# Supplementary Material

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# Supplemental Methods

## Definitions of comorbid disease

Coronary artery disease was defined as acute coronary syndrome or symptom-driven revascularization by percutaneous coronary intervention or coronary artery bypass grafting.

Heart failure was defined as left ventricular ejection fraction <45% or an unscheduled hospital admission for heart failure, characterized by typical signs and symptoms and diagnostic testing consistent with a diagnosis of heart failure, including elevated natriuretic peptides, radiological evidence of congestion or echocardiographic evidence of elevated filling pressures.

Cerebrovascular disease was defined as stroke (sudden onset of a focal neurological deficit consistent with the territory of a major cerebral artery) or carotid artery revascularization.

Peripheral vascular disease was defined as clinical evidence of limb ischemia due to atherosclerotic vascular disease requiring revascularization or amputation.

Abdominal vascular disease was defined as revascularization for or evidence of bowel ischemia, or repair or presence of an aortic aneurysm >5.5 cm.

Diabetes was defined as a hemoglobin A1c level of ≥6.5% and/or the use of oral antidiabetic drugs and/or insulin.

Chronic obstructive pulmonary disease was defined as presence of airflow obstruction caused by chronic bronchitis or emphysema and at least GOLD stage I.

Liver disease was defined as a Child-Pugh score of at least Class A.

Immunodeficiency was defined as solid organ transplantation with current use of immunosuppressive drugs, allogeneic stem cell transplantation, HIV infection with CD4 <200/µL, primary immunodeficiency or use of immunosuppressive therapy or chemotherapy for other reasons.

Malignancy was defined as solid or hematologic malignancy active or requiring therapy (surgery, radiotherapy or chemotherapy) within the past 5 years. Hormonal therapy alone without signs of active disease and basocellular epitheliomas of the skin were not taken into consideration.

## Laboratory analyses

Serum albumin was measured in all participating centers with the bromocresol green (BCG) colorimetric assay (Roche Diagnostics, Mannheim, Germany).

# Supplemental Tables

## Supplemental **Table 1: Laboratory Parameters at Baseline**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | All hemodialysis(n=543) | BNT162b2 recipients (n=322) | mRNA-1273 recipients (n=221) | \*\*P |
| Hemoglobin, g/dL Ferritin, ng/mLTransferrin saturation, % | 11.2 (10.5-11.9)387 (247-580)23 (18-29) | 11.2 (10.4-11.9)387 (226-559)23 (17-28) | 11.2 (10.5-11.8)387 (256-628)24 (19-30) | 0.9450.2850.054 |
| C3, g/LC4, g/LLeucocyte count, n/µLLymphocyte count, n/µLImmunoglobulin G, g/LImmunoglobulin M, g/LImmunoglobulin A, g/LExtra fraction, % (no.) | 1.01 (0.87-1.13)0.25 (0.20-0.30)6160 (4848-7900)1080 (768-1403)9.2 (7.5-11)0.59 (0.36-0.89)2.1 (1.5-2.9)14 (73) | 1.04 (0.93-1.16)0.24 (0.20-0.30)6400 (5000-8000)1000 (700-1385)9.4 (7.6-12)0.60 (0.39-0.94)2.1 (1.5-3.0)16 (50) | 0.96 (0.83-1.08)0.25 (0.20-0.31)5880 (4543-7518)1125 (830-1490)9.0 (7.4-11)0.54 (0.31-0.85)2.1 (1.5-2.8)11 (23) | <0.0010.3950.0140.0030.2010.0310.7400.073 |
| Serum albumin, g/L | 39 (37-41) | 39 (37-41) | 40 (37-42) | 0.001 |
| iPTH – pg/mL25-hydroxy-vitamin D – ng/mL | 270 (162-432)32 (26-42) | 287 (173-427)32 (26-42) | 254 (140-444)29 (24-43) | 0.2670.325 |
| Hemoglobin A1c – mmol/mol\* | 6.2 (5.6-6.9) | 6.3 (5.6-6.9) | 6.2 (5.6-7.0) | 0.646 |

Numbers displayed are median (interquartile range); 1in patients with diabetes; \*\*according to Fisher’s exact test or Mann-Whitney U test.

## Supplemental **Table 2: Baseline immunosuppressant medication**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Immunosuppressant | All hemodialysis(n=543) | BNT162b2 recipients (n=322) | mRNA-1273 recipients (n=221) | \*P |
|  Glucocorticoid – % (no.)Calcineurin inhibitor – % (no.)Biological – % (no.)Other – % (no.) | 6.4 (35)3.7 (20)1.1 (6)1.8 (10) | 6.8 (22)3.4 (11)1.5 (5)2.2 (7) | 5.9 (13)4.1 (9)0.5 (1)1.4 (3) | 0.7240.8170.4090.747 |

\*according to Fisher’s exact test.

## **Supplemental Table 3: Humoral response in Covid-19-naïve patients**: proportion of patients with titer above threshold

|  |  |  |  |
| --- | --- | --- | --- |
|  | Hemodialysis(n=478) | Healthy volunteers(n=75) | \*P |
| BNT162b2 recipients (n=285) | mRNA-1273 recipients (n=193) | P | BNT162b2 recipients (n=37) | mRNA-1273 recipients (n=38) | P |  |
| % >50 AU/mL 4/5 weeks 8/9 weeks% >1050 AU/mL 4/5 weeks 8/9 weeks% >3550 AU/mL 4/5 weeks 8/9 weeks% >4160 AU/mL 4/5 weeks 8/9 weeks% >6950 AU/mL 4/5 weeks 8/9 weeks | 74.4% (212)91.6% (261)36.8% (105)62.5% (178)18.6% (53) 30.2% (86)15.1% (43)26.0% (74)   7.0% (20) 12.6% (36)  | 86.0% (166)97.4% (188)62.2% (120)76.2% (147)41.5% (80) 54.9% (106)41.5% (80) 50.8% (98) 31.1% (60) 37.8% (73) |  P=0.0020P=0.010P<0.0001P=0.0019P<0.0001P<0.0001P<0.0001P<0.0001P<0.0001P<0.0001 | 100.0% (37) 100.0% (37)94.6% (35) 100.0% (37)  83.8% (31)  91.9% (34)  78.4% (29) 83.8% (31)  64.9% (24)  56.8% (21)  | 100.0% (38) 100.0% (38)  100.0% (38) 100.0% (38) 97.4% (37) 100.0% (38) 97.4% (37) 97.4% (37) 94.7% (36) 92.1% (35)  | -- --P=0.942--P=0.075P=0.953P=0.033P=0.075P=0.0046P=0.0015  |  P=0.996P=0.994P=0.938P=0.996P=0.457P=0.935P=0.397P=0.429P=0.565P=0.303 |

\*Testing the interaction between vaccine type and subject type

## **Supplemental Table 4: Cellular response (Antigen 1)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Hemodialysis(n=543) | Healthy volunteers(n=75) | \*P |
| BNT162b2 recipients (n=322) | mRNA-1273 recipients (n=221) | P | BNT162b2 recipients (n=37) | mRNA-1273 recipients (n=38) | P |
| GMCOverall Baseline 4/5 weeks 8/9 weeksCovid-naïve Baseline 4/5 weeks 8/9 weeksCovid-experienced Baseline 4/5 weeks 8/9 weeks | 0.0150.3740.1180.0120.3210.1010.1131.2000.418 | 0.0170.6230.2280.0130.5710.1990.1261.2160.691 | P=0.159 P=0.0019P<0.0001P=0.013 P=0.0008P<0.0001P=0.836 P=0.979 P=0.308 | 0.0140.8470.2190.0140.8480.219------  | 0.0121.7380.5690.0121.7280.569------  | P=0.117P=0.013P=0.0008P=0.117P=0.013P=0.0008------ | P=0.230P=0.653P=0.479P=0.014P=0.759P=0.495------ |
| % ≥ 0.15 IU/mlOverall 4/5 weeks 8/9 weeksCovid-naïve 4/5 weeks 8/9 weeksCovid-experienced 4/5 weeks 8/9 weeks | 66.4% (211/318)42.1% (130/309)64.1% (180/281)37.5% (103/275)83.8% (31/37)79.4% (27/34) | 77.3% (167/216)60.6% (126/208)76.4% (146/191)58.4% (108/185)84.0% (21/25)78.3% (18/23) | P=0.0060P<0.0001P=0.0045P<0.0001P=0.999 P=0.999 | 91.7% (33/36) 62.2% (23/37) 91.7% (33/36) 62.2% (23/37) ----  | 94.6% (35/37) 86.8% (33/38)94.6% (35/37) 86.8% (33/38)----  | P=0.487P=0.018P=0.487P=0.018---- | P=0.932P=0.298P=0.889P=0.383---- |

\*Testing the interaction between vaccine type and subject type

## Supplemental **Table 5: Characteristics of Covid-19-naïve patients with adequate and impaired immune response**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristics | Adequatehumoral + cellular(n=120, 26%) | Adequate humoral(n=46, 10%) | Adequate cellular(n=114, 25%) | Impairedhumoral + cellular (n=180, 39%) | P\* |
| Age – yr. | 73.6 (63.7-80.1) | 75.2 (59.0-82.1) | 75.5 (68.3-82.0) | 78.3 (69.2-83.6) | P=0.0067 |
| Male – % (no.)  | 66.7% (80)  | 56.5% (26) | 50.0% (57) | 69.4% (125) | P=0.0051 |
| Ethnicity – Other % (no.)  | 5.8% (7)  | 6.5% (3)  | 1.8% (2) | 4.4% (8) | P=0.325 |
| Nursing home resident – % (no.) | 0.0% (0)  | 4.3% (2)  | 0.0% (0)  | 2.2% (4) | P=0.044 |
| BMI – kg/m2 | 26.2 (23.5-29.6) | 26.2 (23.0-31.5) | 25.7 (22.8-28.9) | 24.9 (21.9-28.8) | P=0.150 |
| Smoking – % (no.) History of Active | 53.3% (64)8.3% (10)  | 41.3% (19)13.0% (6) | 34.2% (39)15.8% (18) | 41.7% (75)16.1% (29) | P=0.091 |
| Comorbid disease – % (no.) Coronary artery disease Heart failure Cerebrovascular disease Peripheral vascular disease Abdominal vascular disease COPD Diabetes type 1, type 2 Liver disease Immunodeficiency Malignancy | 30.0% (36) 18.3% (22) 20.8% (25) 17.5% (21) 8.3% (10) 13.3% (16) 34.2% (41) 1.7% (2) 3.3% (4) 11.7% (14)  | 32.6% (15) 19.6% (9) 17.4% (8) 8.7% (4) 10.9% (5) 0.0% (0) 28.3% (13) 4.3% (2) 8.7% (4) 10.9% (5)  | 36.8% (42) 14.9% (17) 17.5% (20) 14.0% (16) 6.1% (7) 6.1% (7) 36.8% (42) 1.8% (2) 7.0% (8) 14.0% (16)  | 40.6% (73)26.7% (48)23.3% (42)27.8% (50)13.9% (25)12.8% (23)47.8% (86)3.3% (6)11.1% (20)22.2% (40) | P=0.293 P=0.091 P=0.656 P=0.0041P=0.163 P=0.0081P=0.026 P=0.622 P=0.087P=0.057 |
| Hepatitis B vaccine non-responder – % (no.) | 5.8% (6)  | 5.1% (2)  | 7.2% (7) | 19.2% (29) | P=0.0020 |
| Influenza vaccination in 2020 – % (no.) | 88.3% (106) | 84.8% (39) | 94.7% (108) | 91.1% (164) | P=0.376 |
| ESRD Causes – % (no.) Diabetes Vascular disease Glomerular disease Tubulointerstitial disease ADPKD or other genetic disease Other | 24.2% (29)35.0% (42) 5.8% (7) 15.0% (18) 5.8% (7) 14.2% (17) | 19.6% (9) 30.4% (14) 2.2% (1) 21.7% (10)10.9% (5) 15.2% (7) | 23.7% (27)30.7% (35) 7.9% (9) 11.4% (13) 3.5% (4) 22.8% (26) | 25.0% (45)37.2% (67) 7.2% (13)12.8% (23) 6.1% (11)11.7% (21) | P=0.444 |
| Dialysis vintage – yr. | 2.01 (0.92-3.56) | 1.94 (1.05-3.88) | 1.84 (0.77-4.97) | 2.72 (1.19-5.25) | P=0.117 |
| Hemodiafiltration – % (no.) | 55.0% (66)  | 58.7% (27)  | 65.8% (75) | 57.8% (104) | P=0.158 |
| Online Kt/V urea | 1.33 (1.15-1.50) | 1.38 (1.20-1.60) | 1.40 (1.20-1.65) | 1.36 (1.18-1.60) | P=0.099 |
| Medication – % (no.) ACEI/ARB Immunosuppressive drugs | 30.0% (36) 3.3% (4)  | 26.1% (12) 8.7% (4)  | 33.3% (38) 10.5% (12) | 27.8% (50)16.1% (29) | P=0.732 P=0.0034 |
| Lymphocyte count, n/µLImmunoglobulin G, g/LSerum albumin, g/L | 1200 (900-1600)  9.2 (7.9-11.1) 39.6 (37.6-41.4) | 1040 (750-1400) 10.3 (8.0-11.2) 39.8 (36.9-41.8) | 1130 (800-1510)  8.9 (7.2-11.1) 39.6 (37.7-41.5) | 1000 (700-1300)  8.9 (7.3-11.5) 38.4 (36.2-40.0) | P=0.0002P=0.464P=0.0003 |
| mRNA-1273 vaccine  | 61.7% (74) | 43.5% (20) | 36.8% (42) | 27.2% (49) | P<0.0001 |

Numbers displayed are median (interquartile range) unless otherwise specified; adequate humoral response is defined as anti-S IgG >4160 AU/ml; adequate cellular response is defined as QuantiFERON ≥0.15 IU/ml; \*according to Fisher’s exact test or Kruskal-Wallis test.

## Supplemental Table 6: Multivariate analysis of factors associated with combined impaired humoral and cellular response\* at 8/9 weeks

**A. All hemodialysis patients**

|  |  |
| --- | --- |
| **Variable** | **Impaired humoral AND cellular response** |
| β (SE) | Wald χ²-statistic | P |
| Immunosuppressive drugsVaccine type (mRNA-1273)Hepatitis B vaccine non-responderDialysis vintageSARS-CoV-2 experiencedDiabetesSerum albuminLn(Lymphocyte count) | +1.597 (0.367)-0.909 (0.239)+1.195 (0.343)+0.101 (0.030)-1.340 (0.411)+0.687 (0.232)-0.099 (0.036)-0.541 (0.251) | 19.0014.4512.1211.0110.62 8.77 7.78 4.63 | P<0.0001P=0.0001P=0.0005P=0.0009P=0.0011P=0.0031P=0.0053P=0.031  |

**B. Covid-naive hemodialysis patients**

|  |  |
| --- | --- |
| **Variable** | **Impaired humoral AND cellular response** |
| β (SE) | Wald χ²-statistic | P |
| Vaccine type (mRNA-1273)Immunosuppressive drugsHepatitis B vaccine non-responderDialysis vintageDiabetesSerum albuminLn(Lymphocyte count) |  -1.058 (0.254)+1.491 (0.383)+1.330 (0.376)+0.112 (0.032)+0.798 (0.245)-0.111 (0.038)-0.581 (0.265) |  17.3815.1912.4811.9310.63 8.32 4.82 |  P<0.0001P<0.0001P=0.0004P=0.0006P=0.0011P=0.0039P=0.028 |

\*Defined as anti-S IgG ≤4160 AU/ml and QuantiFERON <0.15 IU/ml.

## Supplemental Table 7: Immune response at 8/9 weeks in Covid-19-experienced dialysis patients according to disease severity

|  |  |  |  |
| --- | --- | --- | --- |
|  | **N** | **Humoral response** *GMT* | **QuantiFERON** *GMC* |
| Positive serology or QuantiFERONPCR documented - mild diseasePCR documented - severe disease*Significance* | 242417 | 32374352255897*P<0.0001* | 0.1961.3662.207*P<0.0001* |

# Supplemental Figures

## Supplemental Figure 1: Study flow chart



## Supplemental Figure 2: Immune response by age category

Geometric mean titers (GMT) of the SARS-CoV-2 spike antibody (Panel A) and geometric mean concentration (GMC) of the QuantiFERON response to Antigen 2 (Panel B) at week 8/9 after BNT162b2 or mRNA-1273 vaccination in hemodialysis patients (red) and healthy volunteers (green) for the different age categories.

**A**



**B**



## Supplemental Figure 3: Cellular response

Median (interquartile range) QuantiFERON response to Antigen 1 at week 4 and week 8 after BNT162b2 vaccination in hemodialysis patients (red dashed line) and healthy volunteers (red solid line) and at week 5 and week 9 after mRNA-1273 vaccination in hemodialysis patients (green dashed line) and healthy volunteers (green solid line).

