SARS CoV-2 vaccination in patients receiving kidney replacement therapies: where are we now with the protective immune response?

Nestor Toapanta, Oriol Bestard, and María José Soler

Nephrology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Research, Barcelona, Spain

In the new pandemic COVID-19 era that started in 2020, early studies demonstrated that patients with advanced chronic kidney disease (CKD) such as hemodialysis and kidney transplant patients are at high risk of mortality from SARS CoV-2[1–5]. For this reason several scientific societies taking care of these patients have recommended to prioritize their vaccination[6,7,8]. The higher mortality rate in this group of patients may be in part ascribed to a dysregulation in their immune system[9]. However, studies in COVID-19 convalescent immunosuppressed solid organ transplant (SOT) recipients have showed the capacity of these patients to achieve a robust adaptive immune response, similar to immunocompetent convalescent individuals, despite a concerning initial delay, thus suggesting that an optimal immune response may be also achieved among these high-risk patient population after vaccination[10].

Vaccination against SARS CoV-2 infection has raised hopes for ending the pandemic protecting high risk population such as haemodialysis or kidney transplant patients. Notably, studies reported by Dagan et al. demonstrated that the BNT162b2 (Pfizer-BioNTech) vaccine against SARS CoV-2 is effective for preventing symptomatic COVID-19 and reducing the rates of severe COVID19 infections in the general population, being the antibody response of up to 94% after a second dose[11]. However little is known about the immune response in patients receiving kidney replacement because few of these patients have been included in the initial clinical trials on vaccines against SARS CoV-2 and most importantly, because the actual follow-up of these patients after vaccination is short.

Patients undergoing haemodialysis are known to have frequent infections, as well as a suboptimal response to vaccines, in part due to alterations in both innate and adaptive immunity[12,13]. Grupper et al. evaluated the humoral response in 56 patients on haemodialysis

against a control group composed of 95 health care worked after receiving two doses of the BNT162b2 vaccine (Pfizer-BioNTech). They demonstrated that hemodialysis patients developed a lower titre of anti-SARS-CoV-2 antibody than the control group 21 days after vaccination (median dialysis patients 171 U/ml, IQR: 477.7, versus median controls 2500 U/ml, IQR 943.5), with an inverse correlation between age and IgG6 levels[14]. In another study, of 81 haemodialysis patients and 80 healthy controls who were vaccinated with mRNA vaccine BNT162b, 43 patients on haemodialysis (53%) had an antibody titre lower than 200 U/ml, 22 patients (27%) had a titre lower than 29 U/ml and seven patients (9%) had no detectable antibodies while in control group all patients had titers greater than 200U/ml[15]. In concordance with the previous studies, Torreggiani et al. demonstrated that about one-third of patients on haemodialysis develop neutralizing antibodies after the first dose of BNT162b2 COVID-19 mRNA vaccine, and that these are at low titers, mainly observed in a high-comorbidity cohort (median Charlson comorbidity index= 8)[16].

Yanai et al. from Israel, demonstrated lower response rate to the vaccine, with lower anti–spike antibody level, and a higher rate of COVID-19 infection (38 of 148 patients) after SARS-CoV-2 BNT162b2 mRNA vaccine in 160 patients on chronic dialysis (127 haemodialysis and 33 peritoneal dialysis)[17]. Frantzen et al. with the same vaccine also demonstrated in a large haemodialysis population (n=326) a 91% antibody positivity rate, and only 60% of them presenting an antibody level above 200 U/ml[18]. Agur et al. studied the seropositivity against the BNT162b2 vaccine in two types of dialysis patients (122 patients on haemodialysis and 22 patients on peritoneal dialysis), who received two doses 21 days apart and a follow-up of up to 8 weeks after the second dose; 93.4% of them developed antibodies at 36 days (IQR 32-40). Of note that younger age was associated with higher antibody titers, while lack of response to the vaccine was associated with lower albumin and higher doses of iron sucrose administered[19]. In these dialysis patients, there were no observed differences regarding seropositive response for SARS-CoV-2 anti-S IgG at 2-6 weeks following the second dose of BNT162b2 vaccination between the two main dialysis techniques[19]. Another group, studied seropositivity after vaccination against SARS CoV-2 infection in 186 patients haemodialysis with two vaccines: BNT162b2/Pfizer (N=148) and mRNA-1273/Moderna (N=18). Overall, no differences were found between the two vaccines. Seropositive rate was 165/186 (88.7%) with 70% at maximum titre with IgG levels, although in patients who had previously SARS CoV-2 infection, the seropositivity was 100% (97% with IgG levels at the maximum titre)[20].

Attias et al. assessed the humoral response after the BNT162b2 mRNA vaccine using anti–spike(S)1 IgG antibody in a single-center cohort of 69 patients receiving maintenance haemodialysis, thirteen patients (19%) had a history of previous COVID-19 or positive baseline serology, overall seropositive rate at last follow-up was 86%. Of mention that patients aged >70 years were less likely to reach seropositivity at last follow-up (28 of 37 [75%]; P = 0.01)[21]. Roseanne et al. showed that the antibody response against SARS-CoV-2 spike protein 28 days after the first dose of either the BNT162b2 or AZD1222 vaccine in 94 patients receiving maintenance haemodialysis were detectable in 75 patients (79.8%) and not detectable in 19 patients (20.2%). Median antibody level was 2.4 [interquartile range, 8.8] relative light units. In concordance with the previous report, patients with detectable antibodies were younger than patients without detectable antibodies (60.2±11.6 years vs. 69.8±11.8 years; P = 0.002)[22]. These results suggest that older patients in maintenance haemodialysis have worse antibody response against SARS CoV-2 vaccines and maybe at risk for COVID-19 infection. Table 1 summarized all of these studies including the time after vaccination.

As previously mentioned, kidney transplant (KT) patients on immunosuppressive therapy are also at risk for severe complications of COVID-19 infection[1,2]. Boyarsky et al, reported that, only 17% of transplant recipients who received a single dose of SARS-CoV-2 vaccine developed detectable anti-spike antibody (compared to 100% of the non-immunocompromised subjects in the pivotal trials) and after 2 doses response increased to 54% in transplant recipients[23, 24]. Grupper et. al, analyzed the humoral response following full vaccination with the BNT162b2 (Pfizer- BioNTech) in 136 kidney transplant recipients, and compared to 25 controls. All controls developed a positive response to spike protein, while only 51/136 transplant recipients (37.5%) had positive antibody response (p<0.001). Mean anti IgG spike level was also higher in the controls (KT: 31.05 (41.8) vs. controls: 200.5 (65.1) AU/mL, p<0.001). The older age, high corticosteroids dose in the last 12 months, maintenance with triple immunosuppression, and regimen that includes mycophenolate were associated with a low humoral response[25]. Moreover, transplant recipients receiving antimetabolite maintenance immunosuppression therapy were less likely to develop an antibody response than those not receiving such immunosuppression therapy (37% vs 63%, respectively; adjusted incidence rate ratio [IRR], 0.22 [95% CI, 0.15-0.34]; P < 0.001). As reported in hemodialysis patients, older transplant recipients were less likely to develop an antibody response (adjusted IRR, 0.83 [95% CI, 0.73-0.93] per 10 years; P = 0.002). Those

who received mRNA-1273 were more likely to develop an antibody response than those receiving BNT162b2 (69% vs 31%, respectively; adjusted IRR, 2.15 [95% CI, 1.29-3.57]; P = 0.003)[23]. Nevertheless, the serological immune response to a second dose of mRNA SARS-CoV-2 vaccine was detectable in the majority of transplant recipients, although patients without a response after the first dose had generally low antibody levels. Likewise, after dose, a poorer humoral response was persistently associated with use of antimetabolite immunosuppression[23]. In concordance, Rozen-Zvi B et al. also demonstrated a poor response of BNT162b2 vaccine in kidney transplant recipients. Of 308 kidney transplant recipients included in their study, only 112 (36.4%) tested positive for anti-S antibodies 2-4 weeks after receiving the second dose of BNT162b2 vaccine. Median antibody titer was 15.5 AU/mL. Higher estimated glomerular filtration rate, lower mycophenolic acid dose, younger age and lower calcineurin inhibitors (CNI) blood level were independent factors for antibody response. Of mention that no serious adverse events to the vaccine were reported[26].

Benotmane et al. also examined 242 kidney transplant recipients who received the first injection of Moderna mRNA-1273 vaccine, only 26 (10.8%) kidney transplant recipients had a positive serology response at 28 days after injection, with a median IgG titer of 224 AU/ ml (IQR, 76-496 AU/ml) compared with a median IgG titer of <6.8 AU/ml in seronegative. Patients who seroconverted had longer time from transplantation, less immunosuppression, and better renal function[27]. Korth et al. investigated the SARS- CoV-2 immune response via SARS-CoV-2 IgG detection in 23 renal transplant recipients after two doses of the mRNA-based SARS-CoV-2 vaccine BNT162b2, only 5 of 23 (22%) renal transplant recipients were tested positive for SARS-CoV-2 IgG antibodies after the second dose of vaccine (15.8±3.0 days after the second dose) [28].

Chavarot et al. evaluated the serological and T-cell immune status using an enzyme-linked immunospot (ELISPOT). assay measuring interferon-γ produced by specific SARS-CoV-2 T-cells) vaccinal responses to BNT162b2 mRNA anti-SARS- CoV2 vaccine in kidney transplant recipients treated with the costimulatory blocker belatacept. They observed that at twenty-eight days after the first injection only 2/101 patients (2.0%) developed anti-spike antibodies. Among the 35/101 patients (34.7%) with serology testing 1 month after the second dose, only 2 patients (5.7%) developed anti-spike antibodies. Furthermore, when they assessed the functional SARS-CoV-2-specific T-cell immune response, only 2/40 patients(5.0%) and 7/23

patients(30.4%) showed detectable T-cell frequencies on day 28, and 1 month after the second injection, respectively [29] (Table1).

Recently, Boyarsky et al evaluated 12 transplant recipients who received the Janssen vaccine, observing in only 2 of 12 patients a detectable anti-RBD (receptor-binding domain) antibody response, being significantly lower than that observed among recipients of the mRNA vaccine series, with significantly lower titers than those of the mRNA group, suggesting that the Janssen vaccine may result in an even lower humoral immunity than the mRNA vaccines in these patients[30]. To date 16 clinical trials are registered at https://clinicaltrials.gov that evaluate the response to the vaccine in patients on hemodialysis or kidney transplant patients (Table 2).

Vaccination with two doses of BNT162b2 against SARS-CoV-2 infection was highly effective in the general population, even in older adults, with marked and sustained decreases in the incidence of SARS-CoV-2 and COVID-19-related hospitalizations, severe disease and death, including those caused by the B.1.1.7 SARS-CoV-2 variant favoring control of the pandemic as demonstrated by Hass et al in the Israeli population[31]. In concordance Martinez-Baz et al., reported a reduction in symptomatic COVID-19 and hospitalization in the populations of Navarra, Spain[32]. However it is of interest to mention that 14 patients developed COVID-19 infection after completing vaccination, so we believe there is sufficient evidence to issue warnings that immunocompetent populations should continue with strict COVID-19 precautions after vaccination[33]. Caillard et al. demonstrated that 55 solid organ transplant recipients (52 kidney and 3 simultaneous kidney-pancreas) developed COVID-19 after receiving 2 doses of mRNA-based severe acute respiratory syndrome coronavirus (SARS-CoV-2) vaccines. A total of 9 and 46 patients received the mRNA-1273 (Moderna) and the BNT162b2 (Pfizer-Bio-NTech) vaccine, respectively, 15 (27%) required hospitalization for oxygen therapy. Of these, 6 were admitted to an intensive care unit, and 3 died[34]. In addition, it is of interest to mention that cases of reinfection have been reported in individuals infected with SARS-CoV-2, which calls into question the protective nature of humoral immunity against this highly infectious pathogen. Bartsch YC et al. defined the relationship between titers and functional antibody activity to SARS-CoV-2 over time notably, neutralization, Fc-function, and SARS-CoV-2 specific T cell responses were only observed in subjects that elicited RBD-specific antibody titers above a threshold[35].

As a consequence of the low antibody responses after 2 doses of SARS-CoV-2 vaccine, Kamar et al. tested the effect of three doses of BNT162b2 (Pfizer-Bio-NTech) COVID-19 vaccine in solid-organ transplant recipients. The study showed that the administration of a third dose of the BNT162b2 vaccine to solid-organ transplant recipients significantly improved the immunogenicity of the vaccine (68% (95% CI, 58 to 77; 67 of 99 patients) 4 weeks after the third dose), without cases of COVID-19 infection reported[36]. These results suggest that three shots of COVID-19 vaccine should be considered in solid-organ transplant recipients, special population at high risk for severe COVID-19 disease.

In conclusion, the evidence to date suggests that the majority of renal replacement patients remain at high risk for COVID-19 despite vaccination. Among haemodialysis patients the seroconversion after the administration of the two doses of the vaccine ranges from 80 to 96%, being the eldest patients at especial higher risk of developing a suboptimal antibody response. Of especial concern seem to be the kidney transplant patient population, in whom seroconversion rates after the administration of the two doses varies between 22 - 37.5%. Maintenance immunosuppression therapy with antimetabolites, the co-stimulation blocker belatacept, as well as older age and worse renal function seem to be risk factors for a low serological response to the vaccine. Considering that these patient populations on haemodialysis and kidney transplant is mostly within the elderly age, it is urgent to clarify whether these poor serological responses are in line with an impaired adaptive immune response at the T and B-cell memory compartments, which may highlight the need of additional doses of the vaccine to booster effective recall immune responses. Notably, the significantly lower immune responses achieved by vaccinated patients as compared to those that developed COVID19 infection, and especially those with a severe presentation, highlights the lower immunogenicity triggered by current vaccines covering a single immunogenic viral protein. For this reason, studies to assess long term efficacy and safety of SARS-CoV-2 vaccination and booster doses in patients on dialysis or after kidney transplantation are urgently needed. Furthermore, in these high risk population it seems that social isolation barriers should be maintained to avoid COVID-19 infection because of the unknown response of the vaccines to the different variants of COVID-19 circulating around the world.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Ortiz A, Cozzolino M, Fliser D, et al. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrology Dialysis Transplantation*. 2021;36(1):87-94. doi:10.1093/ndt/gfaa314
2. Gansevoort RT, Hilbrands LB. CKD is a key risk factor for COVID-19 mortality. *Nature Reviews Nephrology*. 2020. doi:10.1038/s41581-020-00349-4
3. Zúñiga J, Toapanta N, Ramos N, et al. Infección por SARS-CoV-2 en pacientes con enfermedad renal crónica en hemodiálisis. Evolución de la PCR de SARS-CoV-2. *Nefrología*. 2021;(December). doi:10.1016/j.nefro.2020.12.008
4. Favà A, Cucchiari D, Montero N, et al. Clinical characteristics and risk factors for severe COVID-19 in hospitalized kidney transplant recipients: A multicentric cohort study. *American Journal of Transplantation*. 2020;20(11):3030-3041. doi:10.1111/ajt.16246
5. Toapanta N, Castañeda Z, Zúñiga J, et al. Seropositividad frente al SARS CoV-2 en pacientes en hemodiálisis. *Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia*. May 2021:10.1016/j.nefro.2021.04.004. doi:10.1016/j.nefro.2021.04.004
6. Caillard S, Anglicheau D, Matignon M, et al. An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants. *Kidney international*. 2020;98(6):1549-1558. doi:10.1016/j.kint.2020.08.005
7. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-436. doi:10.1038/s41586-020-2521-4
8. Glenn DA, Hegde A, Kotzen E, et al. Systematic review of safety and efficacy of COVID-19 vaccines in patients with kidney disease. *Kidney International Reports*. 2021;6(5):1407-1410. doi:10.1016/j.ekir.2021.02.011
9. Kato S, Chmielewski M, Honda H, et al. Aspects of immune dysfunction in end-stage renal disease. *Clinical Journal of the American Society of Nephrology*. 2008;3(5):1526-1533. doi:10.2215/CJN.00950208
10. Favà A, Donadeu L, Sabé N, et al. SARS-CoV-2-specific serological and functional T cell immune responses during acute and early COVID-19 convalescence in solid organ transplant patients. *American Journal of Transplantation*. April 2021. doi:10.1111/ajt.16570

11. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *New England Journal of Medicine*. 2021;384(15):1412-1423. doi:10.1056/nejmoa2101765
12. Lim WH, Kireta S, Leedham E, Russ GR, Coates PT. Uremia impairs monocyte and monocyte-derived dendritic cell function in hemodialysis patients. *Kidney International*. 2007;72(9):1138-1148. doi:10.1038/sj.ki.5002425
13. Eleftheriadis T, Liakopoulos V, Leivaditis K, Antoniadi G, Stefanidis I. Infections in hemodialysis: A concise review. Part II: Blood transmitted viral infections. *Hippokratia*. 2011;15(2):120-126.
14. Grupper A, Sharon N, Finn T, et al. Humoral Response to the Pfizer BNT162b2 Vaccine in Patients Undergoing Maintenance Hemodialysis. *Clinical Journal of the American Society of Nephrology*. 2021;16:CJN.03500321. doi:10.2215/cjn.03500321
15. Simon B, Rubey H, Treipl A, et al. Hemodialysis Patients Show a Highly Diminished Antibody Response after COVID-19 mRNA Vaccination Compared to Healthy Controls. *medRxiv*. 2021;(1):2021.03.26.21254259.
16. Torreggiani M, Blanchi S, Fois A, Fessi H, Piccoli GB. Neutralizing SARS-CoV-2 antibody response in dialysis patients after the first dose of the BNT162b2 mRNA Covid-19 vaccine. The war is far from being won. *Kidney international*. 2021:9-10. doi:10.1016/j.kint.2021.04.010
17. Yanay NB, Freiman S, Shapira M, et al. Experience with SARS-COV-2 BNT162b2 mRNA vaccine in dialysis patients. *Kidney international*. 2021;(April):9-10. doi:10.1016/j.kint.2021.04.006
18. Frantzen L, Cavaille G, Thibeaut S, El-Haik Y. Efficacy of the BNT162b2 mRNA Covid-19 Vaccine in a hemodialysis cohort. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2021. doi:10.1093/ndt/gfab165
19. Agur T, Ben-Dor N, Goldman S, et al. Antibody response to mRNA SARS-CoV-2 vaccine among dialysis patients - a prospectivecohort study. *Nephrology Dialysis Transplantation*. 2021. doi:10.1093/ndt/gfab155
20. Lacson E, Argyropoulos CP, Manley HJ, et al. Immunogenicity of SARS-CoV-2 Vaccine in Dialysis. *medRxiv : the preprint server for health sciences*. April 2021:6. doi:10.1101/2021.04.08.21254779
21. Attias P, Sakhi H, Rieu P, et al. Antibody response to BNT162b2 vaccine in maintenance hemodialysis patients. *Kidney international*. 2021:4-5.

doi:10.1016/j.kint.2021.04.009

22. Billany RE, Selvaskandan H, Adenwalla SF, et al. Seroprevalence of antibody to S1 spike protein following vaccination against COVID-19 in patients receiving hemodialysis: a call to arms. *Kidney international*. 2021;(82):18-20. doi:10.1016/j.kint.2021.04.008
23. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients. *JAMA - Journal of the American Medical Association*. 2021;325(17):1784-1786. doi:10.1001/jama.2021.4385
24. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. *JAMA*. 2021;325(21):2204-2206. doi:10.1001/jama.2021.7489
25. Grupper A, Rabinowich L, Schwartz D, et al. Reduced humoral response to mRNA SARS-Cov-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*. 2021. doi:10.1111/ajt.16615
26. Rozen-Zvi B, Yahav D, Agur T, et al. Antibody response to mRNA SARS-CoV-2 vaccine among kidney transplant recipients - Prospective cohort study. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. May 2021. doi:10.1016/j.cmi.2021.04.028
27. Benotmane I, Gautier-Vargas G, Cognard N, et al. Weak anti–SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. *Kidney International*. 2021:2-3. doi:10.1016/j.kint.2021.03.014
28. Korth J, Jahn M, Dorsch O, et al. Impaired Humoral Response in Renal Transplant Recipients to SARS-CoV-2 Vaccination with BNT162b2 (Pfizer-BioNTech). *Viruses*. 2021;13(5):4-9. doi:10.3390/v13050756
29. Chavarot N, Ouedrani A, Marion O, et al. Poor Anti-SARS-CoV-2 Humoral and T-cell Responses After 2 Injections of mRNA Vaccine in Kidney Transplant Recipients Treated with Belatacept. *Transplantation*. 2021;Publish Ah. doi:10.1097/tp.0000000000003784
30. Boyarsky BJ, Chiang TP-Y, Ou MT, et al. Antibody Response to the Janssen COVID-19 Vaccine in Solid Organ Transplant Recipients. *Transplantation*. 9000;Online First.
31. Haas EJ, Angulo FJ, McLaughlin JM, et al. Impact and effectiveness of mRNA

BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet (London, England)*. 2021;397(10287):1819-1829. doi:10.1016/S0140-6736(21)00947-8

32. Martínez-Baz I, Miqueleiz A, Casado I, et al. Effectiveness of COVID-19 vaccines in preventing SARS-CoV-2 infection and hospitalisation, Navarre, Spain, January to April 2021. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*. 2021;26(21):2100438. doi:10.2807/1560-7917.ES.2021.26.21.2100438
33. Ali NM, Alnazari N, Mehta SA, et al. Development of COVID-19 Infection in Transplant Recipients After SARS-CoV-2 Vaccination. *Transplantation*. 9000;Online First.
34. Caillard S, Chavarot N, Bertrand D, et al. Occurrence of severe COVID-19 in vaccinated transplant patients. *Kidney international*. May 2021:S0085-2538(21)00509-3. doi:10.1016/j.kint.2021.05.011
35. Bartsch YC, Fischinger S, Siddiqui SM, et al. Discrete SARS-CoV-2 antibody titers track with functional humoral stability. *Nature communications*. 2021;12(1):1018. doi:10.1038/s41467-021-21336-8
36. N K, F A, O M, C C, J I, A DB. Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. *The New England journal of medicine*. June 2021. doi:10.1056/NEJMC2108861

Table 1. Studies that demonstrate the response to the vaccine against SARS CoV-2 in hemodialysis and kidney transplant patients after 2nd dose

Study	Nº of patients in HD/KT	Age	Measured of antibodies time (days)	Seroconversion (%)	Level of anti–spike antibody (AU/mL)
Grupper[14]	56 (HD)	74±11	30 (27-34)	96.0	2900 (1128-5651)
Simon[15]	81 (HD)	67 (34-86)	21	80.0	171±477.7
Torreggiani[16]	101 (HD)*	69±15	21	35.0	8.22 (1.73-28.70)
Yanay[17]	127/33 (HD/PD)	69 (62-78)	21 - 35	90	116.5 (66-160)
Frantzen[18]	244 (HD)	76±13	30	91.0	Unknown
Agur[19]	122/23 (HD/PD)	72±12	36 (32-40)	93.4	1599 (419.5-3976.9)
Lacson[20]	186 (HD)	68±12	23±8	88.7	Not reported
Attias[21]	64 (HD)	70±12	16.8	86	16.8 ±14.9
Roseanne[22]	94 (HD) [a]	62±12	27.8±4.2	79.8	2.4 (IQR: 8.8)[a]
Boyarski[24]	322 (KT)	±56	±20	48	Not reported
Grupper[25]	136 (KT)	58±12	15.6±6.2	37.5	200.5 ±65.1
Rozen-Zvi[26]	308 (KT)	58±14	28 (22-34)	36.4	15.5 (3.5-163)
Benotmane[27]	242 (KT)*	58 (49-68)	28	10.8	224 (76-496)
Korth[28]	23 (KT)	58±14	15.8±3	22	50.9±138.7
Chavarot[29]	101 (KT)[b]	64 (53-73)	30	5.7	Unknown

HD: Hemodialysis, KT: Kidney Transplants, PD: Peritoneal Dialysis, AU Arbitrary Unit.

*Determinations of antibodies at 21 days after the first dose

[a]Determinations of antibodies at 28 days after the first dose and level expressed in relative light unit (RLU)

[b]Kidney transplant patients treated with belatacept, 35/101 patients with serology testing 1 month after the second dose. Specific anti-spike T-cell response occurred in 2/40 (5%) patients on day 28 and in 7/23 (30.4%) patients on day 60.

Table 2. Clinical trials registered at https://clincialtrial.gov until July 2nd, 2021 evaluating the response to the vaccine in hemodialysis and kidney transplant patients

Study	Identifier	Conditions	Sponsor
The Malaysian Study On Hemodialysis Patients SARS-COV-2 Vaccination Immune Response: A Prospective Observational Cohort Study	NCT04872751	Immune Response Post Covid 19 Vaccination	Penang Hospital, Malaysia
COVADIAL - Immunogenicity of COVID-19 Vaccine in Hemodialysis Patients	NCT04728828	Covid 19	Centre Hospitalier de Cornouaille
The LESS CoV-2 Study - Long Term Efficacy and Safety of SARS-CoV-2 Vaccination in Patients in Patients With Chronic Kidney Disease Stage G4-G5, on Dialysis or After Kidney Transplantation	NCT04841785	Covid19, SARS-CoV Infection, CKD	University Medical Center Groningen
Response of Haemodialysis Patients to BNT162b2 mRNA Cov-19 Vaccine	NCT04881396	COVID-19 Vaccines, Hemodialysis Complication	Hospices Civils de Lyon
Evaluation of Protective Antibody Production After COVID-19 Vaccination Among Patients Under Hemodialysis	NCT04871945	Covid19, Vaccine Reaction, Hemolysis, End-stage Renal Disease	Hanyang University Seoul Hospital
Observational Study on the Effects of SARS-CoV-2 Vaccination in Dialysis and Kidney Transplant Patients	NCT04743947	CKD Stage 5 on Dialysis, CKD Stage 5 With Transplant Vaccine Response Impaired	Heinrich-Heine University, Duesseldorf
Phenotyping Seroconversion Following Vaccination Against COVID-19 in Patients on Haemodialysis Study	NCT04815850	End Stage Kidney Disease	University of Leicester
Multi Center Study to Assess the	NCT04905862	Chronic Kidney Disease	Medical

Humoral and Cellular Response After Vaccination Against COVID-19 in Dialyzed Patients.		Requiring Chronic Dialysis	University of Gdansk
Immunological Follow-up After COVID 19 Vaccination in Kidney Transplant Recipients	NCT04757883	Kidney Transplant Recipients	University Hospital, Strasbourg, France
The Immune-response and Safety of COVID-19 Vaccination in Patients With Chronic Kidney Disease, on Dialysis, or Living With a Kidney Transplant - A Prospective, Controlled, Multicenter Cohort Study by the RECOVAC Consortium	NCT04741386	Covid19, Chronic Kidney Disease	University Medical Center Groningen
Investigation of the Immune Response Before and After COVID-19 Disease or SARS-CoV-2 Vaccination in Dialysis Patients, Solid Organ Recipients and Medical Staff	NCT04799808	SARS-CoV-2 infection, Active Immunization, Immune Response, Immunosuppression	Technische Universität Dresden
Monitoring of COVID-19 Vaccine Response in Organ Transplant Patients	NCT04828460	Covid19, Kidney Transplantation	University Hospital, Strasbourg, France
SARS-CoV-2 Cellular and Humoral Immune Response Following Vaccination of Kidney Transplant Recipients and Healthy Controls	NCT04747522	Kidney Transplant infection, SARS-CoV-2 infection	Oslo University Hospital
COVID-19 Serology in Nephrology Health Care Workers	NCT04347694	SARS-CoV-2, Immunization, Infection	Medical University of Vienna

A Phase 3b, Open-Label, Safety and Immunogenicity Study of SARS-CoV-2 mRNA-1273 Vaccine in Adult Solid Organ Transplant Recipients and Healthy Controls	NCT04860297	SARS-CoV-2	ModernaTX, Inc.
IgG Antibodies After SARS-CoV2 mRNA Vaccine in Kidney Transplantation	NCT04832841	Kidney Transplant	Institute for Clinical and Experimental Medicine