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Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Xia S, Zhang Y, Wang Y, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial. *Lancet Infect Dis* 2020; published online Oct 15. https://doi.org/10.1016/S1473-3099(20)30831-8.

Appendix

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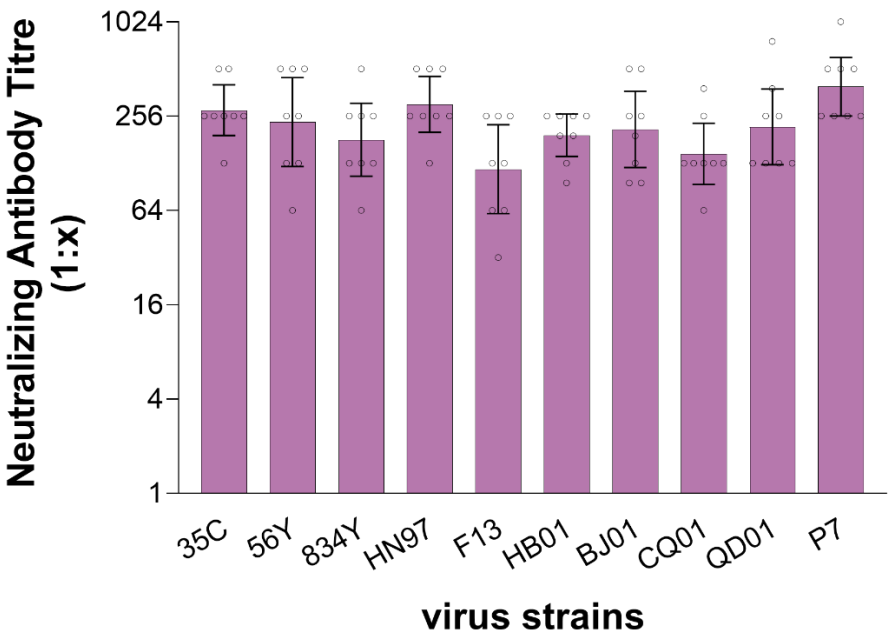
Appendix 1. Neutralizing antibodies against multiple SARS-CoV-2 strains.



Note: The neutralizing antibodies GMT at day 42 from 6 vaccine recipients randomly selected from 4 μg/dose cohorts were determined. Abbreviations: 35T, human-BetaCoV-IVDC-35T-2020; 56Y, human-BetaCoV-IVDC-56Y-2020; 834Y, human-BetaCoV-IVDC-834Y-2020; HN97, human-BetaCoV-IVDC-HN97-2020; F13, environment-BetaCoV-IVDC-F13-2020; HB01, 19nCoV-CDC-Tan-Strain01; CQ01, 19nCoV-CDC-Tan-Strain03 (CQ01); QD01, 19nCoV-CDC-Tan-Strain04; BJ01, 19nCoV-CDC-Tan-Strain05 (BJ01); P7, passage 7 virus stock for vaccine manufacture. Data were shown as geometric mean with 95% CIs.

Appendix 2. Abnormal changes of laboratory tests on day 4 for 18-59 year-old group after the first and the second vaccinations.

Abnormal in Laboratory measures		2 μg (n=32)		4 μg (n=32)		8 μg (n=32)		Total (n=96)	
		vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=72)	placebo (n=24)
WBC	Any	0	0	0	0	0	0	0	0
	Grade 1	0	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
HGB	Any	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 1	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
ALT	Any	0	0	0	0	0	0	0	0
	Grade 1	0	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
BUN	Any	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 1	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
AST	Any	0	0	0	0	0	0	0	0
	Grade 1	0	0	0	0	0	0	0	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0

GLU	Any	7(29.2%)	0	0	2(25%)	0	0	7(9.7%)	2(8.3%)
	Grade 1	4(16.7%)	0	0	2(25%)	0	0	4(5.6%)	2(8.3%)
	Grade 2	3(12.5%)	0	0	0	0	0	3(4.2%)	0
	Grade 3	0	0	0	0	0	0	0	0
TBIL	Any	4(16.7%)	1(12.5%)	4(16.7%)	2(25%)	6(25%)	0	14(19.4%)	9(37.5%)
	Grade 1	4(16.7%)	1(12.5%)	4(16.7%)	1(12.5%)	6(25%)	0	14(19.4%)	8(33.3%)
	Grade 2	0	0	0	1(12.5%)	0	0	0	1(4.2%)
	Grade 3	0	0	0	0	0	0	0	0
PRO	Any	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 1	0	0	1(4.2%)	0	0	0	1(1.4%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
U-GLU	Any	1(4.2%)	0	0	0	0	0	1(1.4%)	0
	Grade 1	1(4.2%)	0	0	0	0	0	1(1.4%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0

Data are n (%). WBC, white blood cells; HGB, hemoglobin; ALT, alanine aminotransferase; BUN, blood urea nitrogen; AST, aspartate aminotransferase; GLU, blood glucose; TBIL, serum total bilirubin; PRO, urinary protein; U-GLU, urinary glucose.

Appendix 3. Abnormal changes of laboratory tests on day 4 for ≥60 year-old group after the first and the second vaccinations.

Abnormal in Laboratory measures		2 μg (n=32)		4 μg (n=32)		8 μg (n=32)		Total (n=96)	
		vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=72)	placebo (n=24)
WBC	Any	0	0	1(4.2%)	0	0	1(4.2%)	1(1.4%)	0
	Grade 1	0	0	0	0	0	0	0	0
	Grade 2	0	0	1(4.2%)	0	0	1(4.2%)	1(1.4%)	0
	Grade 3	0	0	0	0	0	0	0	0
HGB	Any	0	0	0	0	3(12.5%)	0	3(4.2%)	0
	Grade 1	0	0	0	0	3(12.5%)	0	3(4.2%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
ALT	Any	0	0	2(8.3%)	1(12.5%)	0	0	2(2.8%)	1(4.2%)
	Grade 1	0	0	2(8.3%)	1(12.5%)	0	0	2(2.8%)	1(4.2%)
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
BUN	Any	4(16.7%)	1(12.5%)	0	0	0	0	4(5.6%)	1(4.2%)
	Grade 1	4(16.7%)	1(12.5%)	0	0	0	0	4(5.6%)	1(4.2%)
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
AST	Any	1(4.2%)	0	2(8.3%)	0	1(4.2%)	0	4(5.6%)	0
	Grade 1	1(4.2%)	0	2(8.3%)	0	1(4.2%)	0	4(5.6%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
GLU	Any	2(8.3%)	2(25%)	0	4(50%)	8(33.3%)	4(50%)	10(13.9%)	10(41.7%)
	Grade 1	2(8.3%)	2(25%)	0	3(37.5%)	8(33.3%)	4(50%)	10(13.9%)	9(37.5%)

	Grade 2	0	0	0	1(12.5%)	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
TBIL	Any	8(33.3%)	4(50%)	1(4.2%)	0	0	0	9(12.5%)	4(16.7%)
	Grade 1	7(29.2%)	3(37.5%)	1(4.2%)	0	0	0	8(11.1%)	3(12.5%)
	Grade 2	1(4.2%)	1(12.5%)	0	0	0	0	1(1.4%)	1(4.2%)
	Grade 3	0	0	0	0	0	0	0	0
PRO	Any	3(12.5%)	0	0	0	0	0	3(4.2%)	0
	Grade 1	3(12.5%)	0	0	0	0	0	3(4.2%)	0
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0
U-GLU	Any	0	0	1(4.2%)	0	0	0	0	1(4.2%)
	Grade 1	0	0	1(4.2%)	0	0	0	0	1(4.2%)
	Grade 2	0	0	0	0	0	0	0	0
	Grade 3	0	0	0	0	0	0	0	0

Data are n (%). WBC, white blood cells; HGB, hemoglobin; ALT, alanine aminotransferase; BUN, blood urea nitrogen; AST, aspartate aminotransferase; GLU, blood glucose; TBIL, serum total bilirubin; PRO, urinary protein; U-GLU, urinary glucose.

Appendix 4. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 0

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	2.1189	2	2.1189	2	2.1189	2
Lower 95%CI , Upper 95% CI	1.9508,2.3014	2,2	1.9508,2.3014	2,2	1.9508,2.3014	2,2
Median	2	2	2	2	2	2
Min, Max	2,4	2,2	2,4	2,2	2,4	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-0.3281,0.3281	--	--	--	--	--
t-test 95% CI vs. 8 μg	-0.3281,0.3281	--	-0.3281,0.3281	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	>0.99	--	--	--	--	--
t-test p-value vs. 8 μg	>0.99	--	>0.99	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 5. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 7

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	3.9718	2	4.7233	2	5.2757	2
Lower 95%CI, Upper 95% CI	3.156,4.9986	2,2	3.6775,6.0665	2,2	4.0865,6.8109	2,2
Median	4	2	4	2	4	2
Min, Max	2,12	2,2	2,16	2,2	2,32	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-0.7718,2.7718	--	--	--	--	--
t-test 95% CI vs. 8 μg	-0.7238,4.5571	--	-1.8804,3.7137	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.46	--	--	--	--	--
t-test p-value vs. 8 μg	0.28	--	0.97	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 6. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 14

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	9.334	2	11.9605	2	12.1642	2
Lower 95%CI, Upper 95% CI	7.785,11.1912	2,2	9.384,15.2444	2,2	9.6324,15.3614	2,2
Median	8	2	14	2	14	2
Min, Max	4,32	2,2	4,32	2,2	2,32	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-0.3995,7.5662	--	--	--	--	--
t-test 95% CI vs. 8 μg	-0.1446,6.9779	--	-4.3413,4.008	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.21	--	--	--	--	--
t-test p-value vs. 8 μg	0.17	--	>0.99	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 7. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 28

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	22.5783	2	29.2805	2	36.7105	2,2
Lower 95%CI, Upper 95% CI	18.9087,26.9600	2,2	23.8135,36.0026	2,2	29.8274,45.1819	2,2
Median	28	2	32	2	32	2
Min, Max	12,48	2,2	12,64	2,2	12,128	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	0.6589,15.6745	--	--	--	--	--
t-test 95% CI vs. 8 μg	6.3805,27.6195	--	-2.8534,20.5201	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.13	--	--	--	--	--
t-test p-value vs. 8 μg	0.0093	--	0.58	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 8. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 32

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	41.9082	2	84.8271	2	94.3385	2
Lower 95%CI, Upper 95% CI	33.472,52.4706	2,2	65.3675,110.0797	2,2	80.0485,111.1795	2,2
Median	48	2	96	2	96	2
Min, Max	12,96	2,2	32,256	2,2	48,192	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	27.9666,79.0334	--	--	--	--	--
t-test 95% CI vs. 8 μg	35.8098,72.5236	--	-28.2923,29.6256	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	<0.001	--	--	--	--	--
t-test p-value vs. 8 μg	<0.001	--	>0.99	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 9. Statistical Analysis of neutralizing antibody GMT in 18-59 year-old group: Day 42

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)
Subjects with a Valid Assay	24	8	24	8	24	8
Geometric Mean	87.7423	2	211.2041	2	228.695	2
Lower 95%CI, Upper 95% CI	64.9066,118.6122	2,2	158.95,280.6366	2,2	186.0746,281.0777	2,2
Median	96	2	256	2	256	2
Min, Max	16,256	2,2	64,768	2,2	128,768	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	73.6855,230.9805	--	--	--	--	--
t-test 95% CI vs. 8 μg	82.3201,217.0139	--	-97.7631,92.4298	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.0016	--	--	--	--	--
t-test p-value vs. 8 μg	<0.001	--	>0.99	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 10. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 0

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	23	8	24	8	24	8
Geometric Mean	22.1243	2	2.4898	2	2.3107	2
Lower 95%CI, Upper 95% CI	1.9486,2.3159	2,2	2.141,2.8954	2,2	2.0465,2.609	2,2
Median	2	2	2	2	2	2
Min, Max	2,4	2,2	2,6	2,2	2,4	2,2
t-test 95% CI vs. placebo	--	--	---	--	--	--
t-test 95% CI vs. 4 μg	-0.0375,1.0231	--	--	--	--	--
t-test 95% CI vs. 8 μg	-0.1787,0.6642	--	-0.8258,0.3258	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.24	--	--	--	--	--
t-test p-value vs. 8 μg	0.42	--	0.91	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 11. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 7

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	23	8	24	8	24	8
Geometric Mean	2.3253	2.181	3.3235	2	3.668	2
Lower 95%CI, Upper 95% CI	1.9906,2.7162	1.777,2.6769	2.4967,4.4241	2,2	2.7438,4.9035	2,2
Median	2	2	2	2	2	2
Min, Max	2,8	2,4	2,24	2,2	2,16	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-0.1664,3.9562	--	--	--	--	--
t-test 95% CI vs. 8 μg	0.5412,3.7486	--	-2.1811,2.6811	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.24	--	--	--	--	--
t-test p-value vs. 8 μg	0.039	--	0.97	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 12. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 14

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	23	8	24	8	24	8
Geometric Mean	4.6744	2	6.9093	2	6.6652	2
Lower 95%CI, Upper 95% CI	3.2589,6.7048	2,2	4.9472,9.6495	2,2	4.7564,9.3399	2,2
Median	2	2	2	2	2	2
Min, Max	2,24	2,2	2,32	2,2	2,24	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-1.3355,6.2847	--	--	--	--	--
t-test 95% CI vs. 8 μg	-1.421,5.5369	--	-4.1286,3.2953	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.24	--	--	--	--	--
t-test p-value vs. 8 μg	0.42	--	0.97	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 13. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 28

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	23	8	24	8	24	8
Geometric Mean	13.3534	2	18.8931	2	23.7415	2
Lower 95%CI, Upper 95% CI	9.3861,18.9977	2,2	13.4277,26.5831	2,2	19.0374,29.6079	2,2
Median	2	2	2	2	8	2
Min, Max	2,64	2,2	2,64	2,2	8,64	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	-2.1949,16.5645	--	--	--	--	--
t-test 95% CI vs. 8 μg	0.9606,17.822	--	-7.4789,11.8919	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.24	--	--	--	--	--
t-test p-value vs. 8 μg	0.087	--	0.96	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 14. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 32

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**	**vaccination (n=24)**	**placebo (n=8)**
Subjects with a Valid Assay	23	8	24	8	23	7
Geometric Mean	31.3697	2	60.7051	2	73.3171	2
Lower 95%CI, Upper 95% CI	21.6505,45.4519	2,2	46.3498,79.5065	2,2	59.5107,90.3265	2,2
Median	2	2	16	2	24	2
Min, Max	2,128	2,2	16,128	2,2	24,128	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	11.0532,51.0338	--	--	--	--	--
t-test 95% CI vs. 8 μg	21.4778,58.6962	--	12.5433,30.6302	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.018	--	--	--	--	--
t-test p-value vs. 8 μg	<0.001	--	0.91	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 15. Statistical Analysis of neutralizing antibody GMT in ≥60 year-old group: Day 42

	2 μg group (n=32)		4 μg group (n=32)		8 μg group (n=32)	
	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)	vaccination (n=24)	placebo (n=8)
Subjects with a Valid Assay	23	8	24	8	23	7
Geometric Mean	80.6666	2	131.4649	2	170.8679	2
Lower 95%CI, Upper 95% CI	65.3651,99.5501	2,2	108.2188,159.7044	2,2	133.0249,219.4765	2,2
Median	32	2	64	2	128	2
Min, Max	32,256	2,2	64,256	2,2	64,512	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--
t-test 95% CI vs. 4 μg	19.0552,89.3506	--	--	--	--	--
t-test 95% CI vs. 8 μg	53.9459,164.4881	--	-2.0559,112.0849	--	--	--
t-test p-value vs. placebo	--	--	--	--	--	--
t-test p-value vs. 4 μg	0.018	--	--	--	--	--
t-test p-value vs. 8 μg	0.0013	--	0.30	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 16. Statistical Analysis of neutralizing antibody GMT in four immunization schedules: Day 0

	D0 8 μg (n=112)		D0/D14 4 μg (n=112)		D0/D21 4 μg (n=112)		D0/D28 8 μg (n=112)	
	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)
Subjects with a Valid Assay	84	28	84	28	84	28	83	28
Geometric Mean	2	2	2.1189	2	2.0501	2	2	2
Lower 95%CI, Upper 95% CI	2,2	2,2	2.0321, 2.2094	1.9486, 2.1569	1.9933, 2.1085	2,2	2,2	2,2
Median	2	2	2	2	2	2	2	2
Min, Max	2,2	2,2	2,4	2,4	2,4	2,2	2,2	2,2
t-test 95% CI vs. placebo	--	--	--	--	--	--	--	--
t-test 95% CI vs. D0/D14 4 μg	--	--	--	--	--	--	--	--
t-test 95% CI vs. D0/D21 4 μg	--	--	-0.2395, 0.0491	--	--	--	--	--
t-test 95% CI vs. D0/D28 8 μg	--	--	-0.2872, -0.0462	--	-0.1524, 0.0095	--	--	--
t-test 95% CI vs. D0 8 μg	--	--	-0.2865, -0.0469	--	-0.1519, 0.009	--	0,0	--
t-test p-value vs. placebo	--	--	--	--	--	--	--	--
t-test p-value vs. D0/D14 4 μg	0.0067	--	--	--	--	--	--	--
t-test p-value vs. D0/D21 4 μg	0.081	--	0.19	--	--	--	--	--
t-test p-value vs. D0/D28 4 μg	--	--	0.014	--	0.16	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 17. Statistical Analysis of neutralizing antibody GMT in two immunization schedules: Day 14

	D0/D14 (n=112)		D0/D21 (n=112)	
	vaccination (n=84)	**placebo (n=28)**	**vaccination (n=84)**	**placebo (n=28)**
Subjects with a Valid Assay	42	14	42	14
Geometric Mean	104.8727	2	218.9276	2
Lower 95%CI, Upper 95% CI	79.0492,139.1322	2,2	165.5551,289.5066	2,2
Median	128	2	160	2
Min, Max	8,512	2,2	64,1536	2,2
t-test 95% CI vs. placebo	--	--	--	--
t-test 95% CI vs. D0/D14	--	--	--	--
t-test 95% CI vs. D0/D21	64.1611,291.6489	--	--	--
t-test p-value vs. placebo	--	--	--	--
t-test p-value vs. D0/D14	--	--	--	--
t-test p-value vs. D0/D21	0.0077	--	--	--

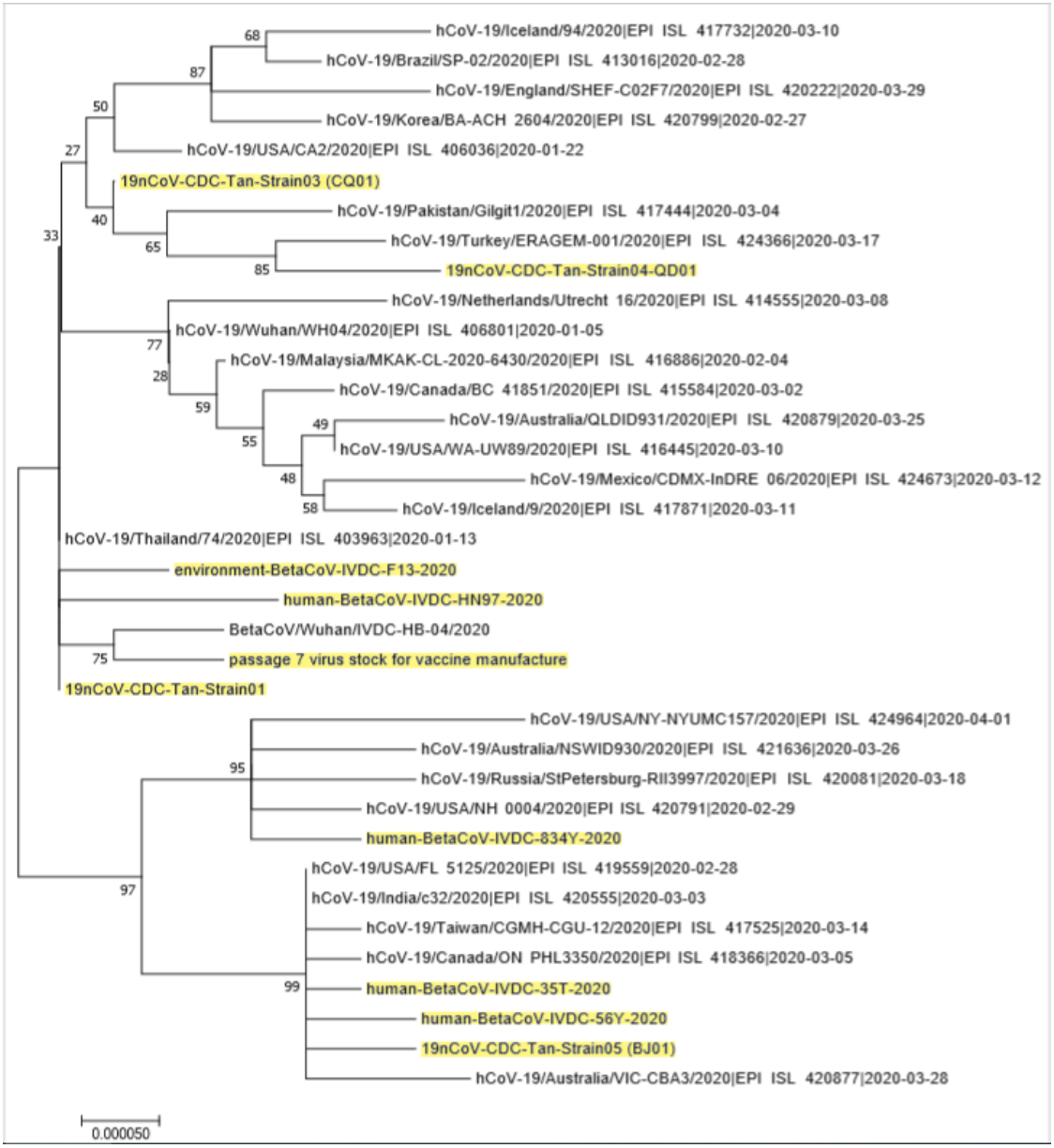
Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 18. Statistical Analysis of neutralizing antibody GMT in four immunization schedules: Day 28

	D0 8 μg (n=112)		D0/D14 4 μg (n=112)		D0/D21 4 μg (n=112)		D0/D28 8 μg (n=112)	
	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)	vaccination (n=84)	placebo (n=28)
Subjects with a Valid Assay	84	28	42	14	39	13	83	28
Geometric Mean	14.7236	2	169.4554	2	282.7149	2	217.992	2
Lower 95%CI, Upper 95% CI	11.5589, 18.7548	2,2	132.2147, 217.1857	2,2	221.1665, 361.3916	2,2	181.8380, 261.3343	2,2
Median	16	2	128	2	256	2	192	2
Min, Max	2,128	2	32,512	2,2	32,1024	2,2	64,1024	2
t-test 95% CI vs. placebo	--	--	--	--	--	--	--	--
t-test 95% CI vs. D0/D14 4 μg	--	--	--	--	--	--	--	--
t-test 95% CI vs. D0/D21 4 μg	--	--	40.7376, 207.6424	--	--	--	--	--
t-test 95% CI vs. D0/D28 8 μg	--	--	-10.6283, 167.2503	--	-140.4675, 48.7085	--	--	--
t-test 95% CI vs. D0 8 μg	--	--	-242.4607, -166.8253	--	-373.0712, -284.5948	--	-339.8796, -226.0284	--
t-test p-value vs. placebo	--	--	--	--	--	--	--	--
t-test p-value vs. D0/D14 4 μg	<0.001	--	--	--	--	--	--	--
t-test p-value vs. D0/D21 4 μg	<0.001	--	0.0081	--	--	--	--	--
t-test p-value vs. D0/D28 4 μg	<0.001	--	0.084	--	0.34	--	--	--

Note: t-test 95% CIs and p-values are calculated using a 2 sample t-test.

Appendix 19. Neighbor-joining phylogenetic tree for SARS-Cov-2 isolates in neutralizing assay



Note： SARS-Cov-2 isolates used in neutralizing assay include human-BetaCoV-IVDC-35T-2020 (35T), human-BetaCoV-IVDC-56Y-2020 (56Y), human-BetaCoV-IVDC-834Y-2020 (834Y), human-BetaCoV-IVDC-HN97-2020 (HN97), environment-BetaCoV-IVDC-F13-2020 (F13), 19nCoV-CDC-Tan-Strain01 (HB01), 19nCoV-CDC-Tan-Strain03 (CQ01), 19nCoV-CDC-Tan-Strain04 (QD01), 19nCoV-CDC-Tan-Strain05 (BJ01), passage 7 virus stock for vaccine manufacture (P7) are highlighted in yellow.

Appendix 20. Method for infectious SARS-Cov-2 neutralizing assay

Serum was successively diluted 1:4 to the required concentration by a 2-fold series, and an equal volume of challenge virus solution was added. After neutralization in a 37 °C incubator for 2 h, a 1.0~2.5×10^5/ml cell suspension was added to the wells (0.1 ml/well) and cultured in a CO2 incubator at 37 ° C for 4 days. Titers expressed as the reciprocal of the highest dilution protecting 50% cell from virus challenge. Convalescent sera is included as a internal positive control in every assay, and the range of the NAb titer is 1:128 – 1:384. Seroconversion is defined as 4-fold increment in antibody titer relative to day 0.

Appendix 21. Detail information for screened subjects in Phase 1/2

	Total screened	Informed consent	Informed consent failure	Physical examination failure	Other withdraws	Total enrolled
Phase 1						
18-59 yrs (2 μg/dose)	63	59	0	27	4	32
18-59 yrs (4 μg/dose)	73	71	1	39	1	32
18-59 yrs (8 μg/dose)	65	60	3	28	2	32
⩾60 yrs (2 μg/dose)	109	96	12	64	1	32
⩾60 yrs (4 μg/dose)	60	58	1	26	1	32
⩾60 yrs (8 μg/dose)	96	88	7	56	1	32
Phase 2						
18-59 yrs (4 μg/dose, D0/D14)	146	139	4	27	3	112
18-59 yrs (4 μg/dose, D0/D21)	143	140	1	28	2	112
18-59 yrs (4 μg/dose,D0/D28)	139	132	2	20	5	112
18-59 yrs (8 μg/dose,D0)	118	118	0	6	0	112