Supplementary Materials

Supplementary to: Tang J, Zhu C, Xu Q, et al. Immunogenicity of Tetravalent Protein Vaccine, SCTV01E-2 against SARS-CoV-2 EG.5 Subvaraint: a Phase 2 Trial.

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

Table S1. Demographic characteristics of participants in the Immunogenicity Per-Protocol Set

	SCTV01E (N = 196) n (%)	SCTV01E-2 (N = 203) n (%)	Total (N = 399) n (%)
Age (Year)			
N	196	203	399
Mean (SD)	55.9 (12.5)	55.0 (11.7)	55.4 (12.1)
Median (Min, Max)	57.5 (20, 81)	58.0 (19, 83)	58.0 (19, 83)
Age subgroups-randomization, n (%)			
18-59 years	120 (61.2)	121 (59.6)	241 (60.4)
≥60 years	76 (38.8)	82 (40.4)	158 (39.6)
Sex, n (%)			
Male	91 (46.4)	93 (45.8)	184 (46.1)
Female	105 (53.6)	110 (54.2)	215 (53.9)
Nation, n (%)			
Han	195 (99.5)	203 (100.0)	398 (99.7)
Others	1 (0.5)	0	1 (0.3)
BMI (kg/m2) ‡			
N	196	203	399
Mean (SD)	26.0 (3.5)	26.5 (3.5)	26.3 (3.5)
Median (Min, Max)	25.8 (18.9, 38.6)	26.6 (16.4, 39.8)	26.1 (16.4, 39.8)
History of SARS-CoV-2 infection, n (%)			
Yes	53 (27.0)	52 (25.6)	105 (26.3)
No	143 (73.0)	151 (74.4)	294 (73.7)
Previous vaccination/infection interval, n (%)			
6-11 months	62 (31.6)	63 (31.0)	125 (31.3)
≥12 months	134 (68.4)	140 (69.0)	274 (68.7)
IgM at baseline			
Positive	0	0	0

	SCTV01E (N = 196) n (%)	SCTV01E-2 (N = 203) n (%)	Total (N = 399) n (%)
Negative	196 (100.0)	203 (100.0)	399 (100.0)
Booster dose of COVID-19 vaccine, n (%)			
Yes	143 (73.0)	145 (71.4)	288 (72.2)
No	53 (27.0)	58 (28.6)	111 (27.8)
Type of last received COVID-19 vaccine-randomization, n (%)			
Inactive vaccine	91 (46.4)	97 (47.8)	188 (47.1)
Adenovirus vector vaccine	38 (19.4)	33 (16.3)	71 (17.8)
Recombinant protein vaccine	67 (34.2)	73 (36.0)	140 (35.1)
Other vaccines	0	0	0
Pre-existing comorbidities, n (%)			
Yes	74 (37.8)	90 (44.3)	164 (41.1)
No	122 (62.2)	113 (55.7)	235 (58.9)

‡ BMI, the body mass index. The body-mass index is the weight in kilograms divided by the square of the height in meters.

Table S2. Geometric Mean Titer (GMT) of Neutralizing Antibodies Against Omicron EG.5 and XBB.1 variants in the Full Analysis Set

	SCTV01E (N = 215)	SCTV01E-2 (N = 214)
EG.5		
Baseline (Day 0)		
n	209	209
GMT (95% CI)	94 (78, 112)	103 (90, 119)
Day 14		
n	207	209
GMT (95% CI)	514 (459, 574)	922 (825, 1032)
GMFI (95% CI)	5.5 (4.6, 6.4)	8.9 (7.6, 10.4)
LS GMR (95% CI)†		1.76 (1.52, 2.04)
P value†		<0.001
XBB.1		
Baseline (Day0)		
n	213	214
GMT (95% CI)	270 (233, 312)	324 (288, 364)
Day 14		
n	211	214
GMT (95% CI)	1422 (1264, 1600)	1879 (1682, 2100)
GMFI (95% CI)	5.3 (4.5, 6.2)	5.8 (5.0, 6.7)
LS GMR (95% CI)†		1.28 (1.09, 1.50)
P value†		0.003

†The immunogenicity data were analyzed based on covariance (ANCOVA) model, covariates included intervention groups, stratification factors and baseline values (in log-transformed scale).

Abbreviations: N, number of participants in the population; n, number of participants in the specific category; GMT, geometric mean titer; GMFI: geometric mean fold increase from baseline; LS GMR, least square geometric mean ratio.

Table S3. Seroconversion Rate (SRR) of Neutralizing Antibodies Against Omicron EG.5 and XBB.1 variants in the Full Analysis Set

	SCTV01E (N = 215)	**SCTV01E-2 (N = 214)**
EG.5		
Day 14		
SRR, n/N	59.4 (123/207)	78.5 (164/209)
SRR (95% CI)†	52.4, 66.2	72.3, 83.8
Difference of SRRs between two groups (95% CI)‡		19.07 (10.24, 27.68)
P value‡		<0.001
XBB.1		
Day 14		
SRR, n/N	60.7 (128/211)	68.7 (147/214)
SRR (95% CI)†	53.7, 67.3	62.0, 74.8
Difference of SRRs between two groups (95% CI)‡		8.10 (-1.00, 17.08)
P value‡		0.081

†Confidential interval of Clopper-Pearson.

‡estimated from the stratified Miettinen-Nurminen method, stratification based on the actual stratification factors.

Abbreviations: N, number of participants in the population; n, number of participants in the specific category; SRR, seroresponse rate.

Table S4. Solicited local adverse reactions of the study vaccines

Preferred Term Intensity	SCTV01E (N = 215) n (%)	SCTV01E-2 (N = 214) n (%)
Number of Participants with at Least One Study Vaccine-Related Solicited Local Adverse Event	60 (27.9)	59 (27.6)
Grade 1	51 (23.7)	49 (22.9)
Grade 2	9 (4.2)	10 (4.7)
Grade 3 and above	0	0
Pain	52 (24.2)	52 (24.3)
Grade 1	47 (21.9)	48 (22.4)
Grade 2	5 (2.3)	4 (1.9)
Grade 3 and above	0	0
Pruritus	9 (4.2)	5 (2.3)
Grade 1	9 (4.2)	5 (2.3)
Grade 2	0	0
Grade 3 and above	0	0
Swelling	5 (2.3)	8 (3.7)
Grade 1	3 (1.4)	3 (1.4)
Grade 2	2 (0.9)	5 (2.3)
Grade 3 and above	0	0
Erythema	1 (0.5)	4 (1.9)
Grade 1	0	2 (0.9)
Grade 2	1 (0.5)	2 (0.9)
Grade 3 and above	0	0
Induration	1 (0.5)	1 (0.5)
Grade 1	0	1 (0.5)
Grade 2	1 (0.5)	0
Grade 3 and above	0	0

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Abbreviations: N, number of participants in the population; n, number of participants in the specific category; %, percentage of participants with N as the denominator.

Table S5. Solicited systemic adverse reactions of the study vaccines

Preferred Term **Intensity**	**SCTV01E** **(N = 215)** **n (%)**	**SCTV01E-2** **(N = 214)** **n (%)**
Number of Participants with at Least One Study Vaccine-Related Solicited Systemic Adverse Event	27 (12.6)	44 (20.6)
Grade 1	16 (7.4)	28 (13.1)
Grade 2	10 (4.7)	10 (4.7)
Grade 3 and above	1 (0.5)	6 (2.8)
Pyrexia	17 (7.9)	25 (11.7)
Grade 1	12 (5.6)	17 (7.9)
Grade 2	4 (1.9)	3 (1.4)
Grade 3 and above	1 (0.5)	5 (2.3)
Fatigue	8 (3.7)	18 (8.4)
Grade 1	4 (1.9)	13 (6.1)
Grade 2	4 (1.9)	5 (2.3)
Grade 3 and above	0	0
Headache	9 (4.2)	16 (7.5)
Grade 1	5 (2.3)	10 (4.7)
Grade 2	4 (1.9)	6 (2.8)
Grade 3 and above	0	0
Myalgia	4 (1.9)	9 (4.2)
Grade 1	2 (0.9)	6 (2.8)
Grade 2	2 (0.9)	3 (1.4)
Grade 3 and above	0	0
Nausea	4 (1.9)	6 (2.8)
Grade 1	3 (1.4)	5 (2.3)
Grade 2	1 (0.5)	1 (0.5)
Grade 3 and above	0	0
Arthritis	3 (1.4)	4 (1.9)
Grade 1	1 (0.5)	1 (0.5)
Grade 2	2 (0.9)	2 (0.9)
Grade 3 and above	0	1 (0.5)
Vomit	0	1 (0.5)
Grade 1	0	0
Grade 2	0	1 (0.5)
Grade 3 and above	0	0
Chill	1 (0.5)	0
Grade 1	0	0
Grade 2	1 (0.5)	0
Grade 3 and above	0	0

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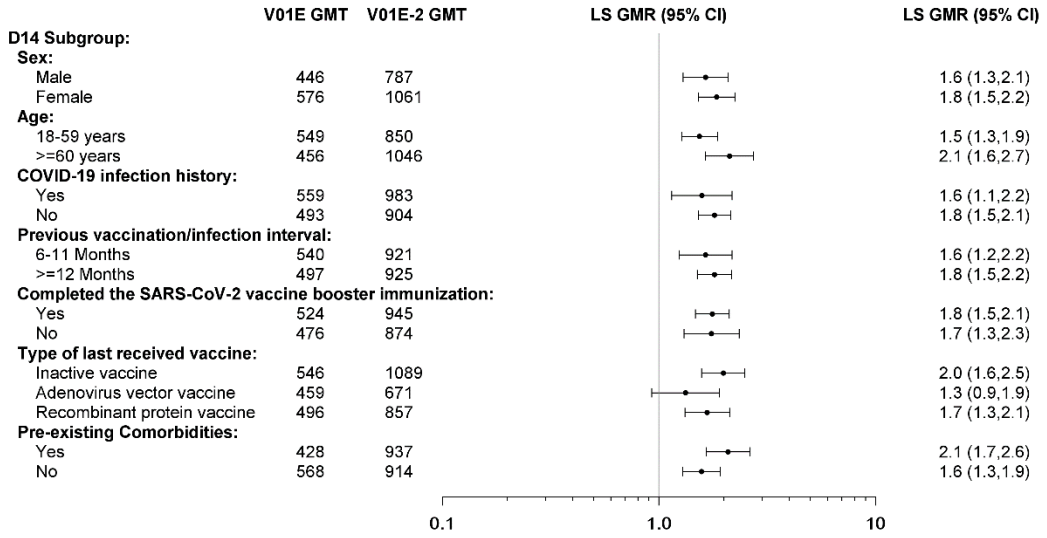
Abbreviations: N, number of participants in the population; n, number of participants

in the specific category; %, percentage of participants with N as the denominator.

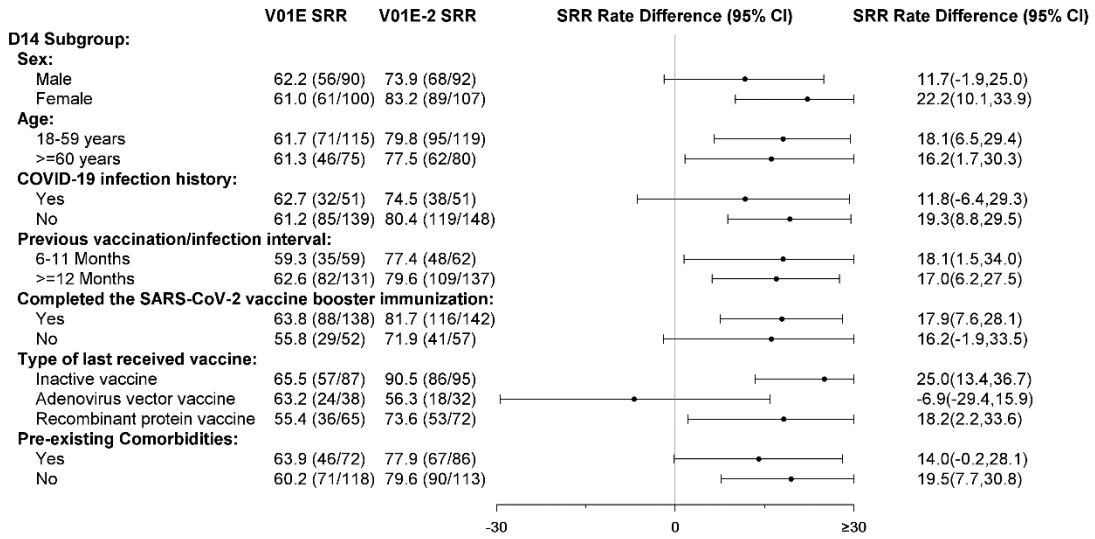
Figure S1. Subgroup analysis of geometric mean titer (GMT) and the least square geometric mean ratio (LS GMR) of live virus nAb against Omicron EG.5.



The subgroup analysis was conducted among the population in the immunogenicity per-protocol set, who had a valid immunogenicity test result prior to the administration of study vaccines and after the administration of study vaccines and had a negative result of anti-spike receptor binding domain (RBD) IgM test at baseline but without major protocol deviations.

Abbreviations: GMT, geometric mean titer; LS GMR, least square geometric mean ratio.

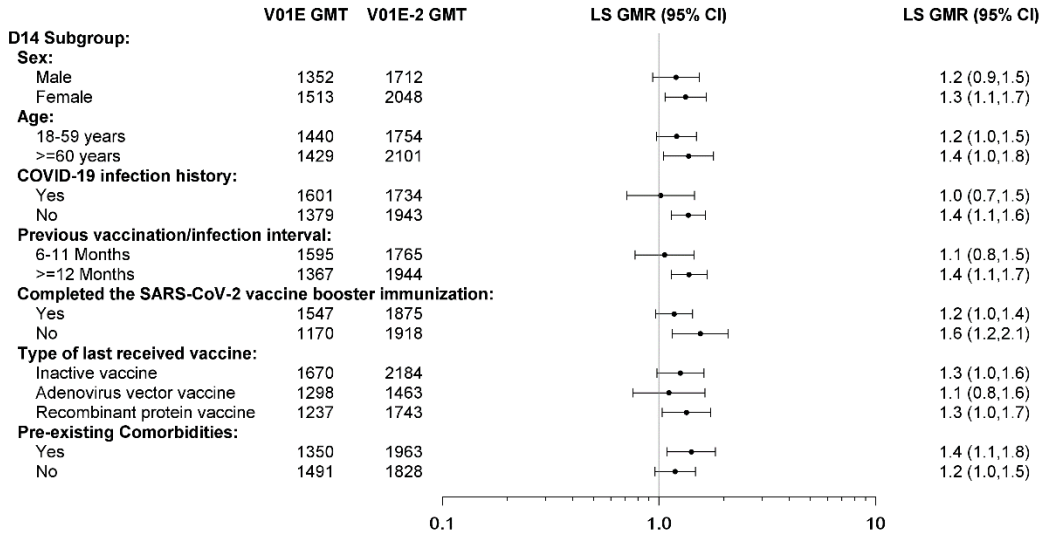
Figure S2. Subgroup analysis of seroresponse rate (SRR) of Live Virus nAb against Omicron EG.5.



The subgroup analysis was conducted among the population in the immunogenicity per-protocol set, who had a valid immunogenicity test result prior to the administration of study vaccines and after the administration of study vaccines and had a negative result of anti-spike receptor binding domain (RBD) IgM test at baseline but without major protocol deviations. Seroresponse was defined as a change from below the low limit of quantitation (LLOQ) to equal to or above LLOQ, or more than a 4-fold rise if the baseline is equal to or above LLOQ in nAb from baseline.

Abbreviations: SRR, seroresponse rate.

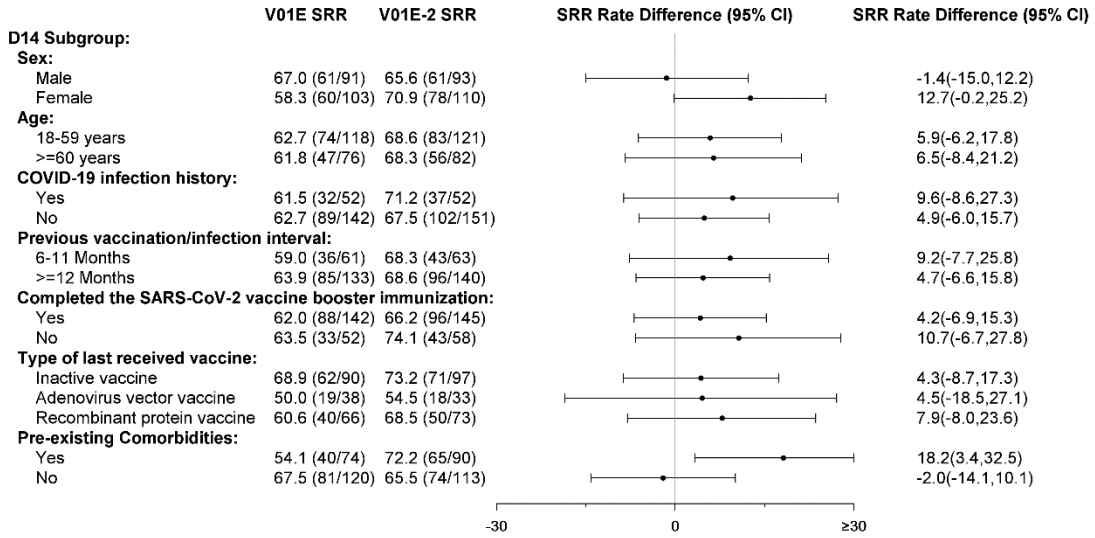
Figure S3. Subgroup analysis of geometric mean titer (GMT) and the least square geometric mean ratio (LS GMR) of live virus nAb against Omicron XBB.1.



The subgroup analysis was conducted among the population in the immunogenicity per-protocol set, who had a valid immunogenicity test result prior to the administration of study vaccines and after the administration of study vaccines and had a negative result of anti-spike receptor binding domain (RBD) IgM test at baseline but without major protocol deviations.

Abbreviations: GMT, geometric mean titer; LS GMR, least square geometric mean ratio.

Figure S4. Subgroup analysis of seroresponse rate (SRR) of live virus nAb against Omicron XBB.1.



The subgroup analysis was conducted among the population in the immunogenicity per-protocol set, who had a valid immunogenicity test result prior to the administration of study vaccines and after the administration of study vaccines and had a negative result of anti-spike receptor binding domain (RBD) IgM test at baseline but without major protocol deviations. Seroresponse was defined as a change from below the low limit of quantitation (LLOQ) to equal to or above LLOQ, or more than a 4-fold rise if the baseline is equal to or above LLOQ in nAb from baseline.

Abbreviations: SRR, seroresponse rate.