Supplementary Appendix

Supplement to: Zou J, Kurhade C, Patel S, et al. Neutralization of BA.4–BA.5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 with bivalent vaccine. N Engl J Med. DOI: 10.1056/NEJMc2214916

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Materials Table of Contents

Supplementary materials

Methods

Biosafety level-3 operation

All virus work was performed in a biosafety level 3 (BSL-3) laboratory with redundant fans in the biosafety cabinets at the University of Texas Medical Branch at Galveston. All personnel wore powered air-purifying respirators (Breathe Easy, 3M) with Tyvek suits, aprons, booties, and double gloves.

Cells

Vero E6 (ATCC® CRL-1586) purchased from the American Type Culture Collection (ATCC, Bethesda, MD) and Vero E6 cells expressing TMPRSS2 purchased from SEKISUI XenoTech, LLC were maintained in a high-glucose Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal bovine serum (FBS; HyClone Laboratories, South Logan, UT) and 1% penicillin/streptomycin at 37°C with 5% CO_2. Culture media and antibiotics were purchased from Thermo Fisher Scientific (Waltham, MA). The cell line was tested negative for *Mycoplasma*.

Human Serum

In participants >55 years of age who previously received three 30-µg BNT162b2 doses, serum samples were collected just prior to and 1 month post-boost with a 4th dose booster of monovalent original 30-µg BNT162b2 (Study C4591031; ClinicalTrials.gov identifier: NCT04955626) or 30-µg BNT162b2 bivalent BA.4/BA.5 vaccine (15 µg original with 15 µg BA.4/BA.5) (Study C4591044; ClinicalTrials.gov identifier: NCT05472038). Study C4591031 compared the original vaccine and Omicron BA.1 modified vaccines and supported authorization of the Omicron BA.1 bivalent vaccine; BA.1 bivalent boosted sera were not analyzed in this study. Study C4591044 groups support the post-authorization commitment assessment of safety and immunogenicity for the Omicron BA.4/5 bivalent vaccine. The protocol and informed consent were approved by

institutional review boards for each of the investigational centers participating in the study. The study was conducted in compliance with all International Council for Harmonisation Good Clinical Practice guidelines and the ethical principles of the Declaration of Helsinki.

Participants in this part of the study were ≥18-years-old and had received three prior 30-μg BNT162b2 doses, within the most recent 150 to 365 days before randomization; were willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures; were healthy; and were capable of giving personal signed informed consent. Participants could not have received or planned to receive radiotherapy or immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids; or blood/plasma products, immunoglobulin, or monoclonal antibodies, from 60 days before study intervention administration.

The median time between dose-3 and -4 for Study C4591031 and C4591044 was 6.3 and 11.3 months, respectively. All participants were screened by SARS-CoV-2 nucleocapsid Ig serological test for preexisting SARS-CoV-2 or RT-PCR for existing infection. The subset of participant's sera (approximately 40 per vaccine group) for neutralization testing were selected to ensure equal distribution between those with and without evidence of infection at baseline (pre-dose-4) by either test and medical history of COVID-19. **Table S1** summarizes the detailed demographic information (e.g., age and gender) of all participants. Human sera were heat-inactivated at 56°C for 30 min before the neutralization test.

Recombinant Omicron sublineages-mNG SARS CoV-2 viruses

Recombinant Omicron sublineage BA.4/5-, BA.4.6-, BA.2.75.2-, BQ.1.1-, and XBB.1-spike mNG SARS-CoV-2s was constructed by engineering the complete spike gene from the indicated

variants into an infectious cDNA clone of mNG USA-WA1/2020 and reported previously[1-5]. Viruses were rescued post 2-3 days after electroporation and served as P0 stock. P0 stock was further passaged once on Vero E6 cells to produce P1 stock. The spike gene was sequenced from all P1 stock viruses to ensure no undesired mutation. The infectious titer of the P1 virus was quantified by fluorescent focus assay on Vero E6 cells. The P1 virus was used for the neutralization test.

Fluorescent focus reduction neutralization test (FFRNT)

Neutralization titers of human sera were measured by FFRNT using the USA-WA1/2020-, BA.4/5, BA.4.6-, BA.2.75.2-, BQ.1.1- and XBB.1-spike mNG SARS-CoV-2s. All sera were tested sequentially, USA-WA1/2020 and BA.4/5 followed by the remaining Omicron sublineages. The details of the FFRNT protocol were reported previously[1,5-8]. Briefly, 2.5×10^4 Vero E6 cells per well were seeded in 96-well plates (Greiner Bio-one™). The cells were incubated overnight. On the next day, each serum was 2-fold serially diluted in the culture medium with the first dilution of 1:20 (final dilution range of 1:20 to 1:20,480). The diluted serum was incubated with 100-150 FFUs of mNG SARS-CoV-2 at 37 °C for 1 h, after which the serum virus mixtures were loaded onto the pre-seeded Vero E6 cell monolayer in 96-well plates. After 1 h infection, the inoculum was removed and 100 μl of overlay medium (supplemented with 0.8% methylcellulose) was added to each well. After incubating the plates at 37 °C for 16 h, raw images of mNG foci were acquired using Cytation™ 7 (BioTek) armed with 2.5× FL Zeiss objective with a wide-field of view and processed using the Gene 5 software settings (GFP [469,525] threshold 4000, object selection size 50-1000 μm). The foci in each well were counted and normalized to the non-serum-treated controls to calculate the relative infectivities. The $FFRNT_{50}$ value was defined as the minimal serum dilution that suppressed >50% of fluorescent foci. The neutralization titer of each serum was determined in duplicate assays, and the geometric mean was taken. All attempts at

replication were successful. Supplementary Table 2 summarizes the $FFRNT_{50}$ results. Data were initially plotted in GraphPad Prism 9 software and assembled in Adobe Illustrator.

Figure S1.

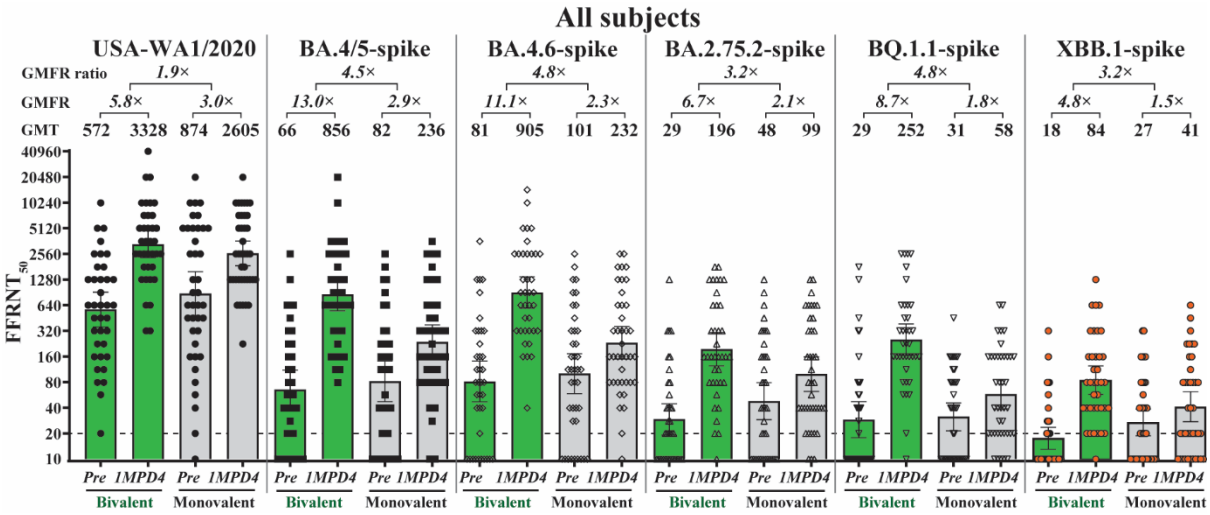

Figure S1. $FFRNT_{50}$s of all subjects regardless of infection status. All sera samples, regardless of previous SARS-COV-2 infection, were analyzed for neutralizing titers against USA-WA1/2020 and indicated Omicron sublineages. The bar heights and the numbers above indicate geometric means of neutralization titers (GMTs). The whiskers indicate 95% CI. Green bars, 4th dose vaccination with bivalent; gray bars, 4th dose vaccination with monovalent BNT16b2. $FFRNT_{50}$s against USA-WA1/2020, BA.4/5-spike, BA.4.6-spike, BA.2.75.2-spike, BQ.1.1-spike, and XBB.1-spike are shown as black circle, black square, rhombus, up-triangle, down-triangle, and red circle with black outline, respectively. Pre, serum samples collected on the day of booster; 1MPD4, one month post dose 4. GMFR, geometric mean fold rises (ratio of titers at 1MPD4 relative to Pre). Numbers above GMFRs indicate the ratios between GMFRs of bivalent to GMFRs of monovalent. The lower bounds of the two-sided 95% CIs for GMFR of bivalent or monovalent booster against USA-WA1/2020, BA.4/5-spike, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 were all >1.

Table S1. Demographics information of subjects.

Characteristic	Vaccine Group	
	C4591044 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg (N[a]=38) n[b] (%)	**C4591031 BNT162b2 30 µg (N[a]=40) n[b] (%)**
Sex		
Male	24 (63.2)	17 (42.5)
Female	14 (36.8)	23 (57.5)
Race		
White	31 (81.6)	36 (90.0)
Black or African American	4 (10.5)	2 (5.0)
American Indian or Alaska Native	1 (2.6)	0
Asian	1 (2.6)	2 (5.0)
Multiracial	1 (2.6)	0
Ethnicity		
Hispanic/Latino	3 (7.9)	9 (22.5)
Non-Hispanic/non-Latino	35 (92.1)	31 (77.5)
Age at vaccination (years)		
Mean (SD)	66.5 (6.82)	65.4 (5.80)
Median	66.0	65.5
Min, max	(57, 79)	(56, 79)
Baseline SARS-CoV-2 status		
Positive[c]	19 (50.0)	20 (50.0)
Negative[d]	19 (50.0)	20 (50.0)
Time from the last dose of BNT162b2 (received prior to the study) to the study vaccination (months)		
n	38	40
Mean (SD)	10.9 (1.41)	6.9 (1.82)
Median	11.3	6.3
Min, max	(5.5, 13.0)	(5.4, 13.1)

Characteristic	Vaccine Group	
	C4591044 BNT162b2 Bivalent (WT/OMI BA.4/BA.5) 30 µg (N^a=38) n^b (%)	C4591031 BNT162b2 30 µg (N^a=40) n^b (%)
≥5 to <7 Months	1 (2.6)	30 (75.0)
≥7 to <9 Months	2 (5.3)	5 (12.5)
≥9 to ≤12 Months	31 (81.6)	4 (10.0)
>12 Months	4 (10.5)	1 (2.5)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test

a. N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of participants with the specified characteristic.
c. Positive N-binding antibody result at baseline, positive NAAT result at baseline, or medical history of COVID-19.
d. Negative N-binding antibody result at baseline, negative NAAT result at baseline, and no medical history of COVID-19.

Table S2. $FFRNT_{50}$ values of all subjects received bivalent BA.4/5 booster.

ID	AGE (years)	Time since last vaccine (months)	SEX	Booster	*$FFRNT_{50}$												With infection at baseline (pre Dose 4)
					USA-WA1/2020		BA.4/5-spike		BA.4.6-spike		BA.2.75.2-spike		BQ.1.1-spike		XBB.1-spike		
					Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	
1	73	10.8	M	Bivalent	5120	5120	640	2560	1280	5120	320	905	320	1280	57	160	YES
2	78	11.6	M	Bivalent	640	20480	80	3620	160	5120	40	1280	40	1810	20	640	YES
3	76	11.3	M	Bivalent	1280	7241	40	905	80	640	40	160	10	320	10	80	NO
4	61	11.0	F	Bivalent	905	3620	113	640	113	320	10	20	57	113	10	20	YES
5	71	11.3	M	Bivalent	113	640	20	160	10	160	10	40	10	57	10	20	NO
6	68	10.7	M	Bivalent	$N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	NA
7	57	11.3	F	Bivalent	3620	3620	1280	640	1280	1280	320	320	320	320	160	160	YES
8	75	12.0	F	Bivalent	2560	10240	226	2560	320	2560	113	640	57	640	80	320	NO
9	64	10.5	M	Bivalent	320	1810	40	640	57	905	20	226	10	320	10	57	YES
10	65	10.3	F	Bivalent	640	2560	40	160	80	320	20	80	28	80	10	40	YES
11	59	7.5	M	Bivalent	226	2560	10	320	20	226	20	160	10	80	10	20	NO
12	71	11.0	F	Bivalent	640	40960	160	20480	226	14482	20	1810	160	2560	10	640	YES
13	77	11.8	M	Bivalent	10240	10240	2560	3620	3620	5120	1280	1280	1810	2560	320	640	YES
14	68	12.0	F	Bivalent	640	2560	57	640	40	905	10	113	10	226	10	80	NO
15	60	11.4	F	Bivalent	1280	7241	320	1810	160	320	10	80	40	160	10	80	YES
16	61	12.3	M	Bivalent	80	1280	10	226	10	320	10	57	10	80	10	40	NO
17	69	11.5	M	Bivalent	1810	5120	80	3620	160	2560	40	640	10	453	20	320	YES
18	79	11.8	M	Bivalent	160	7241	10	2560	10	3620	10	1810	10	453	10	160	NO
19	57	9.7	F	Bivalent	320	2560	113	1280	80	2560	28	1280	10	640	10	320	YES
20	68	11.5	M	Bivalent	320	1280	57	320	113	640	40	160	40	226	10	40	YES
21	63	11.8	M	Bivalent	160	1280	40	320	113	453	20	113	20	160	20	113	NO
22	57	10.5	M	Bivalent	453	10240	28	3620	57	2560	28	640	10	320	10	160	NO
23	58	9.7	M	Bivalent	640	2560	40	1280	57	905	10	160	10	160	10	40	NO
24	66	9.6	M	Bivalent	226	20480	20	10240	40	10240	10	1280	10	2560	10	1280	NO
25	60	11.7	F	Bivalent	1280	5120	160	2560	453	2560	320	1280	80	640	40	320	YES
26	74	11.2	M	Bivalent	5120	10240	640	2560	1280	2560	57	320	1280	2560	28	80	YES
27	58	13.0	M	Bivalent	1280	5120	320	1280	320	640	80	160	80	320	28	57	YES
28	69	11.6	M	Bivalent	453	2560	20	640	40	640	10	80	10	160	10	40	NO
29	63	12.3	M	Bivalent	453	1810	10	160	10	226	10	160	10	57	10	20	NO
30	75	9.3	F	Bivalent	160	640	10	160	10	320	10	80	10	160	10	40	NO
31	66	11.8	F	Bivalent	1280	3620	226	640	320	905	160	160	80	160	80	113	YES
32	59	9.9	F	Bivalent	2560	3620	640	1280	905	2560	80	320	453	640	80	160	YES
@33	63	11.4	M	Bivalent	N/A	N/A	N/A	N/A	10	453	10	80	10	160	10	40	NO
34	72	12.0	M	Bivalent	57	320	10	113	10	160	10	20	10	20	10	20	NO
35	58	11.1	M	Bivalent	2560	5120	453	905	320	1280	160	320	40	160	28	80	YES
36	73	5.5	M	Bivalent	20	320	10	113	10	40	10	10	10	10	10	10	NO
37	69	11.4	F	Bivalent	113	2560	10	640	10	320	10	40	10	226	10	40	NO
38	73	10.5	F	Bivalent	80	1280	10	80	10	160	10	28	10	57	10	20	NO
39	62	8.8	M	Bivalent	1810	1810	57	905	80	1280	20	160	10	160	20	80	YES
40	N/A		N/A	Bivalent	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	NA

*Individual $FFRNT_{50}$ value is the geometric mean of duplicate FFRNT results.
^$FFRNT_{50}$ of <20 was treated as 10 for plot purpose and statistical analysis.
$Not available (N/A)

Table S3. $FFRNT_{50}$ values of all subjects received BNT162b2 monovalent booster.

ID	AGE (years)	Time since last vaccine (months)	SEX	Booster	*$FFRNT_{50}$												With infection at baseline (pre Dose 4)
					USA-WA1/2020		BA.4/5-spike		BA.4.6-spike		BA.2.75.2-spike		BQ.1.1-spike		XBB.1-spike		
					Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	
1	63	6.5	M	BNT162b2	640	1810	57	320	113	320	40	160	40	160	20	80	YES
2	71	10.2	M	BNT162b2	5120	7241	905	640	905	905	640	640	160	320	320	320	YES
3	67	6.0	M	BNT162b2	10240	10240	1810	3620	2560	1810	1280	905	160	226	80	226	YES
4	64	5.5	M	BNT162b2	7241	5120	640	640	905	1280	320	453	113	160	80	160	YES
5	68	10.8	M	BNT162b2	5120	10240	226	640	320	640	160	453	80	160	40	113	YES
6	56	13.1	M	BNT162b2	2560	7241	160	2560	640	2560	320	640	80	320	160	160	YES
7	66	6.0	M	BNT162b2	3620	10240	160	1280	226	640	80	320	80	160	40	80	YES
8	57	5.6	F	BNT162b2	453	640	40	40	28	40	^10	20	10	20	10	10	NO
9	61	5.9	F	BNT162b2	2560	10240	320	1280	453	1280	160	320	113	160	80	226	YES
10	63	6.3	F	BNT162b2	5120	7241	226	320	113	320	160	640	40	160	40	80	YES
11	67	8.0	F	BNT162b2	10	1280	10	160	10	80	10	20	10	20	10	**10**	NO
12	72	10.6	M	BNT162b2	20480	20480	2560	2560	1280	1810	453	640	160	160	160	226	YES
13	64	5.8	F	BNT162b2	1280	1280	113	320	113	160	40	57	**10**	20	10	40	NO
14	56	5.5	F	BNT162b2	10240	10240	1280	1810	640	2560	320	1280	160	640	160	640	YES
15	58	6.0	M	BNT162b2	453	1280	20	80	28	80	10	40	10	20	10	20	NO
16	57	9.0	F	BNT162b2	640	2560	113	160	226	320	80	160	40	80	57	80	NO
17	69	6.6	M	BNT162b2	20	1280	10	113	10	57	10	40	10	**10**	10	10	NO
18	65	6.0	F	BNT162b2	7241	5120	160	160	160	320	28	40	160	80	20	20	NO
19	67	6.4	M	BNT162b2	640	1280	40	160	80	80	40	40	20	28	20	20	YES
20	68	5.6	F	BNT162b2	226	1810	20	320	113	160	20	40	**10**	20	10	10	NO
21	70	6.3	F	BNT162b2	5120	7241	226	453	320	453	113	160	80	160	80	80	YES
22	70	5.5	M	BNT162b2	1280	2560	226	320	320	640	226	320	40	80	40	80	YES
23	65	10.8	M	BNT162b2	80	640	10	10	10	10	10	10	10	10	10	10	NO
24	60	6.3	F	BNT162b2	57	1280	10	80	10	80	10	20	10	20	10	10	YES
25	73	5.9	M	BNT162b2	113	640	**10**	80	40	113	10	20	10	40	10	20	NO
26	70	8.1	F	BNT162b2	160	1280	10	80	10	80	10	40	10	20	10	**10**	NO
27	73	6.7	F	BNT162b2	320	640	10	28	**10**	57	10	40	10	10	10	**10**	NO
28	56	5.5	F	BNT162b2	5120	2560	160	160	113	160	160	160	57	80	40	80	NO
29	65	6.5	F	BNT162b2	160	1280	10	40	10	20	10	10	10	10	10	10	NO
30	75	6.3	M	BNT162b2	905	1280	113	80	160	226	80	113	40	40	20	20	NO
31	61	5.4	F	BNT162b2	160	640	**10**	80	10	80	10	20	10	20	10	10	NO
32	73	5.7	F	BNT162b2	2560	5120	320	320	160	320	40	80	80	160	40	40	NO
33	64	6.4	F	BNT162b2	10240	10240	1280	2560	1810	1810	905	1280	453	640	320	453	YES
34	68	6.5	M	BNT162b2	40	226	10	10	10	40	10	10	10	10	10	10	NO
35	79	6.1	F	BNT162b2	453	2560	40	226	80	160	20	80	20	40	10	20	NO
36	56	6.0	F	BNT162b2	5120	5120	640	1280	1280	1280	320	640	160	320	160	226	YES
37	61	6.1	F	BNT162b2	320	2560	40	113	40	80	**10**	40	10	20	10	20	NO
38	67	6.5	F	BNT162b2	453	1280	20	113	40	160	10	40	**10**	40	10	20	YES
39	62	7.2	F	BNT162b2	905	3620	113	453	80	160	20	80	10	40	20	40	YES
40	69	8.5	M	BNT162b2	640	2560	40	160	40	160	**10**	40	**10**	28	10	20	YES

*Individual $FFRNT_{50}$ value is the geometric mean of duplicate FFRNT results.
^$FFRNT_{50}$ of <20 was treated as 10 for plot purpose and statistical analysis.

Table S4. Geometric mean neutralizing titers (GMT) and geometric mean fold rise (GMFR) from before to 1 month post-dose 4 for bivalent BA.4/5 or BNT162b2 monovalent booster.

Vaccine Group	Subset		FFRNT$_{50}$											
			USA-WA1/2020		BA.4/5-spike		BA.4.6-spike		BA.2.75.2-spike		BQ.1.1-spike		XBB.1-spike	
			Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4	Pre	1MPD4
BNT162b2 Bivalent BA.4/BA.5 30 µg	All	[$]n	37	37	37	37	38	38	38	38	38	38	38	38
		[#]GMT (95% CI)	572.0 (357.4, 915.3)	3327.7 (2317.6, 4778.0)	65.7 (38.8, 111.3)	855.6 (552.2, 1325.8)	81.5 (47.0, 141.4)	905.1 (589.5, 1389.6)	29.3 (19.2, 44.8)	195.6 (124.6, 306.9)	29.1 (17.8, 47.4)	252.4 (164.7, 387.0)	17.6 (13.1, 23.7)	84.5 (57.5, 124.2)
		[†]GMFR (95% CI)		5.8 (4.0, 8.5)		13.0 (8.0, 21.1)		11.1 (7.1, 17.3)		6.7 (4.4, 10.2)		8.7 (5.7, 13.3)		4.8 (3.3, 6.9)
	With Prior Infection	[$]n	19	19	19	19	19	19	19	19	19	19	19	19
		[#]GMT (95% CI)	1376.9 (854.0, 2219.9)	4847.4 (3228.6, 7277.6)	206.6 (115.9, 368.3)	1376.9 (820.1, 2311.6)	281.6 (159.5, 497.2)	1564.4 (938.2, 2608.5)	62.0 (32.5, 118.0)	325.9 (183.0, 580.5)	74.4 (34.7, 159.4)	444.4 (259.4, 761.3)	26.8 (16.2, 44.2)	130.9 (80.0, 214.3)
		[†]GMFR (95% CI)		3.5 (2.1, 6.0)		6.7 (3.5, 12.7)		5.6 (3.1, 9.8)		5.3 (2.8, 9.8)		6.0 (3.2, 11.2)		4.9 (2.8, 8.5)
	Without Prior Infection	[$]n	18	18	18	18	19	19	19	19	19	19	19	19
		[#]GMT (95% CI)	226.3 (125.7, 407.5)	2237.2 (1238.2, 4042.2)	19.6 (12.7, 30.2)	517.8 (260.5, 1029.5)	23.6 (14.1, 39.4)	523.6 (277.3, 988.8)	13.9 (10.1, 19.1)	117.3 (60.6, 227.2)	11.4 (9.3, 13.9)	143.4 (78.7, 261.3)	11.6 (9.1, 14.7)	54.5 (31.0, 95.9)
		[†]GMFR (95% CI)		9.9 (6.2, 15.7)		26.4 (14.4, 48.3)		22.2 (12.7, 38.8)		8.4 (4.6, 15.5)		12.6 (7.1, 22.5)		4.7 (2.8, 7.9)
BNT162b2 30 µg	All	[$]n	40	40	40	40	40	40	40	40	40	40	40	40
		[#]GMT (95% CI)	874.3 (479.7, 1593.3)	2604.7 (1863.6, 3640.7)	82.1 (47.6, 141.8)	236.3 (148.6, 375.7)	101.1 (58.9, 173.5)	232.2 (149.3, 361.1)	48.0 (29.1, 79.0)	99.3 (62.4, 158.1)	31.4 (21.4, 45.9)	58.1 (39.2, 86.1)	27.1 (18.9, 38.8)	41.4 (27.5, 62.3)
		[†]GMFR (95% CI)		3.0 (2.1, 4.3)		2.9 (2.1, 3.9)		2.3 (1.9, 2.8)		2.1 (1.7, 2.5)		1.8 (1.6, 2.2)		1.5 (1.3, 1.8)
	With Prior Infection	[$]n	20	20	20	20	20	20	20	20	20	20	20	20
		[#]GMT (95% CI)	2516.0 (1291.8, 4900.4)	5120.0 (3465.6, 7564.2)	226.3 (110.4, 463.8)	629.0 (371.2, 1066.0)	283.4 (142.6, 563.2)	586.9 (346.9, 993.0)	125.5 (62.1, 253.9)	264.5 (146.3, 478.0)	59.6 (35.0, 101.5)	132.2 (82.5, 212.0)	54.6 (32.5, 92.0)	98.5 (58.0, 167.3)
		[†]GMFR (95% CI)		2.0 (1.4, 2.9)		2.8 (1.9, 4.1)		2.1 (1.5, 2.8)		2.1 (1.6, 2.7)		2.2 (1.8, 2.7)		1.8 (1.5, 2.2)
	Without Prior Infection	[$]n	20	20	20	20	20	20	20	20	20	20	20	20
		[#]GMT (95% CI)	303.8 (137.9, 669.3)	1325.1 (924.2, 1900.1)	29.8 (16.9, 52.5)	88.8 (55.3, 142.6)	36.1 (20.4, 63.6)	91.9 (59.8, 141.1)	18.3 (12.1, 27.7)	37.3 (25.1, 55.4)	16.5 (11.0, 24.8)	25.5 (17.4, 37.4)	13.4 (10.3, 17.5)	17.4 (12.6, 24.1)
		[†]GMFR (95% CI)		4.4 (2.3, 8.2)		3.0 (1.8, 4.9)		2.5 (1.9, 3.5)		2.0 (1.6, 2.6)		1.5 (1.2, 1.9)		1.3 (1.1, 1.6)

[$]Number of participants with valid and determinate assay results for the specific assay.
[#]Geometric mean neutralizing titers (GMT) and 2-sided 95% confidence interval (CI) were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.
[†]Geometric mean fold rise (GMFR) from before to 1 month post-dose 4 and 2-sided 95% CI were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

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