Supplementary Table 1. Relationship between adverse events experienced after either dose (first or second dose) and immune response eight weeks after the first dose (approximately four weeks after the second dose; T2)

Type of AE	SARS-CoV-2 antibody assay	subjects with AEs after 1st or 2nd dose		*p*-value
		no	yes	
Any local AE	Anti-S IgG (U/mL)	N=1 2618.18	N=170 4422.83 (4094.49- 4778.59)	0.307
	ND_{50}	N=0	N=100	NA
Injection site pain	Anti-S IgG (U/mL)	N=3 3820.32 (1688.88- 8643.71)	N=168 4420.79 (4087.90- 4779.69)	0.625
	ND_{50}	N=1 3090.30	N=99 2849.71 (2476.28- 3278.67)	0.909
Injection site redness/ swelling	Anti-S IgG (U/mL)	N=121 4302.29 (3938.22- 4698.94)	N=49 4744.60 (4049.49- 5560.32)	0.257
	ND_{50}	N=64 3034.59 (2532.79- 3635.80)	N=35 2598.36 (2078.35- 3250.87)	0.293
Injection site motion limitation	Anti-S IgG (U/mL)	N=7 3802.77 (2542.14- 5687.22)	N=164 4437.11 (4099.21- 4802.86)	0.435
	ND_{50}	N=0	N=100	NA

Any systemic AE	Anti-S IgG (U/mL)	N=3 3894.04 (1630.80- 9300.37)	N=168 4418.76 (4086.96- 4778.59)	0.672
	ND_{50}	N=0	N=100	NA
Fever (≥37.5°C)	Anti-S IgG (U/mL)	N=44 3944.57 (3332.73- 4668.74)	N=127 4582.47 (4204.36- 4994.59)	0.093
	ND_{50}	N=21 2828.13 (2082.57- 3839.72)	N=79 2858.25 (2437.25- 3351.97)	0.951
Chill	Anti-S IgG (U/mL)	N=47 4030.88 (3419.01- 4753.35)	N=124 4561.42 (4183.12- 4975.08)	0.158
	ND_{50}	N=23 2681.02 (2071.57- 3469.76)	N=77 2904.69 (2460.93- 3429.26)	0.632
Headache	Anti-S IgG (U/mL)	N=42 3939.13 (3292.30- 4713.03)	N=129 4574.04 (4204.36- 4976.22)	0.099
	ND_{50}	N=21 2891.35 (2021.16- 4136.19)	N=79 2841.19 (2439.50- 3309.02)	0.92
Muscle pain	Anti-S IgG (U/mL)	N=12 4441.20 (3550.59- 5555.20)	N=159 4406.56 (4061.63- 4781.89)	0.96
	ND_{50}	N=5 2727.09 (2054.94- 3619.93)	N=95 2858.25 (2413.79- 3308.26)	0.717

Fatigue	Anti-S IgG (U/mL)	N=31 4487.45 (3657.63- 5506.81)	N=140 4392.38 (4039.24- 4776.39)	0.833
	ND_{50}	N=16 2753.59 (1845.02- 4109.60)	N=84 2870.78 (2469.45- 3338.11)	0.829
Joint pain	Anti-S IgG (U/mL)	N=120 4350.11 (3954.58- 4788.30)	N=51 4550.93 (3989.33- 5191.59)	0.599
	ND_{50}	N=69 2732.75 (2308.87- 3234.45)	N=31 3135.45 (2427.17- 4050.42)	0.367
Vomiting	Anti-S IgG (U/mL)	N=153 4470.95 (4114.34- 4859.59)	N=18 3917.42 (3212.18- 4777.49)	0.300
	ND_{50}	N=89 2852.33 (2464.34- 3301.41)	N=11 2847.74 (1686.55- 4808.39)	0.994
Rash	Anti-S IgG (U/mL)	N=150 4420.79 (4082.25- 4786.30)	N=21 4330.12 (3244.890 5778.30)	0.862
	ND_{50}	N=84 2930.89 (2505.53- 3428.47) 2875.41 (2480.85- 3331.96)	N=16 2470.02 (1831.05- 3331.96) 2669.93 (1639.08- 4349.11)	0.373

Data is presented as geometric mean titers (95% confidence interval)

AE, adverse event; NA, not available; ND_{50}, median neutralizing titer

Supplementary Table 2. Univariate and multivariate analyses for predictive factors of strong antibody response at each time point

	Anti-S IgG at T1				Anti-S IgG at T2			
	<250 U/mL (n=134)	≥250 U/mL (n=43)	*p*-value	Adjusted OR (95% CI)	<5400 U/mL (n=111)	≥5400 U/mL (n=60)	*p*-value	Adjusted OR (95% CI)
Age, year (SD)	25.2 (3.6)	25.9 (4.5)	0.322	1.036 (0.953-1.127)[a]	25.3 (2.7)	25.5 (5.4)	0.759	1.009 (0.931-1.094)[a] 1.023 (0.944-1.110)[b]
Male	39 (29.1%)	14 (32.6%)	0.667	1.223 (0.522-2.867)[a]	72 (64.9%)	46 (76.7%)	0.111	1.525 (0.674-3.449)[a] 1.716 (0.718-4.102)[b]
BMI, kg/m^2 (SD)	21.3 (2.8)	22.1 (3.0)	0.103	1.108 (0.970-1.266)[a]	21.8 (2.9)	21.2 (2.9)	0.212	0.969 (0.854-1.100)[a] 0.982 (0.863-1.116)[b]
AE after dose 1								
Any AE	134 (100%)	42 (97.7%)	0.243		110 (99.1%)	60 (100%)	0.461	
Any local AE	132 (98.5%)	42 (97.7%)	0.568		108 (97.3%)	60 (100%)	0.271	
pain	130 (97%)	40 (93%)	0.226	0.471 (0.097-2.288)[a]	105 (94.6%)	59 (98.3%)	0.227	2.638 (0.297-23.399)[a]
swelling	23 (17.2%)	4 (9.3%)	0.212		18 (16.2%)	9 (15.0%)	0.835	
Motion limitation	119 (88.8%)	39 (90.7%)	0.490		95 (85.6%)	57 (95.0%)	0.062	
Any systemic AE	118 (88.1%)	37 (86.0%)	0.728		96 (86.5%)	53 (88.3%)	0.731	
fever	28 (20.9%)	10 (23.3%)	0.743		19 (17.1%)	16 (26.7%)	0.140	
chill	30 (22.4%)	7 (16.3%)	0.391		23 (20.7%)	11 (18.3%)	0.709	
headache	40 (29.9%)	16 (37.2%)	0.367		32 (28.8%)	22 (36.7%)	0.293	
Muscle pain	98 (73.1%)	32 (74.4%)	0.868		77 (69.4%)	48 (80.0%)	0.135	
Fatigue	78 (58.2%)	26 (60.5%)	0.794		66 (59.5%)	33 (55.0%)	0.573	
arthralgia	13 (9.7%)	4 (9.3%)	0.602		10 (9.0%)	6 (10.0%)	0.832	

vomiting	3 (2.2%)	0 (0.0%)	0.432		3 (2.7%)	0 (0.0%)	0.271	
Rash	10 (7.5%)	3 (7.0%)	0.609		10 (9.0%)	3 (5.0%)	0.267	
dyspnea	4 (3.0%)	1 (2.3%)	0.648		4 (3.6%)	1 (1.7%)	0.424	
flushing	4 (3.0%)	1 (2.3%)	0.648		4 (3.6%)	1(1.7%)	0.424	
Facial palsy	4 (3.0%)	1 (2.3%)	0.648		4 (3.6%)	1(1.7%)	0.424	
paresthesia	14 (10.4%)	1 (2.3%)	0.080		12 (10.8%)	3 (5.0%)	0.200	
Antipyretic use	81 (60.4%)	26 (60.5%)	0.998	1.009 (0.491-2.073)[a]	58 (52.3%)	43 (71.7%)	0.014	2.202 (1.110-4.367)[a]
AE after dose 2								
Any AE					108 (97.3%)	60 (100%)	0.271	
Any local AE					107 (96.4%)	57 (95.0%)	0.470	
pain					104 (93.7%)	57 (95.0%)	0.510	0.511 (0.098-2.652)[b]
swelling					21 (18.9%)	17 (28.3%)	0.158	
Motion limitation					98 (88.3%)	54 (90.0%)	0.734	
Any systemic AE					104 (93.7%)	59 (98.3%)	0.161	
fever					76 (68.5%)	49 (81.7%)	0.063	
chill					73 (65.8%)	48 (80.0%)	0.051	
headache					76 (68.5%)	44 (73.3%)	0.507	
Muscle pain					89 (80.2%)	52 (86.7%)	0.287	
Fatigue					86 (77.5%)	48 (80.0%)	0.702	
arthralgia					29 (26.1%)	16 (26.7%)	0.939	
vomiting					12 (10.8%)	4 (6.7%)	0.375	
Rash					6 (5.4%)	5 (8.3%)	0.330	
dyspnea					6 (5.4%)	0 (0.0%)	0.071	
flushing					1 (0.9%)	0 (0.0%)	0.649	

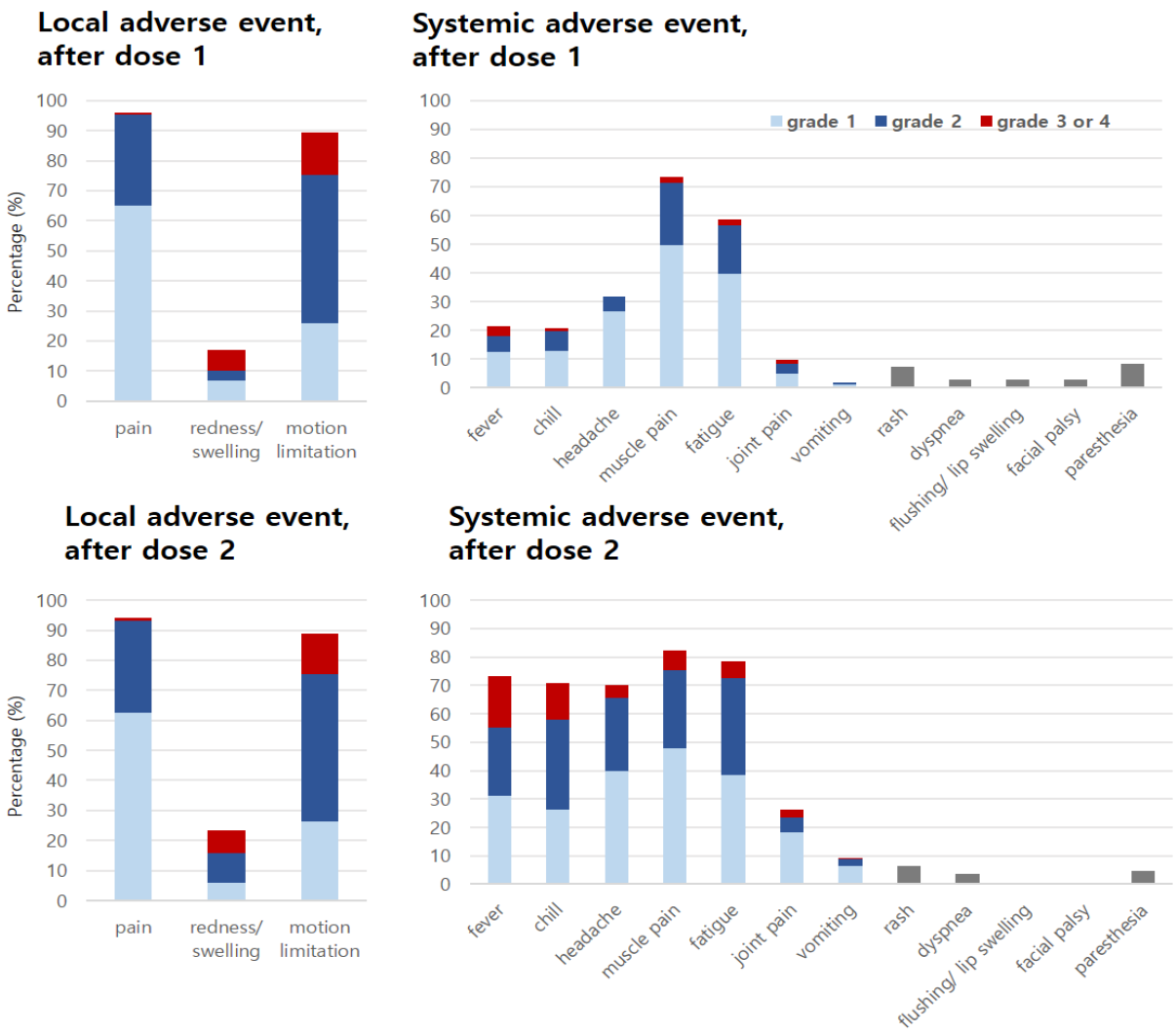
Facial palsy	1 (0.9%)	0 (0.0%)	0.649	
paresthesia	5 (4.5%)	3 (5.0%)	0.578	
Antipyretic use	96 (86.5%)	59 (98.3%)	0.011	10.033 (1.185-84.924)[b]

OR, odds ratio; SD, standard deviation; BMI, body mass index; AE, adverse event.

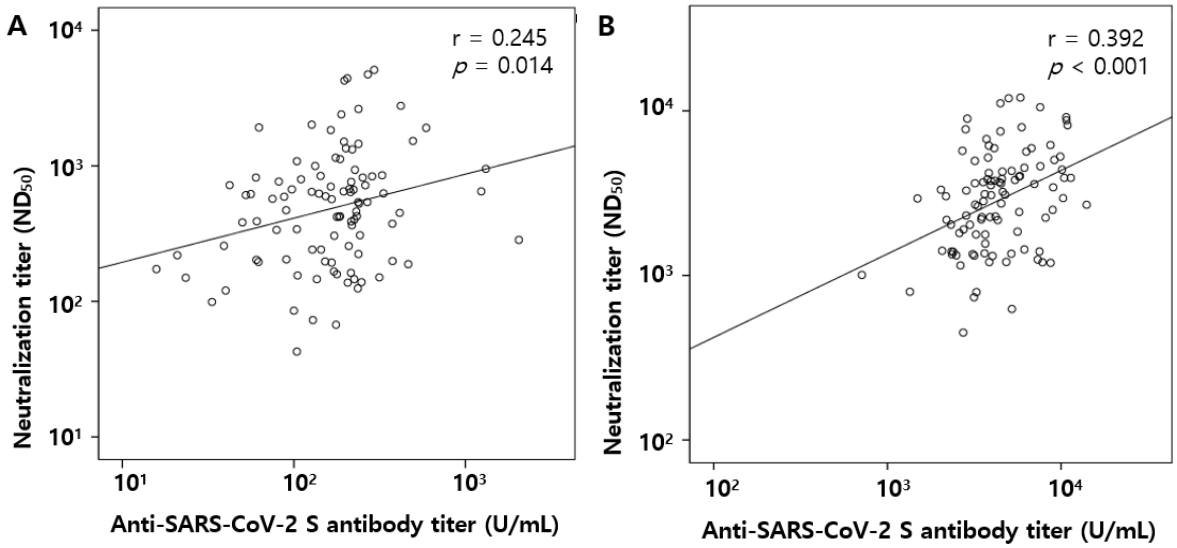
[a] Adjusted for age, sex, BMI, injection site pain after dose 1, and antipyretic use after dose 1

[b] Adjusted for age, sex, BMI, injection site pain after dose 2, and antipyretic use after dose 2

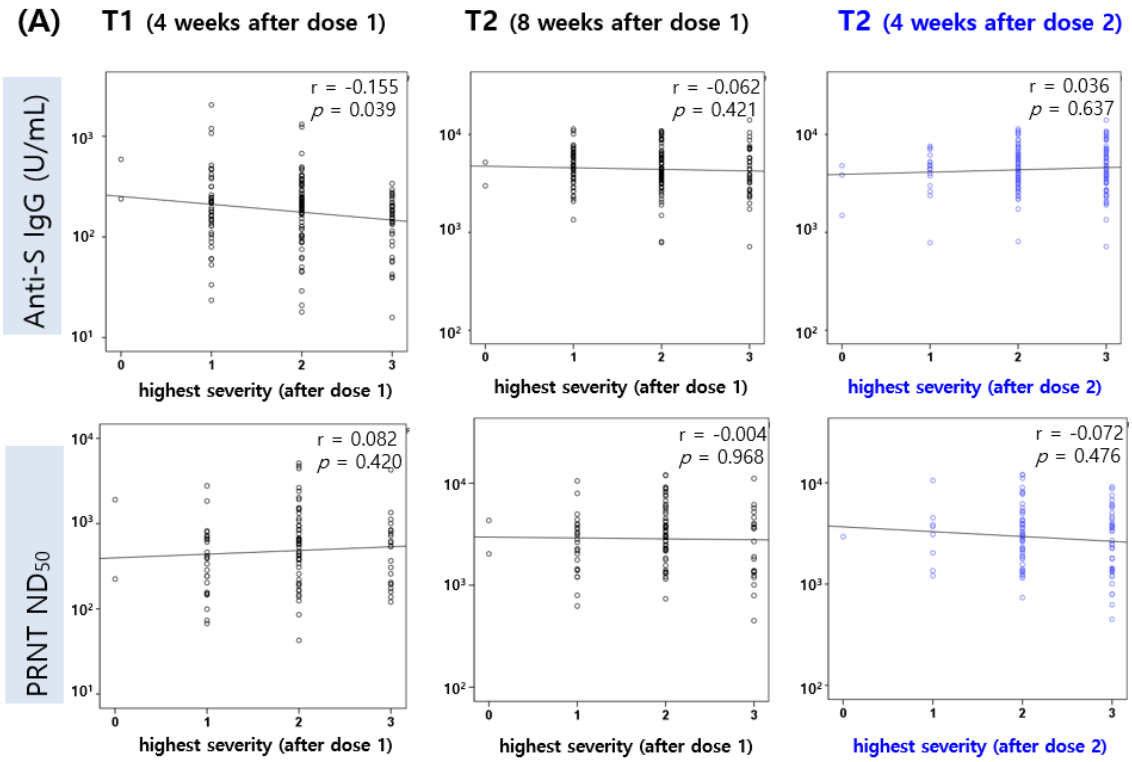
Supplementary Figure 1. Solicited adverse events after each dose

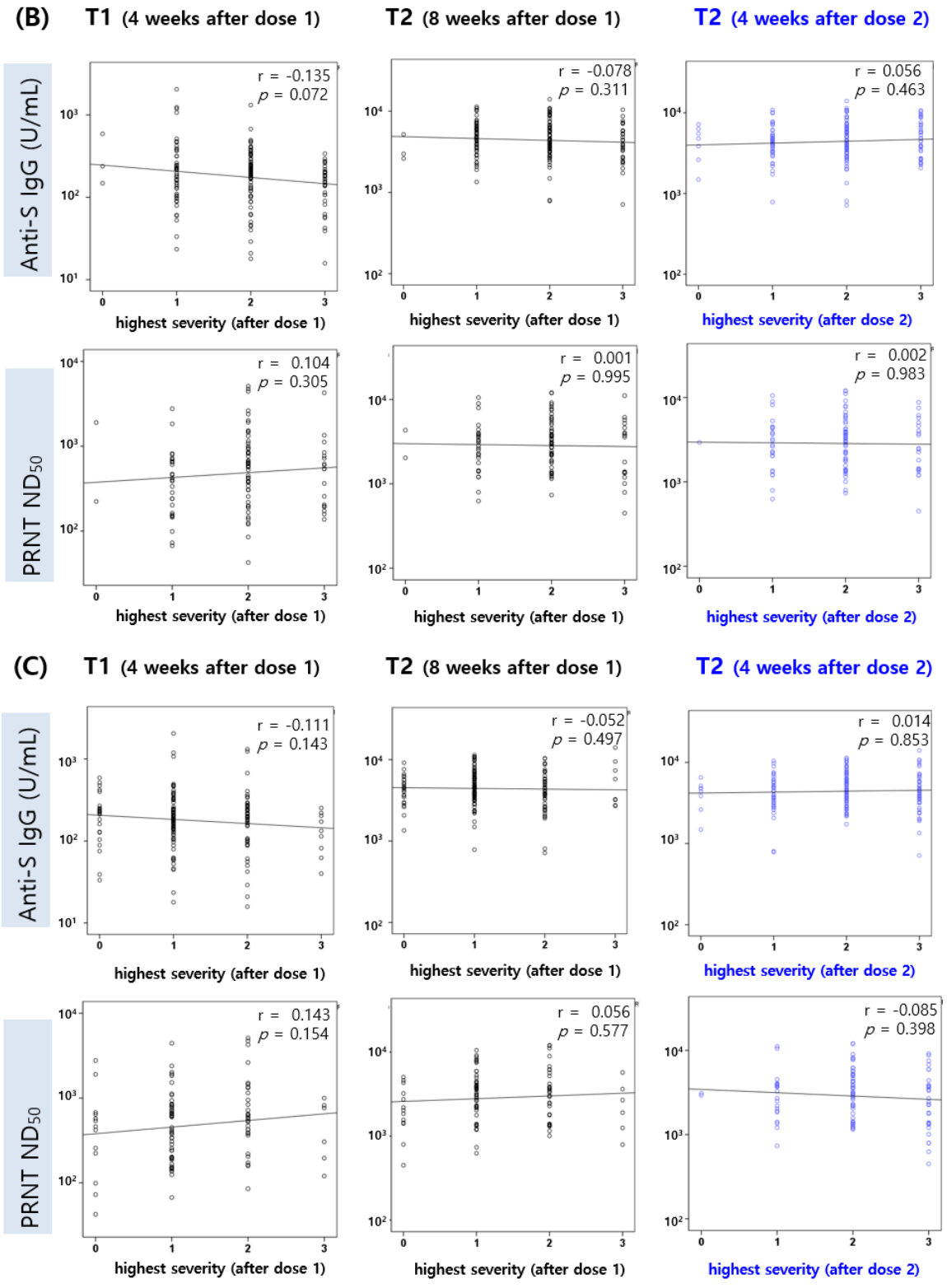


Supplementary Figure 2. Correlation between anti-SARS-CoV-2 S IgG and neutralizing antibody titer at each time point: (A) Four weeks and (B) Eight weeks after first injection.

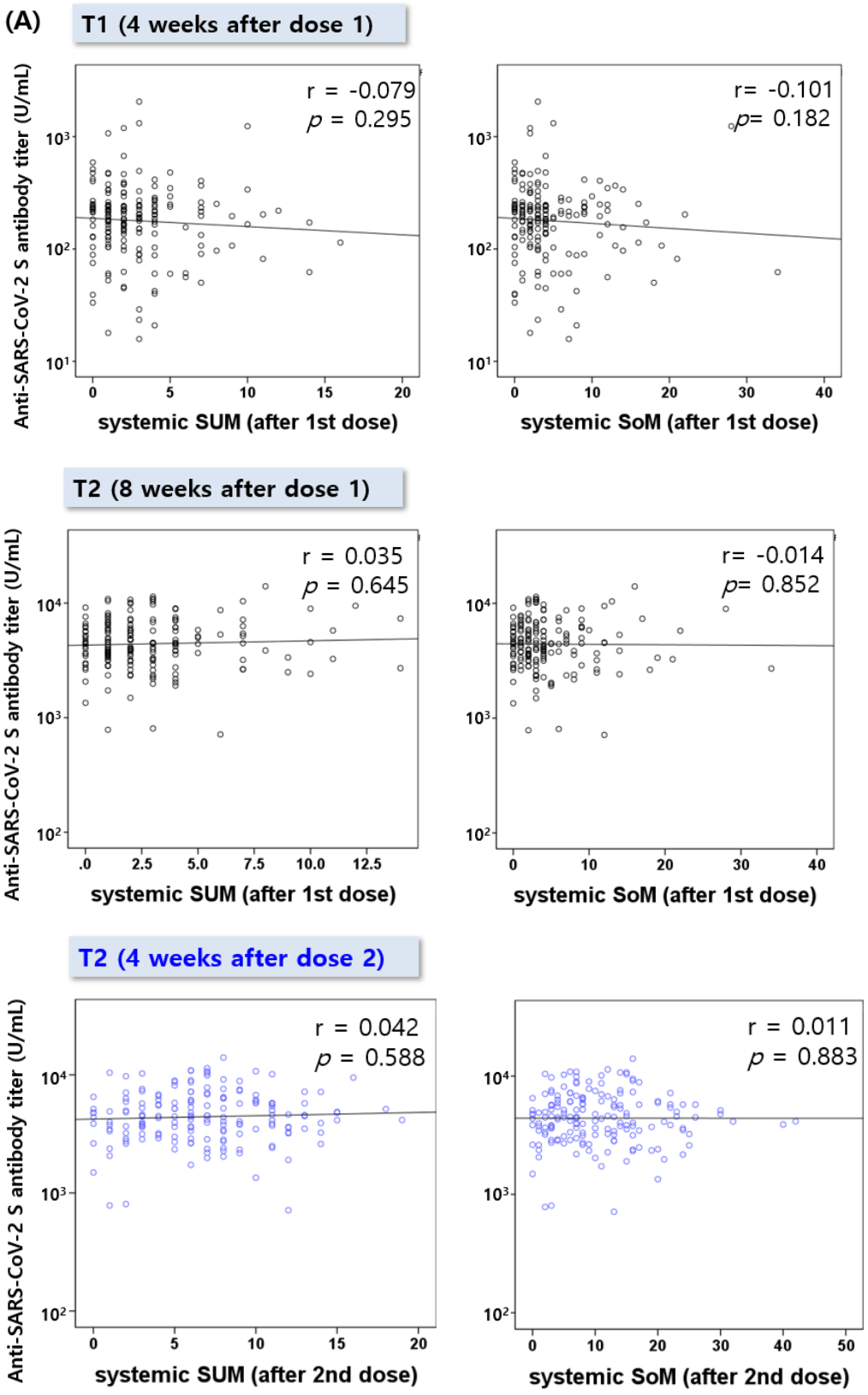


Supplementary Figure 3. Relationship of immune response with (A) highest severity of all adverse events, (B) highest severity of local adverse events, and (C) highest severity of systemic adverse events at each time point. Immune responses are presented as geometric mean titer.

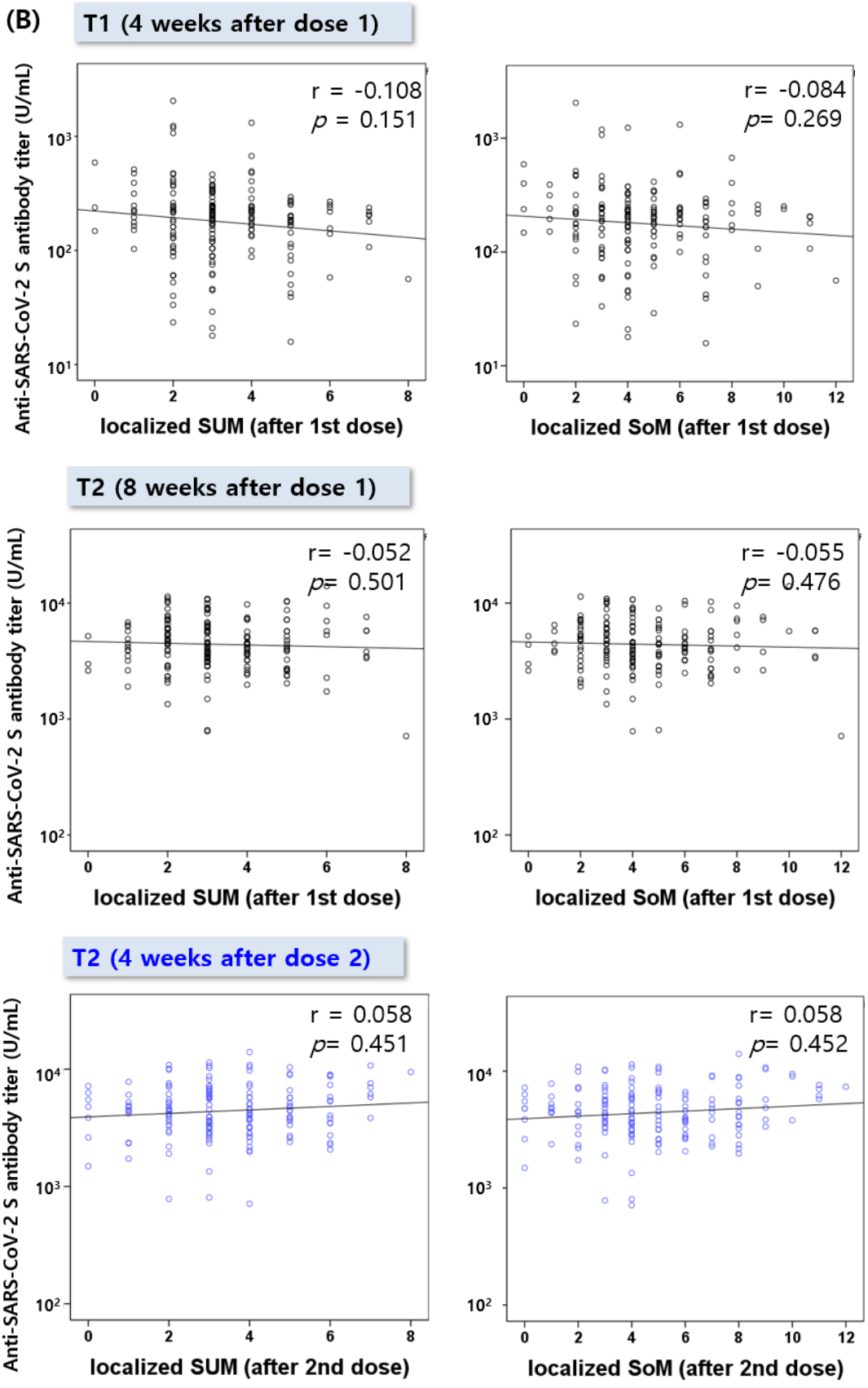



(B)
T1 (4 weeks after dose 1)
T2 (8 weeks after dose 1)
T2 (4 weeks after dose 2)
Anti-S IgG (U/mL)
PRNT ND50
r = -0.135
p = 0.072
r = -0.078
p = 0.311
r = 0.056
p = 0.463
r = 0.104
p = 0.305
r = 0.001
p = 0.995
r = 0.002
p = 0.983
highest severity (after dose 1)
highest severity (after dose 2)
(C)
T1 (4 weeks after dose 1)
T2 (8 weeks after dose 1)
T2 (4 weeks after dose 2)
Anti-S IgG (U/mL)
PRNT ND50
r = -0.111
p = 0.143
r = -0.052
p = 0.497
r = 0.014
p = 0.853
r = 0.143
p = 0.154
r = 0.056
p = 0.577
r = -0.085
p = 0.398
highest severity (after dose 1)
highest severity (after dose 2)

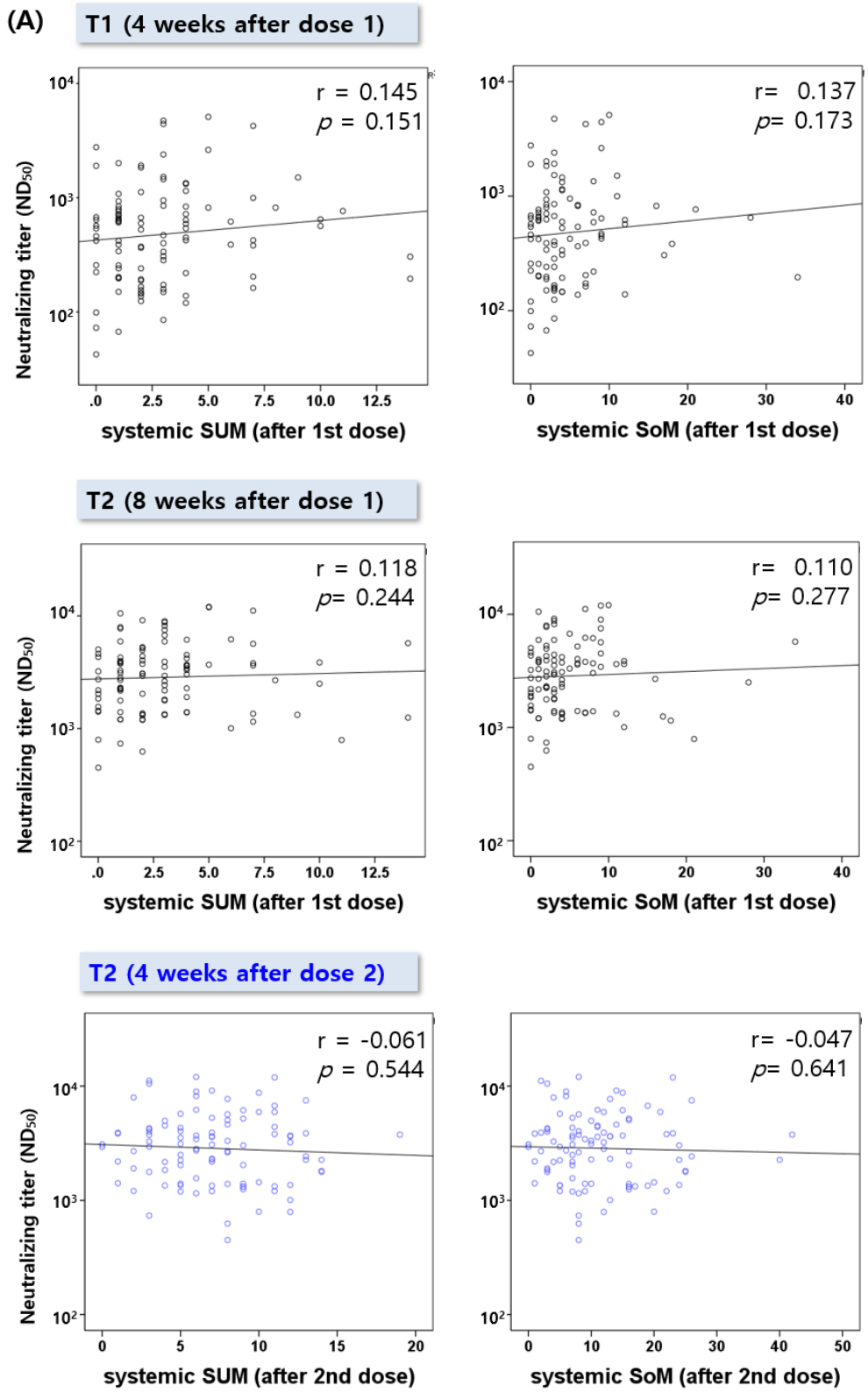
Supplementary Figure 4. Relationship of anti-SARS-CoV-2 S antibody response with (A) systemic SUM and SOM, and (B) localized SUM and SOM at each time point.



(B)

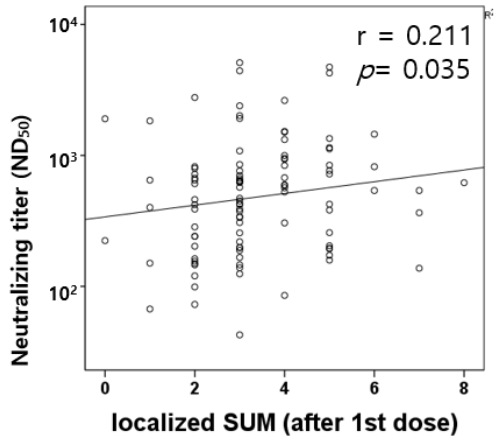

T1 (4 weeks after dose 1)
r = -0.108
p = 0.151
r= -0.084
p= 0.269
Anti-SARS-CoV-2 S antibody titer (U/mL)
localized SUM (after 1st dose)
localized SoM (after 1st dose)
T2 (8 weeks after dose 1)
r= -0.052
p= 0.501
r= -0.055
p= 0.476
localized SUM (after 1st dose)
localized SoM (after 1st dose)
T2 (4 weeks after dose 2)
r = 0.058
p= 0.451
r= 0.058
p= 0.452
localized SUM (after 2nd dose)
localized SoM (after 2nd dose)

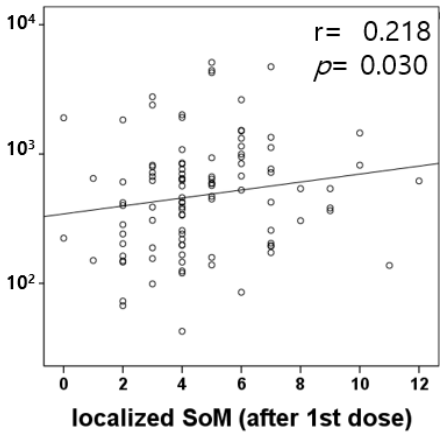
Supplementary Figure 5. Relationship of neutralizing antibody response (PRNT ND_{50}) with (A) systemic SUM and SOM, and (B) localized SUM and SOM at each time point. PRNT: plaque reduction neutralization test.



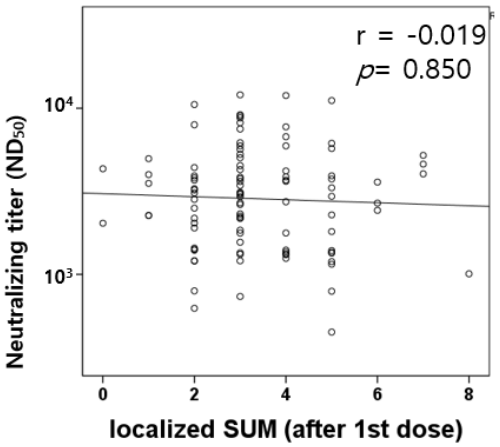
(B)

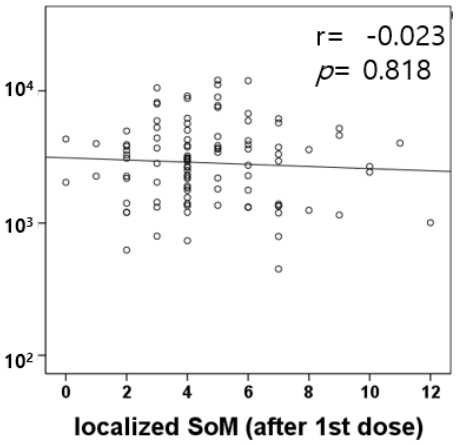
T1 (4 weeks after dose 1)





T2 (8 weeks after dose 1)





T2 (4 weeks after dose 2)