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mRNA-1273 vaccine (Moderna): a better option than BNT162b2 (Pfizer) in kidney transplant recipients and dialysis patients?

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With the roll-out of coronavirus disease 2019 (COVID-19) vaccines, it has become clear that vaccinating the majority of the population worldwide will be the most important element to control and manage the ongoing COVID-19 pandemic. Several reports have shown diminished immunogenicity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines in both kidney transplant recipients (KTRs) and dialysis patients (DPs), as evidenced in a recent narrative review [1]. Furthermore, two recent articles have included comparisons between the immunogenicity of the mRNA-1273 (Moderna) versus the BNT162b2 (Pfizer) vaccine in these populations [2, 3]. Boyarsky et al. [3] studied a cohort of solid organ transplant recipients, including KTRs, and reported lower seroconversion rates after receiving the Pfizer vaccine. Stumpf et al. [2] also described lower seroconversion rates in KTRs and DPs receiving the Pfizer vaccine. However, none of these articles reported the titers of anti-SARS-CoV-2 antibodies. Therefore we here compared the immunogenicity of the two available messenger RNA (mRNA) vaccines±BNT162b2 (Pfizer-BioNTech) versus mRNA-1273 (Moderna)—in both KTRs and DPs regarding both seroconversion rates and, among responding patients, antibody titers.

KTRs and DPs receiving a first dose of a SARS-CoV-2 mRNA vaccine between February and May 2021 were consecutively included. Blood was prospectively sampled at day 1 (before vaccination), 16–21 days after the first dose of the vaccine and 21–35 days after the second vaccine dose. Samples were stored at 'Biobank Antwerp', Antwerp, Belgium (ID: BE 71030031000) [4]. Immunoglobulin G (IgG) antibodies against the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein were measured using an in-house Luminex assay [5]. These measurements were performed by staff unaware of the identity of the samples. In order to investigate only patients without prior SARS-CoV-2 infection, patients with a polymerase chain reaction (PCR)-proven history of SARS-CoV-2 infection and patients who tested positive for anti-RBD IgG antibodies (>1) on the day of vaccination without a PCR-proven history of SARS-CoV-2 infection, as a surrogate of previous SARS-CoV-2 infection, were excluded. Response to first and second vaccinations was defined as anti-RBD IgG positivity (signal:noise ratio >1) at 16–21 days after dose 1 and 21–35 days after dose 2, respectively. The study was performed in accordance with the Declaration of Helsinki and approved by the ethical committee of the Antwerp University Hospital and University of Antwerp (EC 21/05/076).

Multiple logistic regression modelling was used to identify variables associated with a positive antibody response after dose 1 and dose 2. A multiple linear mixed model was used to study factors influencing the mean log-transformed anti-RBD IgG levels in responding patients. Potentially important factors were first identified using a bivariate analysis, with effect sizes expressed as crude odds ratios (ORs) or additive effects, respectively. Also, a stepwise model-building exercise based on Akaike's Information Criterion (AIC) was used

Table 1. Patient characteristics (first-dose response) (univariate analysis)

Characteristics	mRNA-1273 (Moderna)	BNT162b2 vaccine (Pfizer-BioNTech)	P-value
Kidney transplant recipients ($n = 138$)			
Subjects, *n*	44	94	
Male, *n* (%)	26 (59.0)	54 (57.4)	0.855*
Age (years), median (IQR)	54.0 (48.8–61.0)	56.5 (46.0–66.8)	0.293**
Diabetes mellitus, *n* (%)	3 (6.8)	11 (11.7)	0.548*
Immunosuppressive therapy, *n* (%)			
CNI	6 (14.6)	23 (24.4)	0.146*
CNI + MMF	25 (56.8)	39 (41.5)	0.092*
CNI + AZA/mTOR inhibitor	9 (20.5)	19 (20.2)	0.974*
Positive antibody response, *n* (%)	11 (25.0)	8 (8.5)	0.009*
Anti-RBD IgG antibody levels[a], median (IQR)	3.13 (1.93–7.83)	5.03 (3.03–6.71)	0.386**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	3.77 (2.36)	4.80 (2.06)	0.529***
Dialysis patients ($n = 141$)			
Subjects, *n*	61	80	
Male, *n* (%)	39 (63.9)	53 (66.3)	0.775*
Age (years), median (IQR)	70 (60.0–78.0)	70 (62.0–75.0)	0.975**
HD, *n* (%)	40 (65.6)	63 (78.8)	0.081*
Diabetes mellitus, *n* (%)	29 (47.5)	28 (35.0)	0.133*
Positive antibody response, *n* (%)	41 (67.2)	21 (26.3)	< 0.001*
Anti-RBD IgG antibody levels[a], median (IQR)	6.43 (3.28–10.54)	3.03 (1.96–5.03)	0.011**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	5.27 (2.26)	3.17 (1.91)	0.016**
Total ($N = 279$)			
Subjects, *n*	105	174	
Male, *n* (%)	65 (61.9)	107 (61.4)	0.946*
Age (years), median (IQR)	61.0 (50.0–72.0)	63.0 (51.5–71.0)	0.881**
Diabetes mellitus, *n* (%)	32 (30.4)	39 (22.4)	0.134*
Positive antibody response, *n* (%)	52 (49.5)	29 (16.7)	< 0.001*
Anti-RBD IgG antibody levels[a], median (IQR)	5.70 (2.37–10.52)	3.34 (2.05–5.96)	0.054**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	4.91 (2.29)	3.55 (1.98)	0.077***

[a] In responding patients.
* Based on Pearson's chi-squared test (or Fisher's exact test in case of small cell counts).
** Based on Mann–Whitney *U*-test.
*** Based on an unpaired Student's *t*-test comparing two mean log-GMTs.
AZA, azathioprine; CNI, calcineurin inhibitors; MMF, mycophenolate mofetil; mTOR, mechanistic target of rapamycin; SD, standard deviation.

to select all important explanatory variables in the final models. Depending on the selected covariates, all pairwise interaction effects were checked for significance, adjusting for multiplicity. All statistical tests were two-sided. P-values <0.05 were considered statistically significant.

In total, 155 KTRs and 182 DPs were included, of whom 268 patients without prior SARS-CoV-2 infection (80%) were sampled after both vaccine dose 1 and dose 2. To evaluate the antibody response after dose 1, 138 KTRs and 141 DPs were included after exclusion of patients with evidence of prior SARS-CoV-2 exposure ($n = 55$) or loss to follow-up ($n = 3$) (Table 1). Identical exclusion criteria were used to study the antibody response after dose 2, resulting in the inclusion of 133 KTRs and 138 DPs (Table 2).

When zooming in on patients included to study antibody response after dose 1 ($n = 279$), the median age was 62 years, the interquartile range (IQR) was 51–71 years and 62% were men; 62% received the BNT162b2 vaccine (Pfizer-BioNTech), 38% received the mRNA-1273 vaccine (Moderna). At a median of 21 days (IQR 20–23) anti-RBD IgG antibodies were detected in 81 of 279 participants [29% {Clopper–Pearson 95% confidence interval (CI) 24–35}]. Both hemodialysis (HD) patients [adjusted OR (aOR) 6.403 (95% CI 2.970–13.804); P < 0.001] and peritoneal dialysis (PD) patients [aOR 10.379 (95% CI 4.143–26.000); P < 0.001] were more likely to develop antibody responses compared with KTRs (Table 3A). Furthermore, the odds of having an antibody response decreased by a factor of 0.972 (95% CI 0.950–0.994) with a 1-year increase in age. Patients receiving the mRNA-1273 vaccine showed significantly different seroconversion rates 21 days after dose 1 compared with patients receiving the BNT162b2 vaccine [49.5% versus 16.7%; OR 4.941 (95% CI 2.698–9.047); P < 0.001] (Tables 1 and 3A). All pairwise interaction terms included in both models were found to be non-significant at a 5% significance level.

Performing a similar analysis regarding antibody responses after the second vaccine dose, anti-RBD IgG antibodies were detected in 211 of 271 participants [78% (Clopper–Pearson 95% CI 72–83)] at a median of 28 days (IQR 25–31) after second vaccine administration. Again, both HD patients [aOR 6.181 (95% CI 2.828–13.511); P < 0.001] and PD patients [aOR 18.870 (95% CI 2.483–143.380); P = 0.005] were more likely to develop antibody responses compared with KTRs (Table 3A). Patients receiving the mRNA-1273 vaccine showed significantly different seroconversion rates compared with those receiving the BNT162b2 vaccine [90.0% versus 70.8%;

Table 2. Patient characteristics (second dose response) (univariate analysis)

Characteristics	mRNA-1273 (Moderna)	BNT162b2 vaccine (Pfizer-BioNTech)	P-value
Kidney transplant recipients ($n = 133$)			
Subjects, *n*	42	91	
Male, *n* (%)	25 (59.5)	52 (57.1)	0.796*
Age (years), median (IQR)	55.5 (50.0–61.0)	57.0 (46.5–66.5)	0.365**
Diabetes mellitus, *n* (%)	3 (7.1)	10 (11.0)	0.754*
Immunosuppressive therapy, *n* (%)			
CNI	6 (14.3)	22 (24.2)	0.193*
CNI + MMF	25 (59.5)	37 (40.7)	0.043*
CNI + AZA/mTOR inhibitor	8 (19.0)	19 (20.9)	0.807*
Positive antibody response, *n* (%)	32 (76.2)	51 (56.0)	0.026*
Anti-RBD IgG antibody levels[a], median (IQR)	12.39 (3.51–16.18)	5.62 (2.13–14.25)	0.159**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	7.27 (2.63)	5.37 (2.73)	NA***
Dialysis patients ($n = 138$)			
Subjects, *n*	58	80	
Male, *n* (%)	35 (60.3)	53 (66.3)	0.476*
Age (years), median (IQR)	69.5 (60.0–77.8)	70.0 (61.8–75.0)	0.941**
HD, *n* (%)	37 (63.8)	63 (78.8)	0.052*
Diabetes mellitus, *n* (%)	25 (43.1)	29 (36.3)	0.416*
Positive antibody response, *n* (%)	58 (100)	70 (87.5)	0.005*
Anti-RBD IgG antibody levels[a], median (IQR)	16.16 (15.69–16.41)	16.58 (10.22–17.36)	0.194**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	15.22 (1.23)	11.86 (1.98)	NA***
Total ($n = 271$)			
Number of subjects	100	171	
Male, *n* (%)	60 (60.0)	105 (61.4)	0.819*
Age (years), median (IQR)	61.0 (50.8–72.0)	63.0 (53.0–71.0)	0.831**
Diabetes mellitus, *n* (%)	28 (28.0)	39 (22.8)	0.339*
Positive antibody response, *n* (%)	90 (90.0)	121 (70.8)	<0.001*
Anti-RBD IgG antibody levels[a], median (IQR)	16.02 (13.42–16.39)	14.08 (4.89–17.14)	0.449**
Anti-RBD IgG antibody levels[a], geometric mean (SD)	11.70 (2.00)	8.49 (2.51)	NA***

[a] In all responding patients after second vaccine dose.
* Based on Pearson's chi-squared test (or Fisher's exact test).
** Based on Mann–Whitney *U*-test.
*** No P-values were determined for geometric mean anti-RBD IgG antibody levels, given deviations from normality.
AZA, azathioprine; CNI, calcineurin inhibitors; MMF, mycophenolate mofetil; mTOR, mechanistic target of rapamycin; NA, not applicable; SD, standard deviation.

aOR 3.428 (95% CI 1.587–7.406); P < 0.005] (Tables 2 and 3). After selecting patients with an antibody response after the first ($n = 81$) or second ($n = 211$) vaccine dose, antibody levels appeared to be associated with the type of patient, age and vaccine type. Mean log-transformed antibody titre concentrations were 0.289 units higher for Moderna versus Pfizer vaccination, irrespective of the dose (first or second) considered (P = 0.005 in multiple linear mixed model; Table 4).

In this study of the humoral immune response after SARS-CoV-2 mRNA vaccination, low seroconversion rates were noted in both KTRs and DPs after first-dose administration. While in DPs the seroconversion rate levelled up to 92.8% after a second dose of SARS-CoV-2 mRNA vaccination, KTRs lagged behind with a seroconversion rate of 62.4%. Furthermore, vaccination with the mRNA-1273 vaccine resulted in both higher seroconversion rates and mean log-transformed antibody titer concentrations. It is known that mycophenolate mofetil (MMF) treatment reduces the chances to seroconvert in KTRs after vaccination with a SARS-CoV-2 mRNA vaccine [6]. In the present study, even with more patients who were under MMF treatment in the two-dose mRNA-1273 versus BNT162b2 group, the seroconversion rate was higher in the mRNA-1273 group.

Several limitations of our study must be acknowledged. First, although an interesting difference in serological response was observed following administration of mRNA-1273 versus BNT162b2, no further investigation was performed on potential differences in T-cell responses. It is well described in the literature that patients without antibody responses can mount T-cell responses, which could provide some protection against SARS-CoV-2 infection in seronegative patients [7]. Second, no information concerning possible side effects of both SARS-CoV-2 mRNA vaccines was collected. Nevertheless, two studies have already reported fewer local and systemic adverse events after two-dose vaccination with BNT162b2 in dialysis patients compared with healthy controls [8, 9]. Furthermore, Sanders et al. [10] reported fewer systemic adverse events after two-dose vaccination with mRNA-1273 in KTRs compared with controls.

While writing this article, six very recent articles were published reporting on results in various conditions, which support our above-mentioned findings [11–16]. Seroconversion rates in adults with hematologic malignant disease, the majority of whom received B-cell-depleting monoclonal antibodies, were higher in patients vaccinated with mRNA-1273 compared with BNT162b2 (50% versus 33%; P = 0.013) [11].

Table 3A. Multiple logistic regression model for factors associated with antibody response to the first and second dose of SARS-CoV-2 mRNA vaccine

Covariates	No antibody response	Antibody response	Crude OR (95% CI)	P-value	aOR (95% CI)	P-value
First-dose response, *n*	198	81				
Type of patient						
Kidney transplant	119 (60.1)	19 (23.5)	Ref	Ref	Ref	Ref
HD	63 (31.8)	40 (49.3)	3.977 (2.127–7.434)	<0.001	6.403 (2.970–13.804)	<0.001
PD	16 (8.1)	22 (27.2)	8.612 (3.847–19.276)	<0.001	10.379 (4.143–26.000)	<0.001
				Overall* <0.001		Overall* <0.001
Gender						
Male	117 (59.1)	55 (67.9)	Ref	Ref		
Female	81 (40.9)	26 (32.1)	0.682 (0.396–1.179)	0.171	NA	NA
Age (years), median (IQR)	62.5 (52.0–71.0)	62.0 (50.0–72.0)	1.000 (0.982–1.017)	0.977	0.972 (0.950–0.994)	0.013
Diabetes mellitus, *n* (%)						
No	150 (75.8)	58 (71.6)	Ref	Ref		
Yes	48 (24.2)	23 (28.4)	1.239 (0.692–2.218)	0.470	NA	NA
Vaccine type, *n* (%)						
Pfizer	145 (73.2)	29 (35.8)	Ref	Ref	Ref	Ref
Moderna	53 (26.8)	52 (64.2)	4.906 (2.823–8.525)	<0.001	4.941 (2.698–9.047)	<0.001
Second-dose response, *n* (%)	60	211				
Type of patient						
Kidney transplant	50 (83.3)	83 (39.3)	Ref	Ref	Ref	Ref
HD	9 (15.0)	91 (43.1)	6.091 (2.822–13.149)	<0.001	6.181 (2.828–13.511)	<0.001
PD	1 (1.7)	37 (17.5)	22.289 (2.966–167.528)	0.003	18.870 (2.483–143.380)	0.005
				Overall* <0.001		Overall* <0.001
Gender, *n*						
Male	32 (53.3)	133 (63.0)	Ref	Ref	NA	NA
Female	28 (46.7)	78 (37.0)	0.670 (0.376–1.196)	0.176		
Age (years), median (IQR)	58.5 (50.0–68.0)	64.0 (52.5–72.0)	1.021 (1.002–1.041)	0.031	NA	NA
Diabetes mellitus, *n* (%)						
No	51 (85.0)	153 (72.5)	Ref	Ref	NA	NA
Yes	9 (15.0)	58 (27.5)	2.148 (0.994–4.641)	0.052		
Vaccine type, *n* (%)						
Pfizer	50 (83.3)	121 (57.3)	Ref	Ref	Ref	Ref
Moderna	10 (16.7)	90 (42.7)	3.719 (1.789–7.730)	<0.001	3.428 (1.587–7.406)	0.002

*Based on an overall likelihood ratio test.
NA, not applicable; Ref, reference.

A study of individuals in the multi state Mayo Clinic Health System revealed that the mRNA-1273 vaccine was associated with a lower incidence of SARS-CoV-2 infection ($P = 0.0034$) as well as with a significant two-fold risk reduction against breakthrough infection compared with BNT162b2 [12]. Kaiser et al. [13] compared antibody titers between both mRNA vaccines after full vaccination in HD patients [13]. They reported 2.39-fold ($P < 0.005$) higher anti-S-antibody titers in patients vaccinated with mRNA-1273. Hsu et al. [16] also reported a significantly greater seroconversion rate in dialysis patients vaccinated with mRNA-1273 versus BNT162b2 (96% versus 87%; $P < 0.001$). Furthermore, Dębska-Ślizień et al. [15] described the type of vaccine as one of the major determinants of humoral response to mRNA SARS-CoV-2 vaccination in KTRs, showing higher immunization after vaccination with two doses of mRNA-1273 compared with BNT162b2. Rituximab-treated patients appeared to more often develop SARS-CoV-2 anti-spike antibodies after being vaccinated with mRNA-1273 (56.5%) versus BNT162b2 (23.5%) ($P < 0.05$) [14].

Whether observed differences between these two mRNA vaccines relate to a different mRNA sequence, a difference in dosage (100 μg mRNA in Moderna versus 30 μg mRNA in Pfizer) or a difference in vaccine composition remains to be investigated. Furthermore, future studies are needed to assess whether our observed differences are associated with better clinical protection. Meanwhile, mRNA-1273 might be the preferred vaccine in kidney transplant and dialysis patients.

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Table 4. Multiple linear mixed model for factors associated with mean (log-transformed) antibody levels after the first and second dose of SARS-CoV-2 mRNA vaccine

	Multivariable analysis			
Covariates	Regression parameter	Standard error	*t*-Statistic	P-value
Intercept	1.715	0.355	4.828	< 0.001
Type of patient				
Kidney transplant	Ref	Ref	Ref	Ref
HD	0.730	0.122	5.972	< 0.001
PD	0.822	0.148	5.549	< 0.001
				Overall*
				< 0.001
Age	-0.019	0.006	-3.358	< 0.001
Vaccine type				
Pfizer	Ref	Ref	Ref	Ref
Moderna	0.289	0.102	2.828	0.005
Second dose				
No	Ref	Ref	Ref	
Yes	0.092	0.332	0.276	0.783
Age*second dose	0.018	0.005	3.351	< 0.001

*Based on an overall partial *F*-test.

Ref, reference.

First, a multiple linear mixed model was considered to establish factors associated with mean (log-transformed) antibody levels after the first and second dose of SARS-CoV-2 mRNA vaccine. Both HD patients (+0.730 units) and PD patients (+0.822 units) showed higher mean log-transformed antibody levels compared with kidney transplant recipients ($P < 0.001$). Mean log-transformed antibody (Ab) levels were 0.289 units higher for Moderna versus Pfizer vaccination ($P = 0.005$) and the vaccine effect was found to be not significantly different across vaccination moments. The age-effect vanished after the second vaccine dose [decrease of 0.002 units (S.E. 0.004) in mean log-transformed antibody concentration for an increase of 1 year in age, P-value = 0.668]. The mean log-transformed antibody concentration increased with 1.149 units (S.E. 0.082; $P < 0.001$) after a second vaccination, as compared with the mean antibody concentration after the first dose, for an individual of age 60 (irrespective of the vaccine used and the type of patient). Note that since the second-dose effect is age-dependent, the effect should be interpreted conditional on age.

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DATA AVAILABILITY STATEMENT

Requests for original and additional data should be directed to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared. Furthermore, this article has not been published previously in whole or part.

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