**Plaque reduction neutralization test (PRNT)**

CaCo-2 cells (DSMZ, Braunschweig, Germany, no: ACC 169) were cultured in Minimum Essential Medium (MEM) supplemented with 10% fetal calf serum (FCS), 4 mM L-glutamine, 100 IU/mL of penicillin, and 100 µg/mL of streptomycin at 37°C and 5% CO2. All culture reagents were obtained from Sigma (St. Louis, MO, USA). For the experimental procedure of the neutralization assay, FCS supplementation of the culture medium was reduced to 1% and serum samples were inactivated for 30 min at 56°C. Inactivated sera were diluted 1:10 in media and thereafter serially diluted (1:2) and incubated with 4000 TCID50/mL of the delta (B.1.617.2) or omicron variant (B.1.1.529; BA.1) of SARS-CoV-2 for one hour before infecting CaCo-2 cells. 72 hours after inoculation, infected CaCo-2 cells were analysed for cytopathic effect (CPE) formation by light microscopy to define the neutralization titer. Each serum sample was tested in duplicate, in case of discrepancies the lowest observed titer was chosen.

**Table S1** - Spearman correlation analysis between age of either heterologous (AZ/BNT) or homologous (2xModerna) immunised participants and levels of SARS-CoV-2 anti-Spike IgG antibodies for all three follow up examinations.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Follow up I  (1 month) | Follow up II  (3 months) | Follow up III  (6 months) |
| AZ/BNT | **p=0.0107**  r=-0.1622  (-0.2847 to -0.03446 95% CI) | p=0.1187  r=-0.1065  (-0.2403 to 0.03139 95% CI) | p=0.1593  r=0.1809  (-0.07959 to 0.4183 95% CI) |
| 2xModerna | **p=0.0403**  r=-0.2229  (-0.4216 to -0.003912 95%CI) | **p=0.0090**  r=-0.2997  (-0.4983 to -0.07124 95% CI) | p=0.3156  r=-0.1548  (-0.4392 to -0.1577 95% CI) |

**Table S2** -Sex stratified mean SARS-CoV-2 anti-Spike IgG concentrationsof either heterologous (AZ/BNT) or homologous (2xModerna) immunised participants for all three follow up examinations, including p-values of a conducted unpaired t-test.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Follow up I  (1 month) | | Follow up II  (3 months) | | Follow up III  (6 months) | |
|  | SARS-CoV-2 anti-Spike IgG BAU/mL | | | | | |
| Sex | male | female | male | female | male | female |
| AZ/BNT | 1730 (n=66) | 1718  (n=181) | 632.1  (n=48) | 552.9  (n=168) | 278.8  (n=18) | 182.4  (n=44) |
| p=0.5867 | | p=0.4910 | | **p=0.0162** | |
| 2xModerna | 3473  (n=23) | 3301  (n=62) | 1165  (n=21) | 1345  (n=54) | 596.1  (n=13) | 596.9  (n=31) |
| p=0.9461 | | p=0.3127 | | p=0.9142 | |

**Table S3** –PRNT titers against SARS-CoV-2 delta (B.1.617.2) of heterologous and homologous vaccinated participants at Follow-up II (3 months) and Follow-up III (6 months) after second dose.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Follow up II  (3 months) | | Follow up III  (6 months) | |
| AZ/BNT  n=216 | 2xModerna  n=76 | AZ/BNT  n=62 | 2xModerna  n=44 |
| PRNT titer | delta (B.1.617.2) | | | |
| neg. | 1.9%  (4/216) | 1.3%  (1/76) | 48.4%  (30/62) | 9.1%  (4/44) |
| 1:10 | 9.3%  (20/216) | 10.5%  (8/76) | 27.4%  (17/62) | 38.6%  (17/44) |
| 1:20 | 18.1%  (39/216) | 31.6%  (24/76) | 16.1%  (10/62) | 31.8%  (14/44) |
| 1:40 | 26.9%  (58/216) | 28.9%  (22/76) | 8.1%  (5/62) | 9.1%  (4/44) |
| 1:80 | 25.9%  (56/216) | 19.7%  (15/76) | 0%  (0/62) | 4.5%  (2/44) |
| 1:160 | 9.7%  (21/216) | 5.3%  (4/76) | 0%  (0/62) | 4.5%  (2/44) |
| 1:320 | 5.1%  (11/216) | 1.3%  (1/76) | 0%  (0/62) | 2.3%  (1/44) |
| 1:640 | 2.8%  (6/216) | 0%  (0/76) | 0%  (0/62) | 0%  (0/44) |
| 1:1280 | 0.5%  (1/216) | 1.3%  (1/76) | 0%  (0/62) | 0%  (0/44) |

neg. = negative

**Table S4**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | AZ/2xBNT  n=97\* | | AZ/BNT/Moderna  n=10 | | 3xModerna  n=10\*\* | | 2xModerna/BNT  n=8 | |
| PRNT titer | delta (B.1.617.2) | omicron (B.1.1.529; BA.1) | delta (B.1.617.2) | omicron (B.1.1.529; BA.1) | delta (B.1.617.2) | omicron (B.1.1.529; BA.1) | delta (B.1.617.2) | omicron (B.1.1.529; BA.1) |
| neg. | 0%  (0/97) | 8.3% (8/96) | 0%  (0/10) | 20%  (2/10) | 0%  (0/10) | 10%  (1/10) | 0%  (0/8) | 12.5%  (1/8) |
| 1:10 | 10.3%  (1/97) | 20.8%  (20/96) | 0%  (0/10) | 20%  (2/10) | 0%  (0/10) | 10%  (1/10) | 0%  (0/8) | 0%  (0/8) |
| 1:20 | 5.2%  (5/97) | 36.5%  (35/96) | 0%  (0/10) | 20%  (2/10) | 0%  (0/10) | 10%  (1/10) | 0%  (0/8) | 37.5%  (3/8) |
| 1:40 | 8.2%  (8/97) | 21.9%  (21/96) | 10%  (1/10) | 20%  (2/10) | 10%  (1/10) | 20%  (2/10) | 0%  (0/8) | 25%  (2/8) |
| 1:80 | 20.6%  (20/97) | 10.4%  (10/96) | 30%  (3/10) | 10%  (1/10) | 0%  (0/10) | 50%  (5/10) | 0%  (0/8) | 12.5%  (1/8) |
| 1:160 | 24.7%  (24/97) | 1%  (1/96) | 0%  (0/10) | 10%  (1/10) | 40%  (4/10) | 0%  (0/10) | 50%  (4/8) | 12.5%  (1/8) |
| 1:320 | 28.9%  (28/97) | 1%  (1/96) | 50%  (5/10) | 10%  (0/10) | 20%  (2/10) | 0%  (0/10) | 25%  (2/8) | 0%  (0/8) |
| 1:640 | 8.2%  (8/97) | 0%  (0/96) | 0%  (0/10) | 0%  (0/10) | 20%  (2/10) | 0%  (0/10) | 12.5%  (1/8) | 0%  (0/8) |
| 1:1280 | 3.1%  (3/97) | 0%  (0/96) | 10%  (1/10) | 0%  (0/10) | 10%  (1/10) | 0%  (0/10) | 12.5%  (1/8) | 0%  (0/8) |

\*for one sample there was not enough sample volume for the PRNT against omicron

\*\*for one sample there was not enough sample volume for the PRNT against delta and omicron

neg. = negative

**Figure S1** -Levels of SARS-CoV-2 anti-Spike IgG in BAU/mL including mean after receiving a third dose of an mRNA-based vaccine. P-values of a Kruskal-Wallis and post-hoc Dunn's multiple comparisons test are also shown.

