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Supplementary appendix

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

Supplement to: Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020; published online April 29. http://dx.doi.org/10.1016/S0140-6736(20)31022-9.

Appendix

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21 **Table S1.** Outcomes in the PP population.

Characteristics	Total (n = 226)	Remdesivir group (n = 150)	Control group (n = 76)	Difference §
TTCI	22.0 (14.0 to 28.0)	21.0 (13.0 to 28.0)	23.0 (15.0 to 28.0)	1.27 (0.89 to 1.80)†
Day 28 mortality, n (%)	28 (12.4)	19 (12.7)	9 (11.8)	0.8 (-8.2 to 9.8)
Early (≤10 days of symptom onset)	14/115 (12.2)	8/69 (11.6)	6/46 (13.0)	-1.4 (-13.8 to 10.9)
Late (> 10 days of symptom onset)	14/111 (12.6)	11/81 (13.6)	3/30 (10.0)	3.6 (-9.5 to 16.7)
Clinical improvement proportions				
Day 7, n (%)	6 (2.7)	4 (2.7)	2 (2.6)	0.0 (-4.4 to 4.5)
Day 14, n (%)	58 (25.7)	41 (27.3)	17 (22.4)	5.0 (-6.8 to 16.7)
Day 28, n (%)	145 (64.2)	101 (67.3)	44 (57.9)	9.4 (-4.0 to 22.8)
IMV duration (days) &	8.0 (5.0 to 17.0)	7.0 (3.0 to 13.5)	16.0 (8.0 to 21.0)	-8.0 (-19.0 to 0.0)
IMV duration in survivors (days) &	19.0 (17.0 to 42.0)	12.0 (5.0 to 19.0)	42.0 (17.0 to 46.0)	-25.0 (-41.0 to 2.0)
IMV duration in non-survivors (days) &	7.5 (4.5 to 15.5)	7.0 (2.0 to 11.0)	11.5 (6.0 to 16.0)	-4.0 (-13.0 to 3.0)
Length of oxygen support (days)	20.0 (12.0 to 30.5)	19.0 (11.0 to 30.0)	21.0 (14.0 to 31.0)	-3.0 (-6.0 to 1.0)
Hospital length of stay (days)	25.0 (17.0 to 37.0)	25.0 (17.0 to 38.0)	25.0 (18.0 to 36.0)	0.0 (-4.0 to 4.0)
Days from randomization to discharge (days)	21.0 (13.0 to 31.0)	21.0 (13.0 to 32.0)	21.0 (14.0 to 29.0)	0.0 (-4.0 to 3.0)
Days from randomization to death (days)	11.0 (7.0 to 19.0)	11.0 (7.0 to 19.0)	12.0 (7.0 to 18.0)	-1.0 (-7.0 to 7.0)
Six-category scale at day 7				0.71 (0.41 to 1.21)*
1 Discharge (alive)	6/225 (2.7)	4/149 (2.7)	2 (2.6)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	37/225 (16.4)	21/149 (14.1)	16 (21.1)	
3 Hospitalization, requiring supplemental oxygen, n (%)	129/225 (57.3)	86/149 (57.7)	43 (56.6)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	34/225 (15.1)	26/149 (17.4)	8 (10.5)	
5 Hospitalization, requiring ECMO and/or IMV, n (%)	9/225 (4.0)	5/149 (3.4)	4 (5.3)	
6 Death	10/225 (4.4)	7/149 (4.7)	3 (3.9)	
Six-category scale at day 14				1.31 (0.80 to 2.17)*
1 Discharge (alive)	55/225 (24.4)	38/149 (25.5)	17 (22.4)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	31/225 (13.8)	21/149 (14.1)	10 (13.2)	
3 Hospitalization, requiring supplemental oxygen, n (%)	89/225 (39.6)	61/149 (40.9)	28 (36.8)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	21/225 (9.3)	13/149 (8.7)	8 (10.5)	
5 Hospitalization, requiring ECMO and/or IMV, n (%)	11/225 (4.9)	4/149 (2.7)	7 (9.2)	

6 Death	18/225 (8.0)	12/149 (8.1)	6 (7.9)	
Six-category scale at day 28				1.19 (0.69 to 2.05)*
1 Discharge (alive)	134/220 (60.9)	90/145 (62.1)	44/75 (58.7)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	18/220 (8.2)	14/145 (9.7)	4/75 (5.3)	
3 Hospitalization, requiring supplemental oxygen, n (%)	31/220 (14.1)	18/145 (12.4)	13/75 (17.3)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	4/220 (1.8)	2/145 (1.4)	2/75 (2.7)	
5 Hospitalization, requiring ECMO and/or IMV, n (%)	5/220 (2.3)	2/145 (1.4)	3/75 (4.0)	
6 Death	28/220 (12.7)	19/145 (13.1)	9/75 (12.0)	

* Calculated by ordinal logistic regression model.

Abbreviation: TTCI=time-to-clinical improvement; HFNC = high-flow nasal cannula for oxygen therapy; IMV = invasive mechanical ventilation; ECMO = extracorporeal membrane oxygenation.

& In survivors, 2 patients were in remdesivir group, 3 cases in control group; In non-survivors, 10 patients were in remdesivir group, 6 cases in control group.

§ Differences were expressed as rate differences or Hodges-Lehmann estimator and 95% confidence intervals.

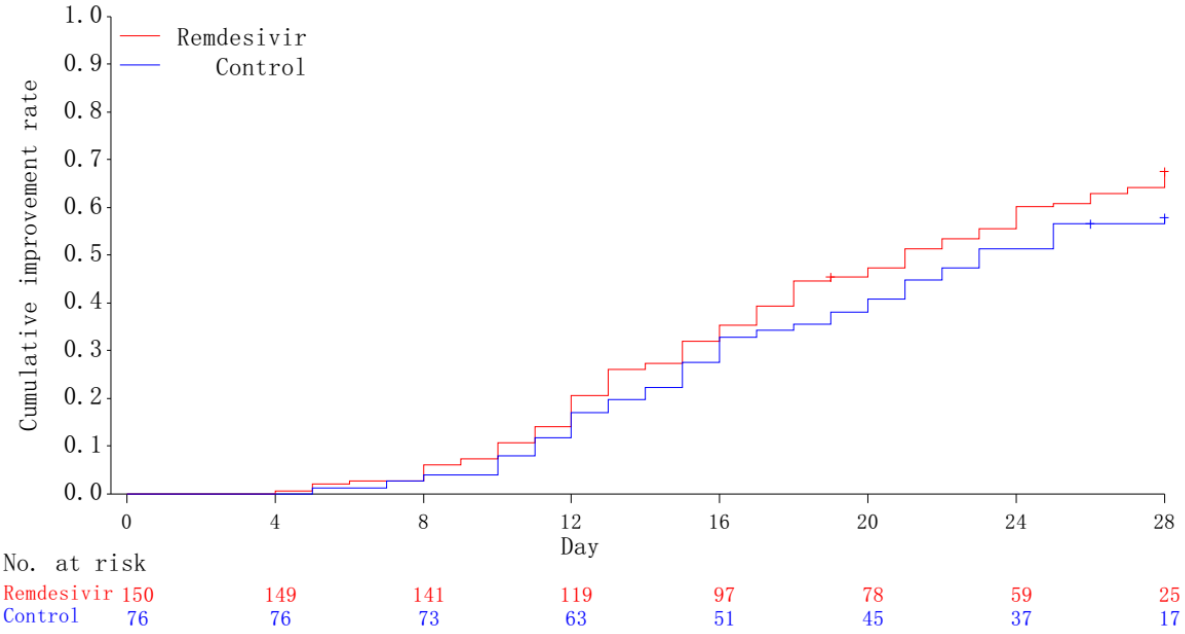
† The hazard ratio was estimated by COX proportional risk model.

Table S2. Accumulated rate of undetectable viral RNA in upper respiratory tract specimens in viral positive population.

Study day	Total (n = 196)	Remdesivir group (n = 131)	Control group (n = 65)	Difference §
Baseline	37/196 (18.9%)	24/131 (18.3%)	13/65 (20.0%)	-1.7 (-13.4 to 10.1)
Day 3, n (%)	56/196 (28.6%)	37/131 (28.2%)	19/65 (29.2%)	-1.0 (-14.5 to 12.5)
Day 5	78/196 (39.8%)	53/131 (40.5%)	25/65 (38.5%)	2.0 (-12.5 to 16.5)
Day 7	98/196 (50.0%)	66/131 (50.4%)	32/65 (49.2%)	1.2 (-13.7 to 16.0)
Day 10	127/196 (64.8%)	82/131 (62.6%)	45/65 (69.2%)	-6.6 (-20.6 to 7.3)
Day 14	142/196 (72.4%)	93/131 (71.0%)	49/65 (75.4%)	-4.4 (-17.4 to 8.6)
Day 21	151/196 (77.0%)	98/131 (74.8%)	53/65 (81.5%)	-6.7 (-18.7 to 5.3)
Day 28	153/196 (78.1%)	99/131 (75.6%)	54/65 (83.1%)	-7.5 (-19.2 to 4.2)
Survivors, n	167	112	55	
Baseline	33/167 (19.8%)	21/112 (18.8%)	12/55 (21.8%)	-3.1 (-16.2 to 10.0)
Day 3, n (%)	49/167 (29.3%)	32/112 (28.6%)	17/55 (30.9%)	-2.3 (-17.1 to 12.5)
Day 5	70/167 (41.9%)	47/112 (42.0%)	23/55 (41.8%)	0.1 (-15.8 to 16.1)
Day 7	89/167 (53.3%)	59/112 (52.7%)	30/55 (54.5%)	-1.9 (-18.0 to 14.2)
Day 10	117/167 (70.1%)	75/112 (67.0%)	42/55 (76.4%)	-9.4 (-23.6 to 4.8)
Day 14	131/167 (78.4%)	85/112 (75.9%)	46/55 (83.6%)	-7.7 (-20.3 to 4.8)
Day 21	138/167 (82.6%)	89/112 (79.5%)	49/55 (89.1%)	-9.6 (-20.8 to 1.5)
Day 28	139/167 (83.2%)	90/112 (80.4%)	49/55 (89.1%)	-8.7 (-19.8 to 2.3)
Non-survivors, n*	29	19	10	
Baseline	4/29 (13.8%)	3/19 (15.8%)	1/10 (10.0%)	5.8 (-19.0 to 30.6)
Day 3, n (%)	7/29 (24.1%)	5/19 (26.3%)	2/10 (20.0%)	6.3 (-25.4 to 38.0)
Day 5	8/29 (27.6%)	6/19 (31.6%)	2/10 (20.0%)	11.6 (-20.8 to 44.0)
Day 7	9/29 (31.0%)	7/19 (36.8%)	2/10 (20.0%)	16.8 (-16.1 to 49.8)
Day 10	10/29 (34.5%)	7/19 (36.8%)	3/10 (30.0%)	6.8 (-28.9 to 42.6)
Day 14	11/29 (37.9%)	8/19 (42.1%)	3/10 (30.0%)	12.1 (-23.9 to 48.2)
Day 21	13/29 (44.8%)	9/19 (47.4%)	4/10 (40.0%)	7.4 (-30.4 to 45.1)
Day 28	14/29 (48.3%)	9/19 (47.4%)	5/10 (50.0%)	-2.6 (-40.9 to 35.6)

***** Totally, 35 patients died during the hospitalization, otherwise there were 32 fatal cases until day 28; Respiratory specimens of 27 patients in remdesivir group and 13 patients in control group were not collected because safety of medical care workers during aerosol generating procedures cannot be guaranteed in one study site

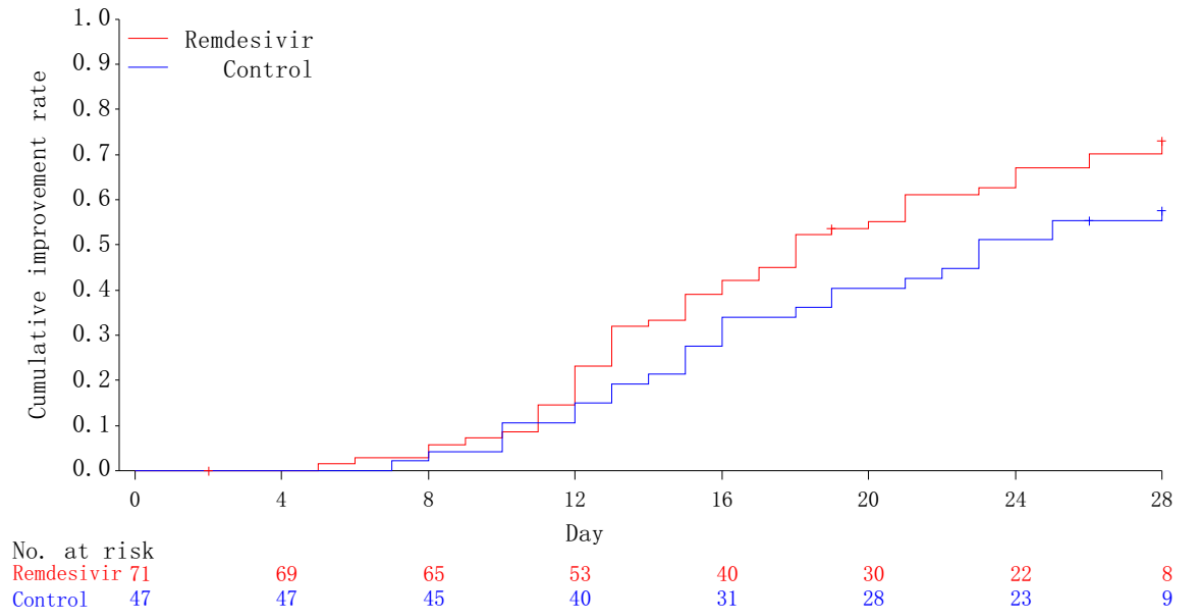
Figure S1. Kaplan Meier plot of time-to-clinical improvement at day 28 in the PP population.



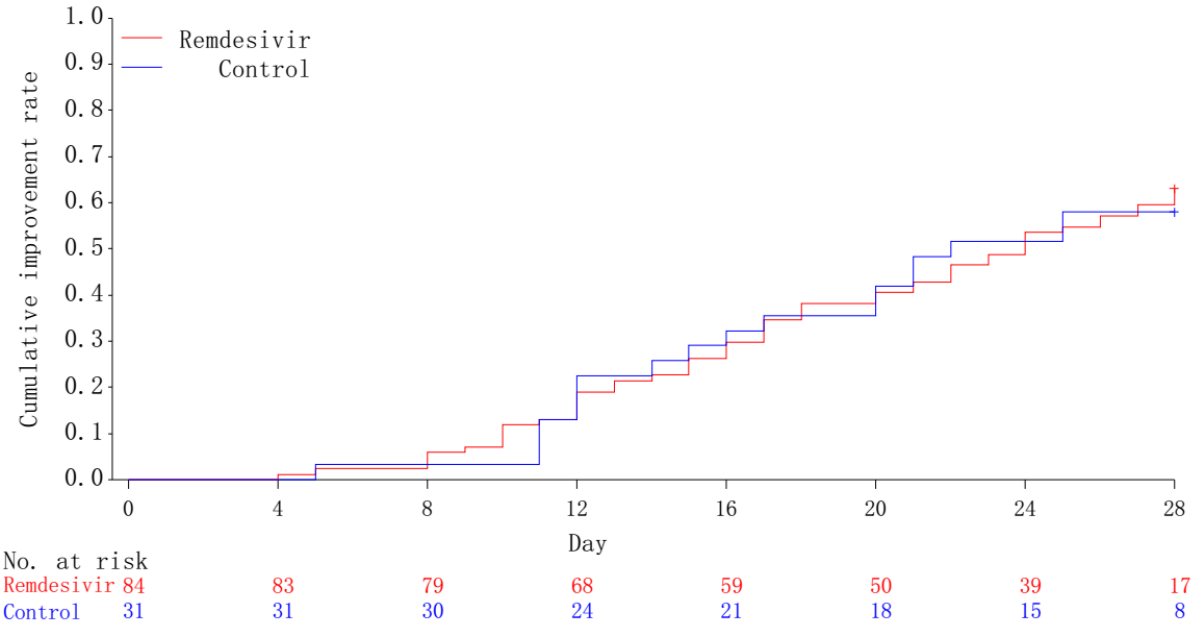
Note. Hazard ratio (HR) for clinical improvement, 1.27; 95% confidence interval [CI], 0.89 to 1.80.

Figure S2. Kaplan Meier plot of time-to-clinical improvement by duration of illness (≤ 10 days [Panel A] vs > 10 days [Panel B]) in the intention-to-treat population.

A

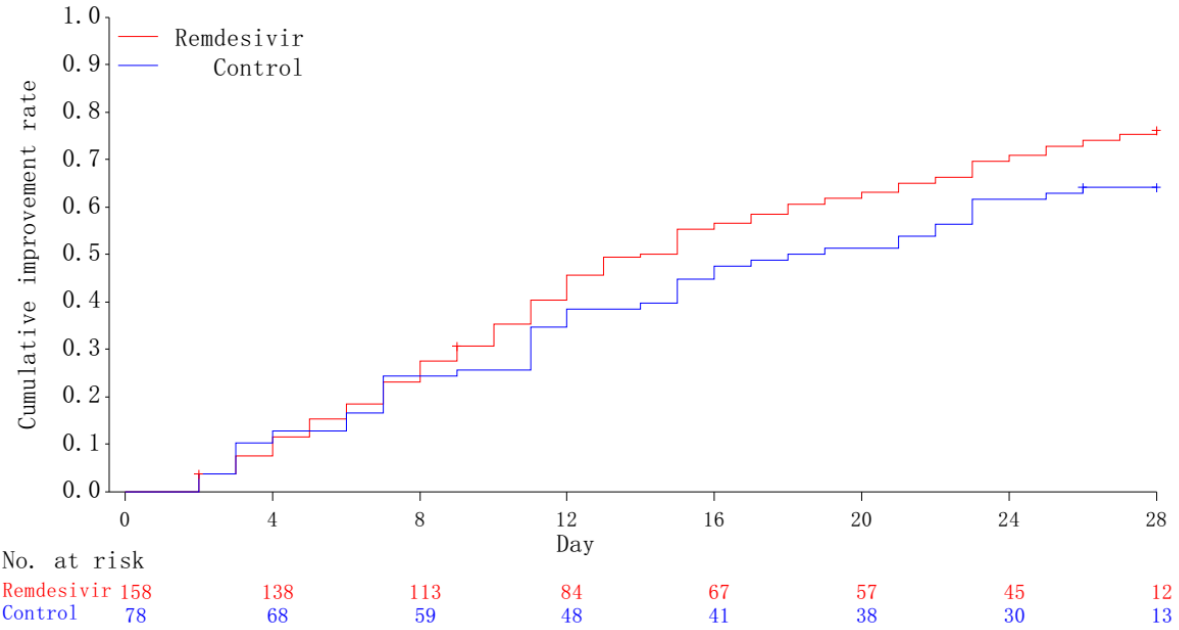


B



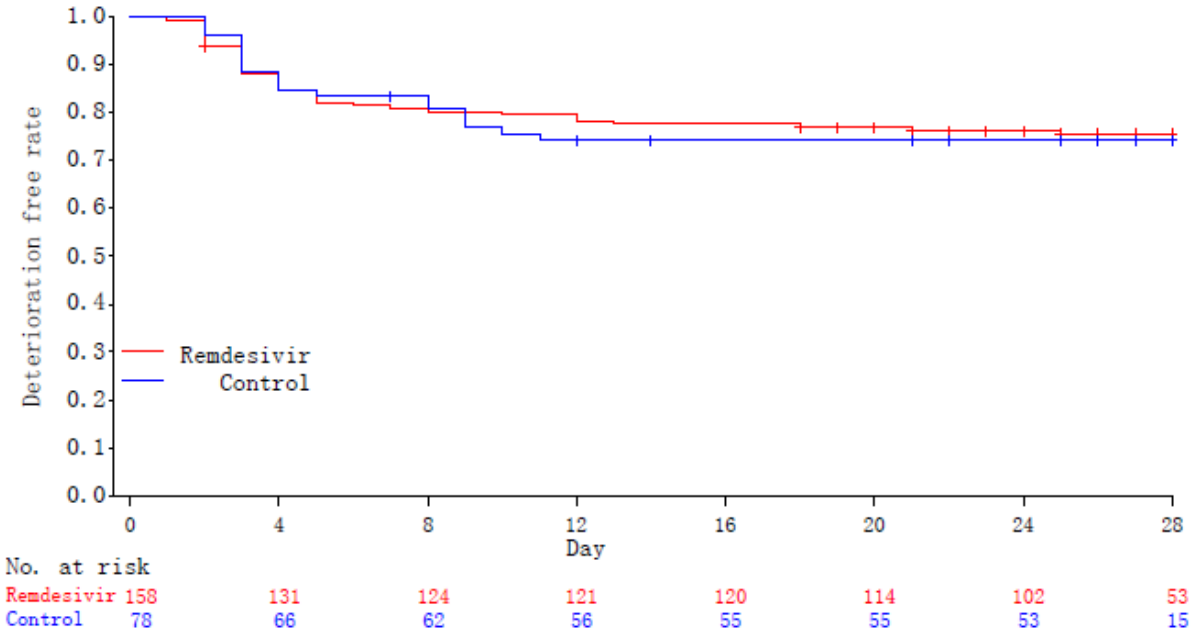
Note. (A) In early treatment group (≤ 10 days), median TTCI 18.0 days (remdesivir) vs. 23 days (control); hazard ratio (HR) for clinical improvement, 1.52; 95% confidence interval [CI], 0.95 to 2.43; and (B) in late treatment group (>10 days), median TTCI 23.0 days (remdesivir) vs. 24 days (control); HR for clinical improvement, 1.07; 95% CI, 0.63 to 1.83.

Figure S3. Kaplan Meier plot of time-to-clinical improvement (defined as one category decline) in the ITT population.



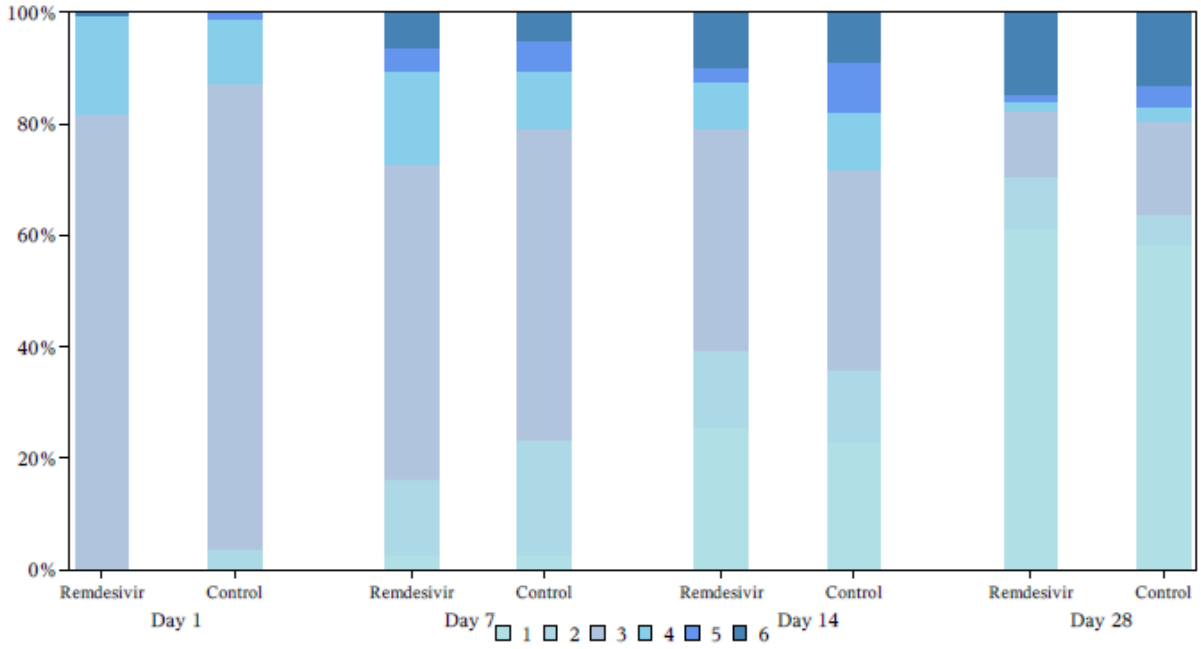
Note. HR for clinical improvement, 1.34; 95% CI, 0.96 to 1.86.

Figure S4. Kaplan Meier of time-to-clinical deterioration (defined as one category increase or death) in the intention-to-treat population.



Note. Hazard ratio for clinical deterioration, 0.95; 95% CI, 0.55 to 1.64.

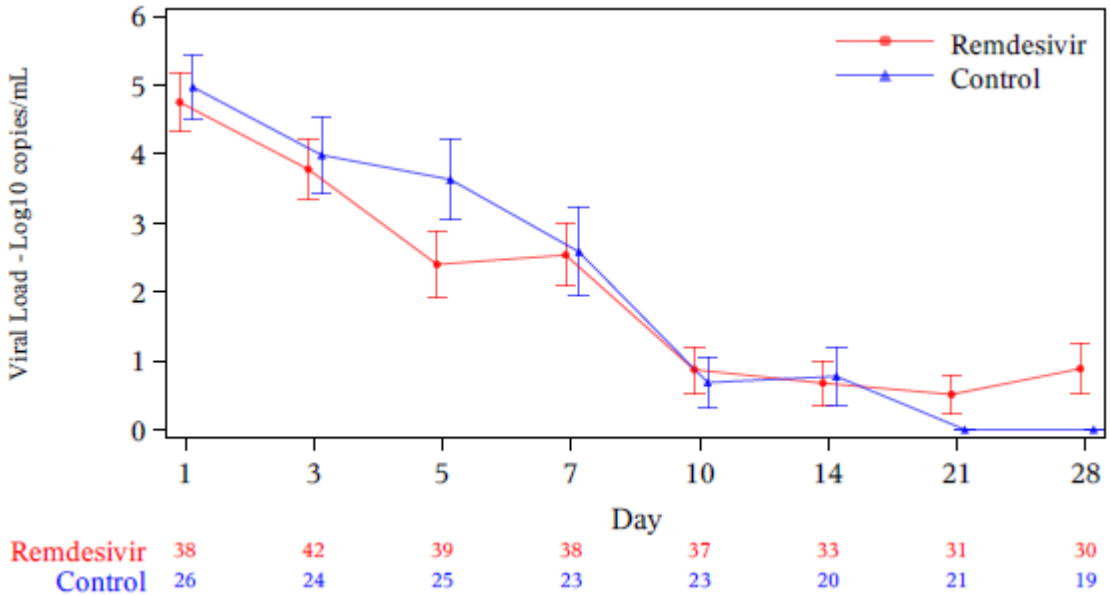
Figure S5. Proportional distribution of primary endpoint categories at day1, 7, 14 and 28 in the intention-to-treat population



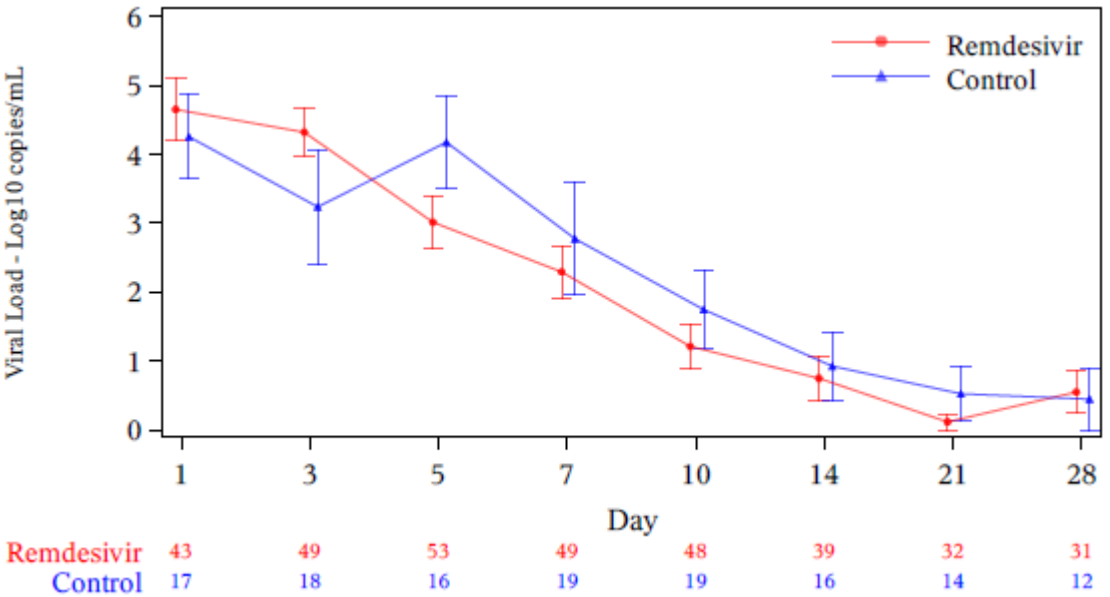
Proportion of severe outcomes according to 6-category ordinal scale that ranges from 1 (discharged with normal activity) to 6 (death). 1 Hospital discharge (alive); 2 Hospitalized, not requiring supplemental oxygen; 3 Hospitalized, requiring supplemental oxygen; 4 Hospitalized, requiring high-flow nasal oxygen (HFNC)and/or non-invasive mechanical ventilation (IMV); 5 Hospitalized, requiring ECMO and/or IMV; 6 Death.

Figure S6. SARS-CoV-2 viral RNA load over time from baseline by qPCR on the upper respiratory tract swabs (viral positive population) by duration of illness (≤ 10 days [Panel A] vs > 10 days [Panel B]) in the viral positive population.

A



B



Note. Based on Wilcoxon rank sum test at each visit, (A) In early treatment group (≤ 10 days), no significant statistical difference between two treatment group, and (B) in late treatment group (>10 days), no significant statistical difference between two treatment group.