

A randomized phase 2 study on demeclocycline in patients with mild-to-moderate COVID-19.

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**Supplementary Table 1.** Concurrent treatments in each group.

		Total	Control group	Demeclocycline 150 mg group	Demeclocycline 300 mg group
Number of patients		20	7	7	6
Concurrent treatment	Casirivimab-Imdevimab	6	2	2	2
	Remdesivir	3	1	0	2
	Favipiravir	14	4	5	5
	Ciclesonide	2	1	1	0

**Supplementary Table 2.** The NEWS score between day 1 and day 29.

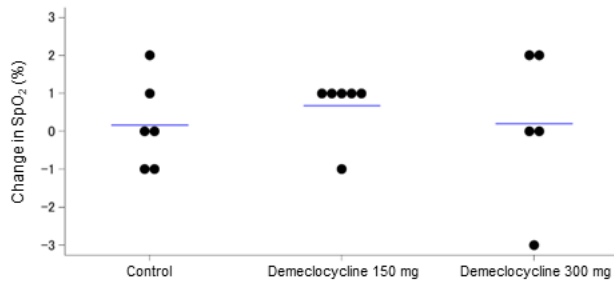
		Day 1	Day 8	Day 15	Day 29
Control group	Number of patients	6	4	1	1
	Mean	0.8	1.0	0.0	1.0
	SD	1.0	0.8	-	-
Demeclocycline 150 mg group	Number of patients	6	4	2	1
	Mean	1.2	1.3	1.5	0.0
	SD	1.2	1.3	0.7	-
Demeclocycline 300 mg group	Number of patients	5	4	2	1
	Mean	2.4	1.0	1.5	1.0
	SD	1.8	0.8	0.7	-

**Supplementary Table 3.** The NEWS scoring system.

	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤ 8		9 - 11	12 - 20		21 - 24	≥ 25
SpO <sub>2</sub> scale (%)	≤ 91	92 -93	94 - 95	≥ 96			
Air or oxygen		Oxygen		Air			
Systolic blood pressure (mmHg)	≤ 90	91 - 100	101 - 110	111 - 219			≥ 220
Pulse (per minute)	≤ 40		41 - 50	51 - 90	91 - 110	111 - 130	≥ 131
Consciousness				Alert			CVPU
Temperature (°C)	≤ 35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥ 39.1	

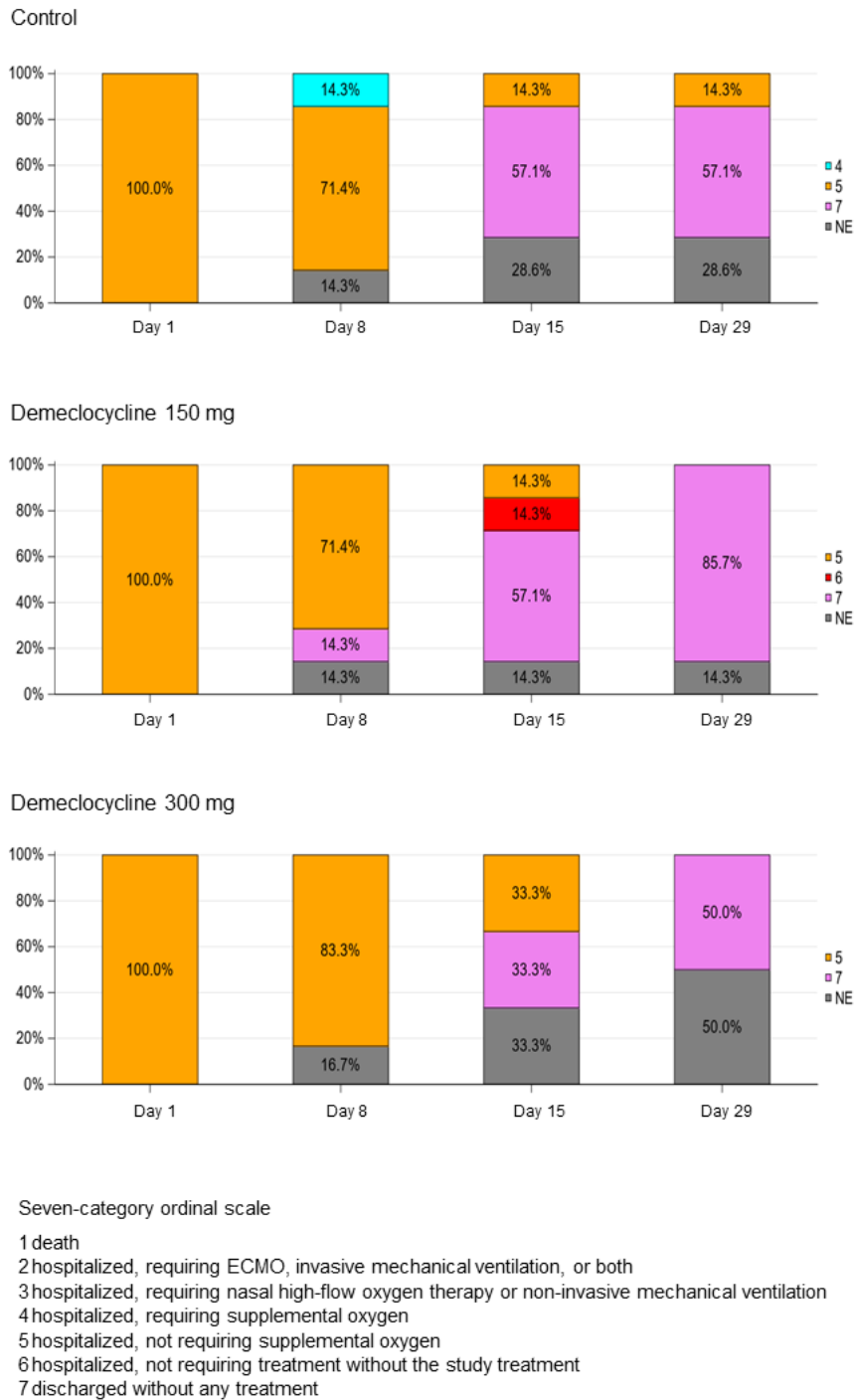
CVPU: confusion, verbal, pain, unresponsive.

### Supplementary Figure 1



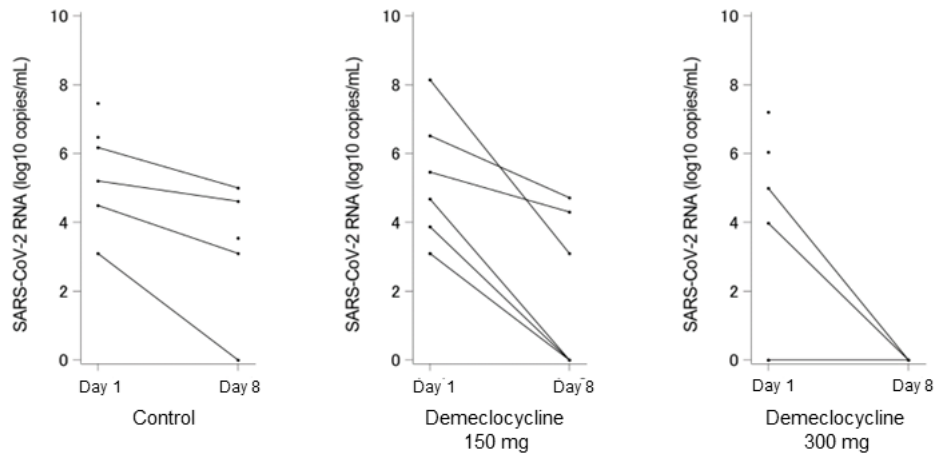
**Supplementary Figure 1.** Changes in SpO<sub>2</sub> from day 1 to day 8 of the study treatment in the control group (n = 6), demeclocycline 150 mg group (n = 6), and demeclocycline 300 mg group (n = 5).

## Supplementary Figure 2



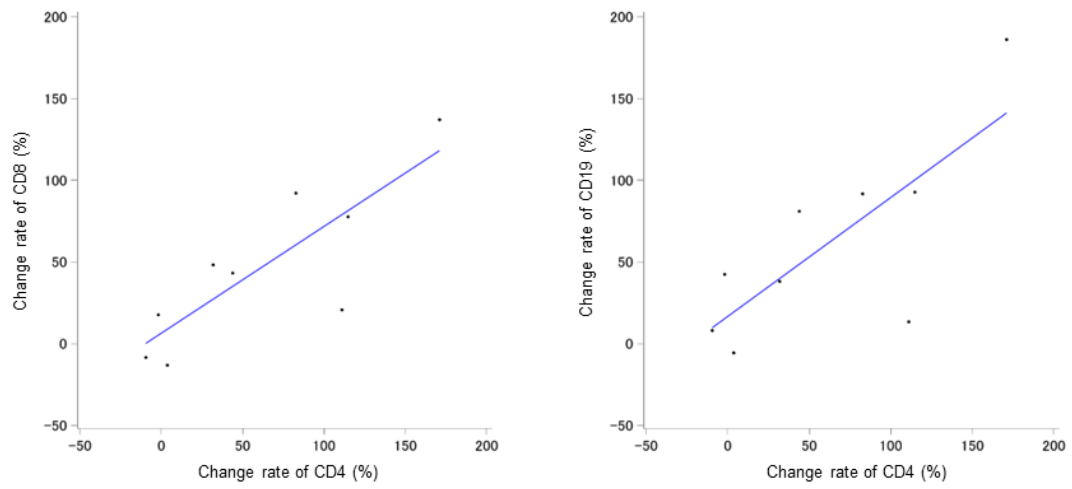
**Supplementary Figure 2.** Clinical status, defined by a seven-category ordinal scale, between day 1 and day 29 in the control group (n = 7), demeclocycline 150 mg group (n = 7), and demeclocycline 300 mg group (n = 6). NE, not evaluable.

### Supplementary Figure 3



**Supplementary Figure 3.** Changes in SARS-CoV-2 RNA from day 1 to day 8 of the study treatment in the control group (n = 4), demeclocycline 150 mg group (n = 6), and demeclocycline 300 mg group (n = 3).

### Supplementary Figure 4

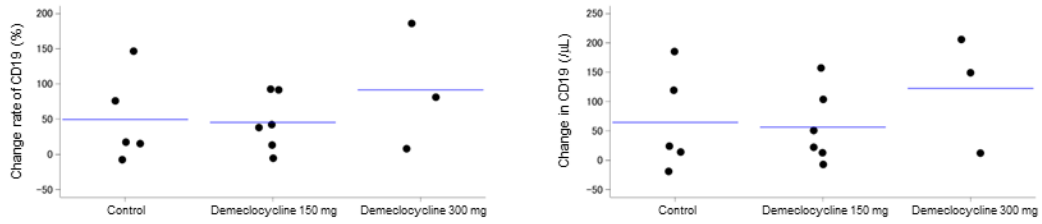


**Supplementary Figure 4.** Relationships between change rates of CD4+ and CD8+ T cells and between CD4+ T cells and CD19+ B cells in demeclocycline treatment groups (n = 9).

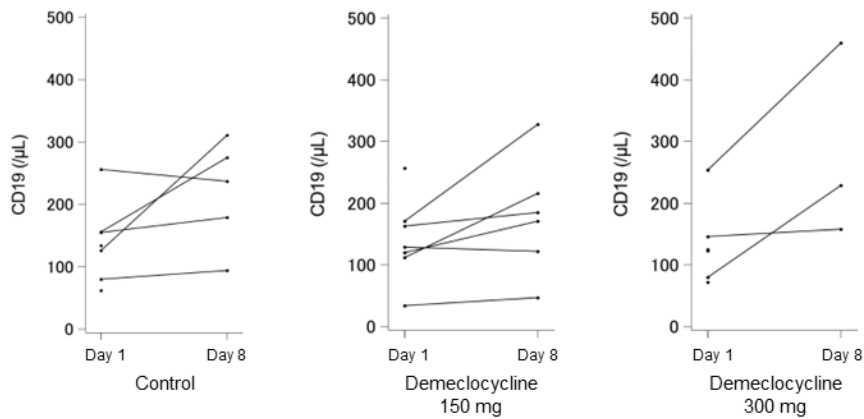


## Supplementary Figure 5

**A**

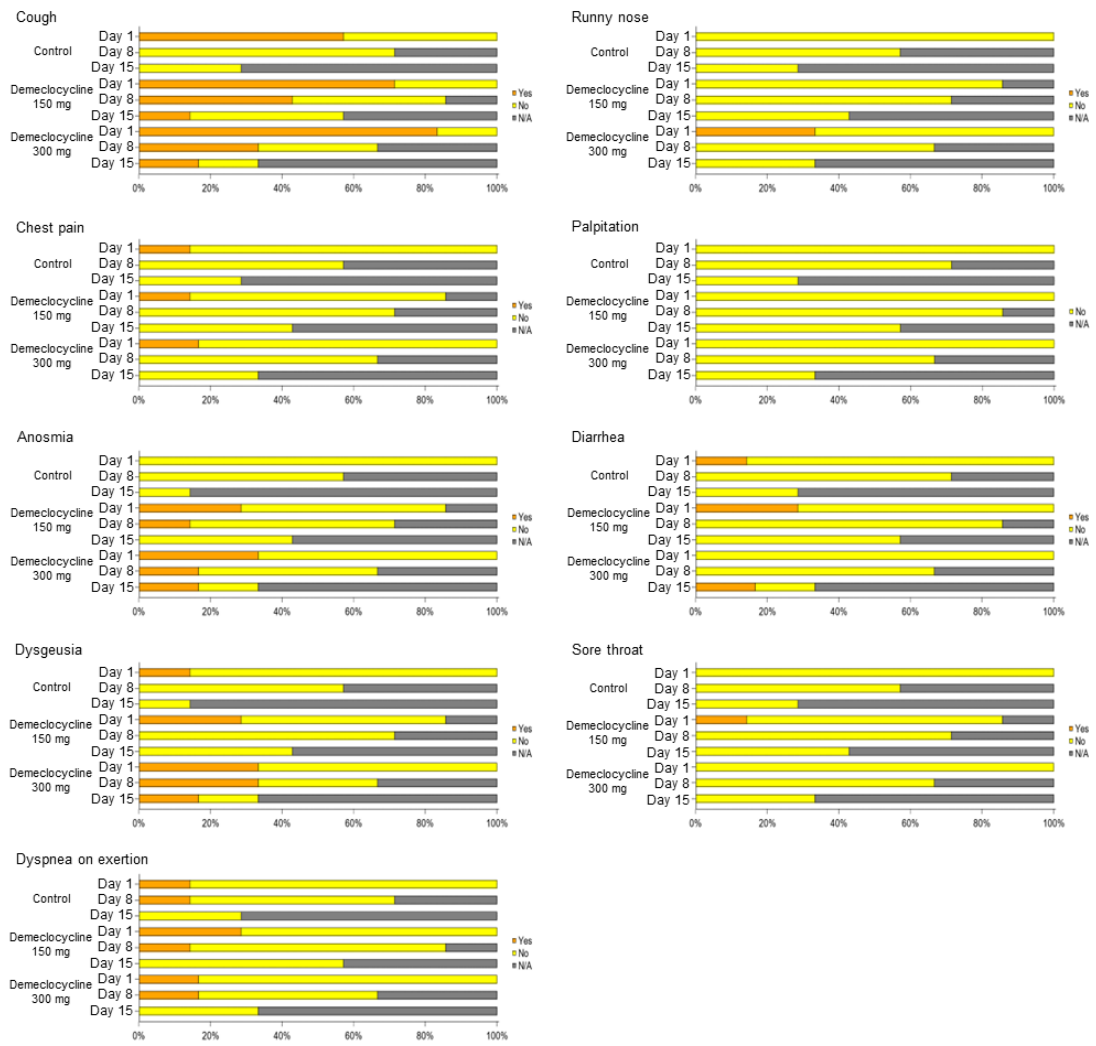


**B**



**Supplementary Figure 5.** (A) Changes in (right) and change rates (left) of CD19+ B cells in the control group (n = 5), demeclocycline 150 mg group (n = 6), and demeclocycline 300 mg group (n = 3). Each bar represents the average for each group. (B) Changes in CD19+ B cells from day 1 to day 8 of the study treatment in the control group (n = 5), demeclocycline 150 mg group (n = 6), and demeclocycline 300 mg group (n = 3).

**Supplementary Figure 6**



**Supplementary Figure 6.** The incidence of nine COVID-19 symptoms between day 1 and day 15 in the control group (n = 7), demeclocycline 150 mg group (n = 7), and demeclocycline 300 mg group (n = 6). N/A, not available.