but lower than LoQ values and 126 (91%) had positive titers, with 55 (40%) considered as high responders.

patients with no antibody response after the two doses were significantly older [median age 56 years (IQR 50–61) versus 46 (IQR 36–56); $P = 0.02$] and were more frequently on maintenance steroid doses (45% versus 8%; $P < 0.001$) than those showing seroconversion after the first dose (Supplementary Table 1).

After the second vaccine dose, five (2.6%) patients developed COVID-19, four of them after 15 days. The median IgG titers of these five patients were 60 AU/mL (IQR 40–75). Three required hospitalization and one died 70 days after the second dose. The five patients who developed COVID-19 after the second dose had antibody titers at the threshold of positivity, suggesting a relationship between the magnitude of the humoral response and protection against infection.

This prospective study suggests that the use of the traditional two-dose regimen of the inactivated whole-virion CoronaVac vaccine in dialysis patients is safe and achieved seroconversion rates of 91.3%, similar to that observed in the general population [9, 10]. Additional strategies deserve to be explored in seronegative patients after the first dose.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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AUTHORS' CONTRIBUTIONS

J.M.P., M.P.C., L.A.V., C.M.T., H.T.S. and D.T.C. participated in the research design. J.M.P., L.A.V., M.P.C., C.M.T., A.L.A., S.R.M. and H.T.S. participated in the writing of the paper. M.P.C., M.R.N., L.A.V., E.F.L., C.M.T. and H.T.S. participated in the data analysis.

CONFLICT OF INTEREST STATEMENT

C.M.T. has been working as a medical manager at AstraZeneca since September 2021. The other authors have no conflicts of interests to declare.

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