Supplementary Appendix

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

Supplement to: Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 — final report. N Engl J Med 2020;383:1813-26. DOI: 10.1056/NEJMoa2007764

Supplementary Appendix to Manuscript Entitled

Remdesivir for the Treatment of COVID-19 – Final Report

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Supplemental Methods:

Additional Study Design Details

The trial was designed, overseen and sponsored by the NIAID's Division of Microbiology and Infectious Diseases (DMID) with input from selected site investigators. The 60 sites and 13 subsites gathered and entered the data into Advantage eClinical ^{SM}, designed by The Emmes Company LLC. The sponsor and staff from Emmes, which is funded by the sponsor, analyzed the data. The first and second author wrote the first draft of the manuscript and tables and figures were prepared the third author and staff from Emmes. The manuscript was subsequently revised and approved by all the authors, who agreed to submit the manuscript for publication.

Additional Study population Details

After informed consent was obtained, participants 18 years of age or older who were hospitalized with symptoms suggestive of COVID-19 were assessed for eligibility. Participants had to meet one of the following criteria suggestive of lower respiratory tract infection at the time of enrollment: radiographic infiltrates by imaging study, peripheral oxygen saturation (SpO2) ≤94% on room air, or requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). There was no limit to the duration of symptoms prior to enrollment. Participants had to have a laboratory-confirmed SARS-CoV-2 infection as determined by a positive reverse transcription, polymerase-chain-reaction (RT-PCR) assay result from any respiratory specimen collected <72 hours prior to randomization. During the study, this criterion was modified due to limitations in testing capacity to also allow a RT-PCR positive specimen that was collected ≥72 hours prior to randomization if the site was unable to obtain a repeat sample and if the participant had progressive disease consistent with ongoing SARS-CoV-2 infection. Other inclusion criteria included agreeing not to participate in another COVID-19 treatment clinical trial through Day 29 and practicing heterosexual abstinence or using study-specified contraception through Day 29 for women of childbearing potential. Exclusion criteria included having either an alanine aminotransferase (ALT) or an aspartate aminotransferase (AST) > 5 times the upper limit of the normal range; impaired renal function as determined by calculating an estimated glomerular filtration rate (eGFR), or need for hemodialysis or hemofiltration; allergy to study product; pregnancy or breast-feeding; and anticipated discharge from the hospital or transfer to another hospital within 72 hours of enrollment.

Randomization was stratified by study site and disease severity at enrollment and was performed using a web-based Internet Data Entry System, Advantage eClinical ^{SM}. Severe disease was defined as participants meeting one or more of the following criteria: requiring invasive or non-invasive mechanical ventilation, requiring supplemental oxygen, an SpO2 ≤ 94% on room air, or tachypnea (respiratory rate ≥ 24 breaths per minute). Mild / moderate disease was defined by a SpO2 > 94% and respiratory rate < 24 breaths per minute without supplemental oxygen requirement. The definition of the two categories of disease severity were chosen to generally align with the two separate remdesivir studies being developed for implementation in Wuhan, China to facilitate comparability of results (NCT04252664, and NCT04257656 (1)).

Additional Study Procedures Details

Participants were assessed daily from Day 1 through Day 29 while hospitalized. Participants discharged from the hospital had study visits at Days 15 and 29. In-person visits were preferred, although restrictions due to local infection control measures often limited participants from leaving their home and returning to the study sites. Follow-up by phone was acceptable in these circumstances. An additional study visit on Day 22 was conducted by phone. The participant's clinical status was captured daily while hospitalized using an 8-category ordinal scale (defined in the main manuscript) and the National Early Warning Score (NEWS) (2, 3). Participants discharged prior to Day 15 had the ordinal scale assessed at all follow-up visits while the NEWS required in-person visits. Blood samples for safety laboratory tests (white blood cell count with differential, hemoglobin, platelet count, creatinine, glucose, total bilirubin, ALT, AST, and prothrombin time), and oropharyngeal (OP) swab samples (nasopharyngeal [(NP]) could be substituted) were collected on Days 1 (before initial infusion), 3, 5, 8, and 11 while hospitalized, and Days 15 and 29 for participants able to attend an in-person visit or who were still hospitalized.

All serious adverse events (SAE), and grade 3-4 adverse events (AE) that represented an increase in severity from Day 1, and any grade 2 or higher suspected drug-related hypersensitivity reactions associated with study product administration were captured in this trial. AEs were assessed by review of the electronic medical record, physical examinations, vital signs, and laboratory studies from the time the informed consent form was signed through Day 29. AEs were classified in accordance with the Medical Dictionary for Regulatory Activities® (MedDRA version 23.0), and their relationship to study product, severity, and outcome were documented.

Additional Statistical Analysis Details

The primary analysis was a log-rank test of time-to-recovery between remdesivir and placebo stratified by disease severity as defined above. The relevant treatment efficacy parameter is the "recovery rate ratio" (for remdesivir relative to placebo), which is akin to the hazard ratio in survival analysis but for the beneficial outcome of recovery. Two practical considerations result from considering time to a beneficial outcome. First, a recovery rate ratio greater than one indicates an improvement for remdesivir. Second, failure to recover and death are both censored at Day 29. Consequently, participants censored on the last observation day reflect two different states: death and failure to recover by Day 29. Hence, a breakdown of deaths by treatment arm is also important to understanding treatment efficacy. The key secondary analysis tested a difference in the ordinal score distribution between remdesivir and placebo at Day 15 using the "common odds ratio" from a proportional odds model, stratifying by baseline disease severity stratum.

The study was designed to achieve 85% power for detecting a recovery rate ratio of 1.35 with a two-sided type-I error rate of 5%. Enrollment continued through April 19, 2020 to ensure at least 400 recoveries and to address subgroup analysis. Because the SAP did not include a provision for correcting for multiplicity when conducting tests for secondary outcomes, results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer definitive treatment effects for secondary outcomes. More details can be found in the statistical analysis plan. Analyses were conducted using SAS version 9.4 and R version 3.5.1.

Supplemental Tables and Figures:

Table S1. Categorical Demographic and Baseline Characteristics by Treatment Group

		Remdesivir (N=541)		Placebo (N=521)		All (N=1062)	
Demographic Category	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**
Sex	Male	352	65	332	64	684	64
	Female	189	35	189	36	378	36
Ethnicity	Not Hispanic or Latino	382	71	373	72	755	71
	Hispanic or Latino	134	25	116	22	250	24
	Not Reported	15	3	14	3	29	3
	Unknown	10	2	18	3	28	3
Race	American Indian or Alaska Native	4	1	3	1	7	1
	Asian	79	15	56	11	135	13
	Native Hawaiian or Other Pacific Islander	2	<1	2	<1	4	<1
	Black or African American	109	20	117	22	226	21
	White	279	52	287	55	566	53
	Multi-Racial	2	<1	1	<1	3	<1
	Unknown	66	12	55	11	121	11
US Sites	US Site	427	79	410	79	837	79
	Non-US Site	114	21	111	21	225	21
Geographic Region	North America	431	80	416	80	847	80
	Europe	84	16	79	15	163	15
	Asia	26	5	26	5	52	5
Age (years)	<40	59	11	60	12	119	11
	40-64	295	55	264	51	559	53
	>=65	187	35	197	38	384	36
Baseline Clinical Status	Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care	75	14	63	12	138	13
	Hospitalized, requiring supplemental oxygen	232	43	203	39	435	41
	Hospitalized, on non-invasive ventilation or high flow oxygen devices	95	18	98	19	193	18
	Hospitalized, on invasive mechanical ventilation or ECMO	131	24	154	30	285	27
Duration of Symptoms prior to enrollment	First Quartile (≤ 6 Days)	158	29	124	24	282	27
	Second Quartile (7 to ≤ 9 Days)	148	27	152	29	300	28
	Third Quartile (10 to ≤ 12 Days)	113	21	108	21	221	21

		Remdesivir (N=541)		Placebo (N=521)		All (N=1062)	
Demographic Category	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**
	Fourth Quartile (13+ Days)	121	22	135	26	256	24
Duration of Symptoms prior to enrollment	≤ 10 Days	356	66	320	61	676	64
	> 10 Days	184	34	199	38	383	36
Duration of Symptoms prior to enrollment	≤ Median (9 Days)	306	57	276	53	582	55
	> Median (9 Days)	234	43	243	47	477	45
Comorbidities	Asthma	63	12	57	11	120	11
	Cardiac failure congestive	31	6	28	5	59	6
	Chronic kidney disease	38	7	29	6	67	6
	Chronic respiratory disease	37	7	41	8	78	7
	Coronary artery disease	69	13	57	11	126	12
	Dependence on oxygen therapy	15	3	4	1	19	2
	Hypertension	269	51	264	51	533	51
	Immune system disorder	32	6	41	8	73	7
	Liver disorder	14	3	12	2	26	2
	Neoplasm malignant	43	8	37	7	80	8
	Obesity	242	46	234	45	476	45
	Type 1 diabetes mellitus	7	1	3	1	10	1
	Type 2 diabetes mellitus	164	31	158	30	322	31
Comorbidities -Presence	Any Comorbidities	435	80	422	81	857	81
	No Comorbidities	97	18	97	19	194	18
	Unknown	9	2	2	<1	11	1
Comorbidities - Number	No Comorbidities	97	18	97	19	194	18
	1 Comorbidity	138	26	137	26	275	26
	2 or more Comorbidities	296	55	283	54	579	55
	Unknown	10	2	4	1	14	1
Comorbidities - Obesity	Obese	242	45	234	45	476	45
	Non-Obese	289	53	284	55	573	54
	Unknown	10	2	3	1	13	1

Table S2. Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	Remdesivir (N=541)	Placebo (N=521)	All (N=1062)
Age (years)	n	541	521	1062
	Mean	58.6	59.2	58.9
	Standard Deviation	14.6	15.4	15.0
	Median	59.0	60.0	59.0
	Minimum	21	21	21
	Maximum	94	95	95
Height (cm)	n	489	474	963
	Mean	170.56	169.94	170.26
	Standard Deviation	11.02	10.02	10.54
	Median	170.20	170.00	170.20
	Minimum	139.7	134.6	134.6
	Maximum	200.7	196.0	200.7
Weight (kg)	n	499	484	983
	Mean	89.50	88.10	88.81
	Standard Deviation	24.77	22.83	23.83
	Median	85.30	84.00	84.90
	Minimum	41.7	46.0	41.7
	Maximum	238.1	190.5	238.1
BMI (kg/m^2)	n	488	474	962
	Mean	30.65	30.54	30.60
	Standard Deviation	7.50	7.54	7.52
	Median	29.20	29.00	29.05
	Minimum	14.4	16.9	14.4
	Maximum	69.5	64.8	69.5
Duration of Symptoms prior to Enrollment (days)	n	540	519	1059
	Mean	9.7	10.0	9.8
	Standard Deviation	5.7	5.0	5.4
	Median	9.0	9.0	9.0
	Minimum	0	1	0
	Maximum	46	34	46
	25^{th} Percentile	6	7	6
	75^{th} Percentile	12	13	12

Table S3. Patients' Status and Treatments Received - As-Treated Population

	All (N=1048)	Remdesivir (N=532)	Placebo (N=516)
Highest level of respiratory support – no. (%)			
Extracorporeal membrane oxygenation	26 (2.5)	11 (2.1)	15 (2.9)
Invasive mechanical ventilation	393 (37.5)	173 (32.5)	220 (42.6)
Non-invasive mechanical ventilation	204 (19.5)	106 (19.9)	98 (19.0)
Other oxygen delivery device	342 (32.6)	194 (36.5)	148 (28.7)
None	83 (7.9)	48 (9.0)	35 (6.8)
Treatments during study – no. (%)			
Antibiotics	863 (82.3)	420 (78.9)	443 (85.9)
Vasopressors	342 (32.6)	147 (27.6)	195 (37.8)
Corticosteroids	241 (23.0)	115 (21.6)	126 (24.4)
Other anti-inflammatory medications	79 (7.5)	42 (7.9)	37 (7.2)
Monoclonal antibodies targeting cytokines	50 (4.8)	23 (4.3)	26 (5.0)
Other biologic therapies	34 (3.2)	21 (3.9)	13 (2.5)
Hydroxychloroquine	373 (35.6)	184 (34.6)	189 (36.6)
Other putative SARS-CoV-2 medications	22 (2.1)	8 (1.5)	14 (2.7)
Other antiviral medications	18 (1.7)	10 (1.9)	8 (1.6)

Table S4. Outcomes Overall and by Baseline Disease Severity – ITT Population

Baseline Disease Severity Stratum	Overall*		Mild-Moderate Disease Stratum		Severe Disease Stratum	
	Remdesivir (n=541)	Placebo (n=521)	Remdesivir (n=55)	Placebo (n=50)	Remdesivir (n=486)	Placebo (n=471)
Recovery						
No. of recoveries	399	352	54	46	345	306
Median time to recovery (95% CI) - days	10 (9, 11)	15 (13, 18)	5 (4, 6)	5 (4, 7)	11 (10, 14)	18 (15, 20)
Restricted Mean Recovery Time (95% CI) - days	14.1 (13.2, 15.1)	16.9 (15.9, 17.8)	6.5 (5.2, 7.8)	7.9 (5.9, 9.8)	15.0 (14.1, 16.0)	17.8 (16.8, 18.8)
Rate ratio (95% CI)†	1.29 (1.12, 1.49); p<0.001		1.22 (0.82, 1.81)		1.31 (1.12, 1.52)	
Mortality over first 14 days‡						
Hazard ratio (95% CI) for data through Day 15	0.55 (0.36, 0.83)		0.45 (0.04, 5.00)		0.55 (0.36, 0.84)	
Number of deaths by Day 15	35	61	1	2	34	59
Kaplan-Meier estimate of mortality by Day 15 – % (95% CI)	6.7 (4.8, 9.2)	11.9 (9.4, 15.0)	1.8 (0.3, 12.2)	4.1 (1.0, 15.3)	7.3 (5.2, 10.0)	12.7 (10.0, 16.1)
Mortality over entire study period‡						
Hazard ratio (95% CI) over entire study period	0.73 (0.52, 1.03); p=0.07		0.60 (0.10, 3.56)		0.74 (0.52, 1.04)	
Number of deaths by Day 29	59	77	2	3	57	74
Kaplan-Meier estimate of mortality by Day 29 – % (95% CI)	11.4 (9.0, 14.5)	15.2 (12.3, 18.6)	3.8 (1.0, 14.3)	6.2 (2.0, 18.0)	12.3 (9.6, 15.7)	16.1 (13.0, 19.8)
Restricted Mean Survival Time (95% CI) - days	26.2 (25.7, 26.7)	25.3 (24.7, 25.9)	27.4 (26.5, 28.4)	27.2 (26.2, 28.1)	26.1 (25.6, 26.6)	25.1 (24.5, 25.8)
Ordinal Scale at day 15 (±2 days) – no. (%)**						
1	157 (29.0)	115 (22.1)	28 (50.9)	22 (44.0)	129 (26.5)	93 (19.7)
2	117 (21.6)	102 (19.6)	14 (25.5)	13 (26.0)	103 (21.2)	89 (18.9)
3	14 (2.6)	8 (1.5)	7 (12.7)	3 (6.0)	7 (1.4)	5 (1.1)
4	38 (7.0)	33 (6.3)	3 (5.5)	5 (10.0)	35 (7.2)	28 (5.9)
5	58 (10.7)	60 (11.5)	1 (1.8)	4 (8.0)	57 (11.7)	56 (11.9)
6	28 (5.2)	24 (4.6)	1 (1.8)	0 (0)	27 (5.6)	24 (5.1)
7	95 (17.6)	121 (23.2)	0 (0)	2 (4.0)	95 (19.5)	119 (25.3)
8	34 (6.3)	58 (11.1)	1 (1.8)	1 (2.0)	33 (6.8)	57 (12.1)
Odds ratio (95% CI)	1.5 (1.2, 1.9); p<0.001		1.5 (0.7, 3.0)		1.6 (1.2, 1.9)	

* P values and confidence intervals have not been adjusted for multiple comparisons. NE denotes not possible to estimate.

† Recovery rate ratios and hazard ratios were calculated from the stratified Cox model; P values for these ratios were calculated with the stratified log-rank test (overall model stratified by actual

disease severity). Recovery rate ratios greater than 1 indicate a benefit for remdesivir; hazard ratios less than 1 indicate a benefit for remdesivir.

‡ Mortality over the first 14 days treats all patients who were still alive through 14 days post enrollment as censored on Day 15, as if 14 days was the maximum follow-up time. Mortality over the entire study period uses the totality of the study data and censors patients who completed follow-up alive at 28 days post enrollment.

** The ordinal score at day 15 is the patient's worst score on the ordinal scale during the previous day. Four patients died 15 days after randomization and are recorded as deceased for the ordinal score at day 15 outcome but not for the mortality by day 15 outcome. Scores on the ordinal scale are as follows: 1, not hospitalized, no limitations of activities; 2, not hospitalized, limitation of activities, home oxygen requirement, or both; 3, hospitalized, not requiring supplemental oxygen and no longer requiring ongoing medical care (used if hospitalization was extended for infection-control reasons); 4, hospitalized, not requiring supplemental oxygen but requiring ongoing medical care (Covid-19–related or other medical conditions); 5, hospitalized, requiring any supplemental oxygen; 6, hospitalized, requiring noninvasive ventilation or use of high-flow oxygen devices; 7, hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); and 8, death. Odds ratios and P values were calculated with the use of a proportional odds model (overall model adjusted for actual disease severity). Odds ratio values greater than 1 indicate a benefit for remdesivir.

Table S5. Outcomes overall According to Score on the Ordinal Scale – ITT Population
(same as Table 2 of the main manuscript, but with additional analyses)

			Ordinal Score at Baseline							
	Overall*		4		5		6		7	
	Remdesivir (n=541)	Placebo (n=521)	Remdesivir (n=75)	Placebo (n=63)	Remdesivir (n=232)	Placebo (n=203)	Remdesivir (n=95)	Placebo (n=98)	Remdesivir (n=131)	Placebo (n=154)
Recovery										
No. of recoveries	399	352	73	58	206	156	57	61	63	77
Median time to recovery (95% CI) - days	10 (9, 11)	15 (13, 18)	5 (4, 6)	6 (4, 7)	7 (6, 8)	9 (7, 10)	15 (10, 27)	19.5 (14, 26)	29 (24, NE)	28 (24, NE)
Restricted Mean Recovery Time (95% CI) - days	14.1 (13.2,15.1)	16.9 (15.9,17.8)	6.7 (5.4,8.0)	8.6 (6.7,10.5)	9.9 (8.8,11.0)	13.1 (11.7,14.5)	17.5 (15.3,19.8)	19.0 (16.9,21.0)	23.5 (22.2,24.9)	23.8 (22.6,25.0)
Rate ratio (95% CI) †	1.29 (1.12, 1.49); p<0.001		1.29 (0.91, 1.83)		1.45 (1.18, 1.79)		1.09 (0.76, 1.57)		0.98 (0.70, 1.36)	
Mortality over first 14 days‡										
Hazard ratio (95% CI) for data through Day 15	0.55 (0.36, 0.83)		0.42 (0.04, 4.67)		0.28 (0.12, 0.66)		0.82 (0.40, 1.69)		0.76 (0.39, 1.50)	
Number of deaths by Day 15	35	61	1	2	7	21	13	17	14	21
Kaplan-Meier estimate of mortality by Day 15 – % (95% CI)	6.7 (4.8, 9.2)	11.9 (9.4, 15.0)	1.3 (0.2, 9.1)	3.2 (0.8, 12.1)	3.1 (1.5, 6.4)	10.5 (7.0, 15.7)	14.2 (8.5, 23.2)	17.3 (11.2, 26.4)	10.9 (6.6, 17.6)	13.8 (9.2, 20.4)
Mortality over entire study period‡										
Hazard ratio (95% CI) over entire study period	0.73 (0.52, 1.03); p=0.07		0.82 (0.17, 4.07)		0.30 (0.14, 0.64)		1.02 (0.54, 1.91)		1.13 (0.67, 1.89)	
Number of deaths by Day 29	59	77	3	3	9	25	19	20	28	29
Kaplan-Meier estimate of mortality by Day 29 – % (95% CI)	11.4 (9.0, 14.5)	15.2 (12.3, 18.6)	4.1(1.3, 12.1)	4.8 (1.6, 14.3)	4.0 (2.1, 7.5)	12.7 (8.8, 18.3)	21.2 (14.0, 31.2)	20.4 (13.7, 29.8)	21.9 (15.7, 30.1)	19.3 (13.8, 26.5)
Restricted Mean Survival Time (95% CI) - days	26.2 (25.7,26.7)	25.3 (24.7,25.9)	27.5 (26.8,28.2)	27.3 (26.6,28.1)	27.3 (26.9,27.8)	25.6 (24.7,26.6)	24.4 (22.7,26.0)	24.1 (22.4,25.7)	24.9 (23.7,26.0)	24.9 (23.7,26.0)
Ordinal Scale at day 15 (±2 days) – no. (%)**										
1	157 (29.0)	115 (22.1)	38 (50.7)	28 (44.4)	90 (38.8)	62 (30.5)	18 (18.9)	14 (14.3)	11 (8.4)	11 (7.1)
2	117 (21.6)	102 (19.6)	20 (26.7)	15 (23.8)	70 (30.2)	58 (28.6)	22 (23.2)	19 (19.4)	5 (3.8)	10 (6.5)
3	14 (2.6)	8 (1.5)	8 (10.7)	4 (6.3)	6 (2.6)	4 (2.0)	0 (0)	0 (0)	0 (0)	0 (0)
4	38 (7.0)	33 (6.3)	3 (4.0)	7 (11.1)	17 (7.3)	13 (6.4)	12 (12.6)	4 (4.1)	6 (4.6)	9 (5.8)
5	58 (10.7)	60 (11.5)	3 (4.0)	5 (7.9)	25 (10.8)	18 (8.9)	2 (2.1)	14 (14.3)	28 (21.4)	23 (14.9)
6	28 (5.2)	24 (4.6)	1 (1.3)	0 (0)	5 (2.2)	7 (3.4)	12 (12.6)	11 (11.2)	10 (7.6)	6 (3.9)
7	95 (17.6)	121 (23.2)	1 (1.3)	3 (4.8)	13 (5.6)	21 (10.3)	16 (16.8)	20 (20.4)	57 (43.5)	74 (48.1)
8	34 (6.3)	58 (11.1)	1 (1.3)	1 (1.6)	6 (2.6)	20 (9.9)	13 (13.7)	16 (16.3)	14 (10.7)	21 (13.6)
Odds ratio (95% CI)	1.5 (1.2, 1.9); p<0.001		1.5 (0.8, 2.7)		1.6 (1.2, 2.3)		1.4 (0.9, 2.3)		1.2 (0.8, 1.9)	

*
P values and confidence intervals have not been adjusted for multiple comparisons. NE denotes not possible to estimate.
†

Recovery rate ratios and hazard ratios were calculated from the stratified Cox model; P values for these ratios were calculated with the stratified log-rank test (overall model stratified by actual disease severity). Recovery rate ratios greater than 1 indicate a benefit for remdesivir; hazard ratios less than 1 indicate a benefit for remdesivir.

‡

Mortality over the first 14 days treats all patients who were still alive through 14 days post enrollment as censored on Day 15, as if 14 days was the maximum follow-up time. Mortality over the entire study period uses the totality of the study data and censors patients who completed follow-up alive at 28 days post enrollment.

**

The ordinal score at day 15 is the patient's worst score on the ordinal scale during the previous day. Four patients died 15 days after randomization and are recorded as deceased for the ordinal score at day 15 outcome but not for the mortality by day 15 outcome. Scores on the ordinal scale are as follows: 1, not hospitalized, no limitations of activities; 2, not hospitalized, limitation of activities, home oxygen requirement, or both; 3, hospitalized, not requiring supplemental oxygen and no longer requiring ongoing medical care (used if hospitalization was extended for infection-control reasons); 4, hospitalized, not requiring supplemental oxygen but requiring ongoing medical care (Covid-19–related or other medical conditions); 5, hospitalized, requiring any supplemental oxygen; 6, hospitalized, requiring noninvasive ventilation or use of high-flow oxygen devices; 7, hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); and 8, death. Odds ratios and P values were calculated with the use of a proportional odds model (overall model adjusted for actual disease severity). Odds ratio values greater than 1 indicate a benefit for remdesivir.

Table S6. Time to Recovery by Treatment Group within Subgroups – ITT Population

				Median Time to Recovery		HR	
Subgroup	**Subgroup Category**	**Treatment Group**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Geographic Region 1	US Site	Remdesivir (N=427)	310	11.0	9.0, 12.0	1.30	1.10, 1.53
		Placebo (N=410)	271	16.0	14.0, 20.0		
	Non-US Site	Remdesivir (N=114)	89	8.0	7.0, 12.0	1.31	0.97, 1.78
		Placebo (N=111)	81	12.0	9.0, 15.0		
Geographic Region 2	North America	Remdesivir (N=431)	313	11.0	9.0, 12.0	1.30	1.10, 1.53
		Placebo (N=416)	276	16.0	14.0, 20.0		
	Europe	Remdesivir (N=84)	63	8.0	6.0, 14.0	1.30	0.91, 1.87
		Placebo (N=79)	56	13.0	9.0, 19.0		
	Asia	Remdesivir (N=26)	23	9.0	7.0, 13.0	1.36	0.74, 2.47
		Placebo (N=26)	20	10.5	9.0, 14.0		
Pooled Duration of Symptoms - Quartiles	First Quartile (≤ 6 Days)	Remdesivir (N=158)	119	10.0	7.0, 14.0	1.92	1.41, 2.60
		Placebo (N=124)	65	24.0	17.0, NE		
	Second Quartile (7 to ≤ 9 Days)	Remdesivir (N=148)	110	10.0	8.0, 13.0	0.99	0.76, 1.28
		Placebo (N=152)	116	12.0	9.0, 15.0		
	Third Quartile (10 to ≤ 12 Days)	Remdesivir (N=113)	86	7.0	5.0, 11.0	1.45	1.07, 1.98
		Placebo (N=108)	76	14.0	9.0, 20.0		
	Fourth Quartile (13+ Days)	Remdesivir (N=121)	84	12.0	9.0, 17.0	1.15	0.86, 1.54
		Placebo (N=135)	94	16.0	12.0, 19.0		
Pooled Duration of Symptoms - ≤ or > 10 days	≤ 10 Days	Remdesivir (N=356)	270	9.0	8.0, 11.0	1.37	1.14, 1.64

				Median Time to Recovery		HR	
Subgroup	**Subgroup Category**	**Treatment Group**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
		Placebo (N=320)	212	15.0	12.0, 19.0		
	> 10 Days	Remdesivir (N=184)	129	11.0	9.0, 13.0	1.20	0.94, 1.52
		Placebo (N=199)	139	15.0	12.0, 19.0		
Pooled Duration of Symptoms - Median	≤ Median (9 Days)	Remdesivir (N=306)	229	10.0	8.0, 13.0	1.32	1.09, 1.61
		Placebo (N=276)	181	16.0	12.0, 20.0		
	> Median (9 Days)	Remdesivir (N=234)	170	10.0	8.0, 12.0	1.29	1.04, 1.59
		Placebo (N=243)	170	14.0	12.0, 18.0		
Race	Asian	Remdesivir (N=79)	63	11.0	9.0, 15.0	1.07	0.73, 1.58
		Placebo (N=56)	43	12.0	9.0, 15.0		
	Black or African American	Remdesivir (N=109)	76	10.0	7.0, 16.0	1.25	0.91, 1.72
		Placebo (N=117)	77	15.0	10.0, 21.0		
	White	Remdesivir (N=279)	207	9.0	8.0, 12.0	1.29	1.06, 1.57
		Placebo (N=287)	196	15.0	12.0, 19.0		
	Other	Remdesivir (N=74)	53	9.0	6.0, 14.0	1.68	1.10, 2.58
		Placebo (N=61)	36	24.0	15.0, NE		
Comorbidities Group - Presence	Any Comorbidities	Remdesivir (N=435)	320	11.0	9.0, 13.0	1.32	1.12, 1.55
		Placebo (N=422)	274	16.0	14.0, 20.0		
	No Comorbidities	Remdesivir (N=97)	79	8.0	6.0, 10.0	1.25	0.91, 1.71
		Placebo (N=97)	78	12.0	9.0, 16.0		
	Unknown	Remdesivir (N=9)	0	NE	NE	1.00	1.00, 1.00
		Placebo (N=2)	0	NE	NE		

				Median Time to Recovery		HR	
Subgroup	**Subgroup Category**	**Treatment Group**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Comorbidities - number	No Comorbidities	Remdesivir (N=97)	79	8.0	6.0, 10.0	1.25	0.91, 1.71
		Placebo (N=97)	78	12.0	9.0, 16.0		
	1 Comorbidity	Remdesivir (N=138)	106	9.5	8.0, 14.0	1.36	1.03, 1.81
		Placebo (N=137)	91	15.0	12.0, 20.0		
	2 or more Comorbidities	Remdesivir (N=296)	213	11.0	9.0, 13.0	1.29	1.06, 1.57
		Placebo (N=283)	183	17.0	13.0, 21.0		
	Unknown	Remdesivir (N=10)	1	25.0	NE	$6.19x10^{11}$	0.00, NE
		Placebo (N=4)	0	NE	NE		
Comorbidities - Obesity	Obese	Remdesivir (N=242)	184	11.0	9.0, 13.0	1.32	1.07, 1.64
		Placebo (N=234)	158	16.0	12.0, 20.0		
	Non-Obese	Remdesivir (N=289)	214	9.0	8.0, 12.0	1.27	1.05, 1.55
		Placebo (N=284)	194	14.0	12.0, 18.0		
	Unknown	Remdesivir (N=10)	1	25.0	NE	$2.40x10^{11}$	0.00, NE
		Placebo (N=3)	0	NE	NE		
Age	<40	Remdesivir (N=59)	51	7.0	5.0, 9.0	1.95	1.28, 2.97
		Placebo (N=60)	40	15.0	10.0, 22.0		
	40-64	Remdesivir (N=295)	228	9.0	7.0, 10.0	1.19	0.98, 1.44
		Placebo (N=264)	198	12.0	9.0, 14.0		
	>=65	Remdesivir (N=187)	120	14.0	12.0, 19.0	1.29	1.00, 1.67
		Placebo (N=197)	114	21.0	16.0, 27.0		
Sex	Male	Remdesivir (N=352)	253	9.0	8.0, 12.0	1.30	1.09, 1.56

				Median Time to Recovery		HR	
Subgroup	**Subgroup Category**	**Treatment Group**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
		Placebo (N=332)	220	15.0	12.0, 19.0		
	Female	Remdesivir (N=189)	146	10.0	8.0, 13.0	1.31	1.03, 1.66
		Placebo (N=189)	132	15.0	12.0, 19.0		
Randomized Disease Severity Stratum	Severe Disease	Remdesivir (N=459)	324	12.0	10.0, 14.0	1.34	1.14, 1.58
		Placebo (N=444)	281	19.0	16.0, 21.0		
	Mild-Moderate Disease	Remdesivir (N=82)	75	5.0	4.0, 6.0	1.10	0.80, 1.53
		Placebo (N=77)	71	7.0	5.0, 9.0		
Actual Disease Severity Stratum	Severe Disease	Remdesivir (N=486)	345	11.0	10.0, 14.0	1.31	1.12, 1.52
		Placebo (N=471)	306	18.0	15.0, 20.0		
	Mild-Moderate Disease	Remdesivir (N=55)	54	5.0	4.0, 6.0	1.22	0.82, 1.81
		Placebo (N=50)	46	5.0	4.0, 7.0		
Baseline Ordinal Score Group 1	Baseline Clinical Status Score 7	Remdesivir (N=131)	63	29.0	24.0, NE	0.98	0.70, 1.36
		Placebo (N=154)	77	28.0	24.0, NE		
	Baseline Clinical Status Score 6	Remdesivir (N=95)	57	15.0	10.0, 27.0	1.09	0.76, 1.57
		Placebo (N=98)	61	19.5	14.0, 26.0		
	Baseline Clinical Status Score 5	Remdesivir (N=232)	206	7.0	6.0, 8.0	1.45	1.18, 1.79
		Placebo (N=203)	156	9.0	7.0, 10.0		
	Baseline Clinical Status Score 4	Remdesivir (N=75)	73	5.0	4.0, 6.0	1.29	0.91, 1.83
		Placebo (N=63)	58	6.0	4.0, 7.0		

NE = Not Estimated.
N= Number of participants in the specified subgroup category, treatment group and analysis population, with data.
n = Number of recovered participants.
HR is the ratio of the hazard of recovery in each treatment group estimated from the Cox model.
The ratio is Remdesivir to Placebo.

Table S7. Time to Recovery by Treatment Group and Randomized Disease Severity: Readmittance Sensitivity Analysis – ITT Population

					Median Time to Recovery		HR	
Analysis Population	**Treatment Group**	**Disease Severity**	**m**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
ITT Population	Remdesivir (N=82)	Mild/Moderate	5	70	6.0	5.0, 8.0	1.05	0.75, 1.47
	Placebo (N=77)		4	67	7.0	5.0, 10.0		
	Remdesivir (N=459)	Severe	21	303	13.0	11.0, 16.0	1.26	1.07, 1.49
	Placebo (N=444)		11	270	20.0	17.0, 22.0		
	Remdesivir (N=541)	Any Severity	26	373	11.0	10.0, 13.0	1.22	1.05, 1.41
	Placebo (N=521)		15	337	16.0	14.0, 20.0		

N= Number of participants in the specified treatment group, disease severity, and analysis population.
m = Number of participants who were readmitted.
n = Number of recovered participants.
HR for the 'Any Severity' group is the ratio of the hazard of recovery in each treatment group estimated from the stratified Cox Model. The ratio is Remdesivir to Placebo.
For this analysis, participants who recovered but were subsequently readmitted were censored at 28 days.

Table S8. Time to Recovery by Treatment Group and Disease Severity: Corticosteroid and Hydroxychloroquine Sensitivity Analysis – ITT Population

Corticosteroid Sensitivity Analysis					Median Time to Recovery		HR	
Analysis Population	**Treatment Group**	**Disease Severity**	**m**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
ITT Population	Remdesivir (N=82)	Mild/Moderate	13	65	5.0	4.0, 6.0	1.17	0.81, 1.67
	Placebo (N=77)		18	55	7.0	5.0, 10.0		
	Remdesivir (N=459)	Severe	102	262	11.0	9.0, 13.0	1.31	1.09, 1.56
	Placebo (N=444)		108	228	17.0	14.0, 20.0		
	Remdesivir (N=541)	Any Severity	115	327	9.0	8.0, 11.0	1.28	1.09, 1.50
	Placebo (N=521)		126	283	14.0	12.0, 16.0		
For this analysis, subjects who reported use of a corticosteroid were censored at earliest reported use of the medication(s).								

Hydroxychloroquine Sensitivity Analysis					Median Time to Recovery		HR	
Analysis Population	**Treatment Group**	**Disease Severity**	**m**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
ITT Population	Remdesivir (N=82)	Mild/Moderate	25	51	5.0	4.0, 8.0	1.01	0.67, 1.51
	Placebo (N=77)		29	44	6.0	4.0, 9.0		
	Remdesivir (N=459)	Severe	160	212	11.0	9.0, 14.0	1.41	1.16, 1.73
	Placebo (N=444)		163	179	20.0	16.0, 23.0		
	Remdesivir (N=541)	Any Severity	185	263	10.0	8.0, 11.0	1.32	1.11, 1.58
	Placebo (N=521)		192	223	16.0	14.0, 20.0		

N= Number of subjects in the specified treatment group, disease severity, and analysis population.
m = Number of subjects who reported use of hydroxychloroquine.
n = Number of recovered subjects without any prior use of hydroxychloroquine.
HR for the 'Any Severity' group is the ratio of the hazard of recovery in each treatment group estimated from the stratified Cox Model. The ratio is Remdesivir to Placebo.
For this analysis, subjects who reported use of hydroxychloroquine were censored at earliest reported use of the medication(s).

Table S9. Time to Recovery: Unblinding and Crossover Treatment Sensitivity Analysis – ITT Population

					Median Time to Recovery		HR	
Unblinding/Crossover Remdesivir Treatment	**Treatment Group**	**Disease Severity**	**m**	**n**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Unblinding	Remdesivir (N=82)	Mild/Moderate	-	75	5.0	4.0, 6.0	1.10	0.80, 1.53
	Placebo (N=77)		1	71	7.0	5.0, 9.0		
	Remdesivir (N=459)	Severe	16	320	12.0	10.0, 14.0	1.37	1.16, 1.61
	Placebo (N=444)		34	268	19.0	16.0, 21.0		
	Remdesivir (N=541)	Any Severity	16	395	10.0	9.0, 11.0	1.31	1.13, 1.52
	Placebo (N=521)		35	339	15.0	13.0, 18.0		
Crossover Remdesivir Treatment	Remdesivir (N=82)	Mild/Moderate	-	75	5.0	4.0, 6.0	1.10	0.80, 1.53
	Placebo (N=77)		1	71	7.0	5.0, 9.0		
	Remdesivir (N=459)	Severe	-	324	12.0	10.0, 14.0	1.34	1.14, 1.57
	Placebo (N=444)		25	274	19.0	16.0, 21.0		
	Remdesivir (N=541)	Any Severity	-	399	10.0	9.0, 11.0	1.29	1.12, 1.49
	Placebo (N=521)		26	345	15.0	13.0, 18.0		

N= Number of participants in the specified treatment group, disease severity, and analysis population.
For the Unblinding analysis, m = Number of participants who were unblinded to their treatment assignment. For the Crossover Treatment analysis, m = Number of participants who were crossover treated with Remdesivir.
n = Number of recovered participants.
HR for the 'Any Severity' group is the ratio of the hazard of recovery in each treatment group estimated from the stratified Cox Model. The ratio is Remdesivir to Placebo.
For the Unblinding analysis, participants who were unblinded to their treatment assignment were censored at the time of unblinding. For the Crossover Treatment analysis, participants who were crossover treated with Remdesivir were censored at the initiation of Remdesivir treatment.

Table S10. Time to Recovery by Treatment Group and Randomized Disease Severity: Fine-competing risk analysis

		HR	
Model	Disease Severity	Estimate	95% CI
Fine-Gray competing risk analysis – Randomized Disease Severity	Mild/Moderate (Randomized)	1.10	0.82, 1.49
	Severe (Randomized)	1.35	1.16, 1.58
	Any Severity (Stratified by Randomized Severity)	1.30	1.13, 1.49
Fine-Gray competing risk analysis – Actual Disease Severity	Mild/Moderate (Actual)	1.22	0.85, 1.75
	Severe (Actual)	1.31	1.13, 1.52
	Any Severity (Stratified by Actual Severity)	1.30	1.13, 1.49
Fine-Gray competing risk analysis – Baseline Ordinal Score 4/5 versus 6/7	Baseline Ordinal Score 4 or 5	1.42	1.22, 1.68
	Baseline Ordinal Score 6 or 7	1.04	0.81, 1.32
	Stratified by Ordinal Score 4/5 vs 6/7	1.27	1.11, 1.46

Table S11. Results of Cox proportional hazards models testing for interactions between treatment effect and baseline ordinal score with respect to recovery and mortality.

Cox Proportional Hazards Model	Group	HR (95% CI)
Recovery		
Model 1 – Time to recovery with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal score treated as continuous • Model terms: treatment, continuous baseline ordinal score, interaction between treatment and ordinal score	Baseline Score 4	1.59 (1.24,2.03)
	Baseline Score 5	1.37 (1.17,1.60)
	Baseline Score 6	1.18 (1.00,1.40)
	Baseline Score 7	1.02 (0.77,1.35)
Model 2 – Time to recovery with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal scores grouped as 4/5 versus 6/7 • Model terms: treatment, grouped baseline ordinal score, interaction between treatment and grouped ordinal score	Baseline Score 4/5	1.47 (1.23,1.76)
	Baseline Score 6/7	1.03 (0.81,1.32)
Model 3 – Time to recovery with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal score treated as categorical • Model terms: treatment, categorical baseline ordinal score, interaction between treatment and categorical ordinal score	Baseline Score 4	1.36 (0.97,1.93)
	Baseline Score 5	1.51 (1.23,1.86)
	Baseline Score 6	1.10 (0.76,1.58)
	Baseline Score 7	0.97 (0.70,1.36)
Mortality		
Model 4 – Mortality with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal score treated as continuous • Model terms: treatment, continuous baseline ordinal score, interaction between treatment and ordinal score	Baseline Score 4	0.34 (0.15,0.76)
	Baseline Score 5	0.50 (0.30,0.85)
	Baseline Score 6	0.75 (0.53,1.07)
	Baseline Score 7	1.13 (0.71,1.79)
Model 5 – Mortality with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal scores grouped as 4/5 versus 6/7 • Model terms: treatment, grouped baseline ordinal score, interaction between treatment and grouped ordinal score	Baseline Score 4/5	0.36 (0.18,0.70)
	Baseline Score 6/7	1.08 (0.73,1.62)
Model 6 – Mortality with interaction term for treatment effect by baseline ordinal score; • Baseline ordinal score treated as categorical • Model terms: treatment, categorical baseline ordinal score, interaction between treatment and categorical ordinal score	Baseline Score 4	0.83 (0.17,4.13)
	Baseline Score 5	0.30 (0.14,0.64)
	Baseline Score 6	1.02 (0.55,1.92)
	Baseline Score 7	1.12 (0.67,1.89)

Table S12. Clinical Status Scores by Treatment Group and Study Visit – ITT Population

		Remdesivir (N=541)			Placebo (N=521)			All Participants (N=1062)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Day 1	Death at or before Study Visit (8)	0	0	0, 1	0	0	0, 1	0	0	0, 0
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	131	24	21, 28	154	30	26, 34	285	27	24, 30
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	95	18	15, 21	98	19	16, 22	193	18	16, 21
	Hospitalized, requiring supplemental oxygen (5)	232	43	39, 47	203	39	35, 43	435	41	38, 44
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	75	14	11, 17	63	12	10, 15	138	13	11, 15
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	0	0	0, 1	0	0	0, 1	0	0	0, 0
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	0	0	0, 1	0	0	0, 1	0	0	0, 0
	Not hospitalized, no limitations on activities (1)	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Hospitalized participants	3	1	0, 2	0	0	0, 1	3	<1	0, 1
	No clinical status score reported – Discharged participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discontinued from study	5	1	0, 2	3	1	0, 2	8	1	0, 1
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0
Day 3	Death at or before Study Visit (8)	3	1	0, 2	7	1	1, 3	10	1	1, 2
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	153	28	25, 32	187	36	32, 40	340	32	29, 35
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	86	16	13, 19	90	17	14, 21	176	17	14, 19
	Hospitalized, requiring supplemental oxygen (5)	202	37	33, 41	169	32	29, 37	371	35	32, 38
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	70	13	10, 16	60	12	9, 15	130	12	10, 14
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	1	<1	0, 1	2	<1	0, 1	3	<1	0, 1
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	0	0	0, 1	0	0	0, 1	0	0	0, 0
	Not hospitalized, no limitations on activities (1)	2	<1	0, 1	0	0	0, 1	2	<1	0, 1
	No clinical status score reported – Hospitalized participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discharged participants	11	2	1, 4	1	<1	0, 1	12	1	1, 2
	No clinical status score reported – Discontinued from study	13	2	1, 4	5	1	0, 2	18	2	1, 3
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0

		Remdesivir (N=541)			Placebo (N=521)			All Participants (N=1062)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Day 5	Death at or before Study Visit (8)	11	2	1, 4	12	2	1, 4	23	2	1, 3
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	152	28	24, 32	191	37	33, 41	343	32	30, 35
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	64	12	9, 15	75	14	12, 18	139	13	11, 15
	Hospitalized, requiring supplemental oxygen (5)	149	28	24, 31	138	26	23, 30	287	27	24, 30
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	81	15	12, 18	55	11	8, 13	136	13	11, 15
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	4	1	0, 2	5	1	0, 2	9	1	0, 2
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	1	<1	0, 1	0	0	0, 1	1	<1	0, 1
	Not hospitalized, no limitations on activities (1)	0	0	0, 1	1	<1	0, 1	1	<1	0, 1
	No clinical status score reported – Hospitalized participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discharged participants	63	12	9, 15	36	7	5, 9	99	9	8, 11
	No clinical status score reported – Discontinued from study	16	3	2, 5	8	2	1, 3	24	2	2, 3
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0
Day 8	Death at or before Study Visit (8)	17	3	2, 5	34	7	5, 9	51	5	4, 6
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	130	24	21, 28	173	33	29, 37	303	29	26, 31
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	48	9	7, 12	47	9	7, 12	95	9	7, 11
	Hospitalized, requiring supplemental oxygen (5)	93	17	14, 21	80	15	13, 19	173	16	14, 19
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	59	11	9, 14	53	10	8, 13	112	11	9, 13
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	8	1	1, 3	7	1	1, 3	15	1	1, 2
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	1	<1	0, 1	0	0	0, 1	1	<1	0, 1
	Not hospitalized, no limitations on activities (1)	0	0	0, 1	1	<1	0, 1	1	<1	0, 1
	No clinical status score reported – Hospitalized participants	2	<1	0, 1	0	0	0, 1	2	<1	0, 1
	No clinical status score reported – Discharged participants	164	30	27, 34	116	22	19, 26	280	26	24, 29
	No clinical status score reported – Discontinued from study	19	4	2, 5	10	2	1, 3	29	3	2, 4
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0
Day 11	Death at or before Study Visit (8)	22	4	3, 6	41	8	6, 11	63	6	5, 8
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	119	22	19, 26	148	28	25, 32	267	25	23, 28

		Remdesivir (N=541)			Placebo (N=521)			All Participants (N=1062)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	31	6	4, 8	38	7	5, 10	69	6	5, 8
	Hospitalized, requiring supplemental oxygen (5)	60	11	9, 14	66	13	10, 16	126	12	10, 14
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	37	7	5, 9	33	6	5, 9	70	7	5, 8
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	12	2	1, 4	11	2	1, 4	23	2	1, 3
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	2	<1	0, 1	2	<1	0, 1	4	<1	0, 1
	Not hospitalized, no limitations on activities (1)	0	0	0, 1	1	<1	0, 1	1	<1	0, 1
	No clinical status score reported – Hospitalized participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discharged participants	237	44	40, 48	170	33	29, 37	407	38	35, 41
	No clinical status score reported – Discontinued from study	21	4	3, 6	11	2	1, 4	32	3	2, 4
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0
Day 15	Death at or before Study Visit (8)	34	6	5, 9	58	11	9, 14	92	9	7, 11
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	83	15	13, 19	115	22	19, 26	198	19	16, 21
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	23	4	3, 6	22	4	3, 6	45	4	3, 6
	Hospitalized, requiring supplemental oxygen (5)	53	10	8, 13	57	11	9, 14	110	10	9, 12
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	37	7	5, 9	33	6	5, 9	70	7	5, 8
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	14	3	2, 4	8	2	1, 3	22	2	1, 3
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	102	19	16, 22	89	17	14, 21	191	18	16, 20
	Not hospitalized, no limitations on activities (1)	157	29	25, 33	115	22	19, 26	272	26	23, 28
	No clinical status score reported – Hospitalized participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discharged participants	13	2	1, 4	10	2	1, 3	23	2	1, 3
	No clinical status score reported – Discontinued from study	25	5	3, 7	14	3	2, 4	39	4	3, 5
	No clinical status score reported – Completed study without reporting score	0	0	0, 1	0	0	0, 1	0	0	0, 0
Day 22	Death at or before Study Visit (8)	50	9	7, 12	67	13	10, 16	117	11	9, 13
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	49	9	7, 12	75	14	12, 18	124	12	10, 14
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	12	2	1, 4	11	2	1, 4	23	2	1, 3

		Remdesivir (N=541)			Placebo (N=521)			All Participants (N=1062)		
Study Visit	**Ordinal Scale Measure**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
	Hospitalized, requiring supplemental oxygen (5)	29	5	4, 8	41	8	6, 11	70	7	5, 8
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	30	6	4, 8	28	5	4, 8	58	5	4, 7
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	8	1	1, 3	5	1	0, 2	13	1	1, 2
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	105	19	16, 23	94	18	15, 22	199	19	17, 21
	Not hospitalized, no limitations on activities (1)	209	39	35, 43	169	32	29, 37	378	36	33, 39
	No clinical status score reported – Hospitalized participants	0	0	0, 1	0	0	0, 1	0	0	0, 0
	No clinical status score reported – Discharged participants	18	3	2, 5	11	2	1, 4	29	3	2, 4
	No clinical status score reported – Discontinued from study	30	6	4, 8	20	4	2, 6	50	5	4, 6
	No clinical status score reported – Completed study without reporting score	1	<1	0, 1	0	0	0, 1	1	<1	0, 1
Day 29	Death at or before Study Visit (8)	58	11	8, 14	76	15	12, 18	134	13	11, 15
	Hospitalized, on invasive mechanical ventilation or ECMO (7)	30	6	4, 8	45	9	7, 11	75	7	6, 9
	Hospitalized, on non-invasive ventilation or high flow oxygen devices (6)	3	1	0, 2	10	2	1, 3	13	1	1, 2
	Hospitalized, requiring supplemental oxygen (5)	23	4	3, 6	22	4	3, 6	45	4	3, 6
	Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) (4)	16	3	2, 5	18	3	2, 5	34	3	2, 4
	Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (3)	3	1	0, 2	4	1	0, 2	7	1	0, 1
	Not hospitalized, limitation on activities and/or requiring home oxygen (2)	107	20	17, 23	100	19	16, 23	207	19	17, 22
	Not hospitalized, no limitations on activities (1)	247	46	42, 50	190	36	32, 41	437	41	38, 44
	No clinical status score reported – Hospitalized participants	0	0	0, 1	1	<1	0, 1	1	<1	0, 1
	No clinical status score reported – Discharged participants	7	1	1, 3	16	3	2, 5	23	2	1, 3
	No clinical status score reported – Discontinued from study	36	7	5, 9	25	5	3, 7	61	6	4, 7
	No clinical status score reported – Completed study without reporting score	11	2	1, 4	14	3	2, 4	25	2	2, 3

N = Number of Participants in the ITT Population.
n = Number of participants who reported the respective score.
95% CI calculated using Wilson CIs.

Table S13. Summary of Change from Baseline in Clinical Ordinal Scores by Treatment Group and Study Visit – ITT Population

Study Visit	All Subjects (N=1062)	Remdesivir (N=541)	Placebo (N=521)	Difference[a]
Mean Ordinal Scale – Mean Change (Standard deviation)[b]				
Day 3	5.7 (1.1)	5.6 (1.1)	5.8 (1.1)	0.2 (1.1)
Day 5	5.7 (1.2)	5.5 (1.2)	5.8 (1.2)	0.3 (1.2)
Day 8	5.5 (1.4)	5.4 (1.3)	5.7 (1.4)	0.3 (1.4)
Day 11	5.4 (1.5)	5.2 (1.4)	5.6 (1.5)	0.3 (1.5)
Day 15	4.0 (2.6)	3.7 (2.5)	4.3 (2.6)	0.6 (2.5)
Day 22	3.4 (2.6)	3.1 (2.5)	3.7 (2.7)	0.6 (2.6)
Day 29	3.1 (2.6)	2.8 (2.5)	3.4 (2.7)	0.5 (2.6)
Change from Baseline Ordinal Scale – Mean Change (Standard deviation)[b]				
Day 3	0.1 (0.6)	0.1 (0.6)	0.2 (0.6)	0.1 (0.6)
Day 5	0.1 (0.9)	-0.0 (0.8)	0.1 (0.9)	0.1 (0.9)
Day 8	-0.1 (1.1)	-0.2 (1.0)	0.0 (1.1)	0.2 (1.0)
Day 11	-0.2 (1.2)	-0.3 (1.1)	-0.1 (1.3)	0.2 (1.2)
Day 15	-1.6 (2.2)	-1.9 (2.1)	-1.4 (2.3)	0.5 (2.2)
Day 22	-2.2 (2.4)	-2.4 (2.2)	-1.9 (2.5)	0.5 (2.4)
Day 29	-2.5 (2.4)	-2.7 (2.3)	-2.3 (2.6)	0.4 (2.4)

N = Number of subjects in the ITT Population.
[a] Defined as the difference in mean change from baseline between Remdesivir and Placebo.
[b]Missing values were imputed using Last Observation Carried Forward. Clinical scores of 8 were carried forward from the dat e of death for subjects who died.

Table S14. Odds Ratio for Better (Lower) Clinical Status Score at Day 15 by Treatment Using a Proportional Odds Model, Remdesivir Relative to Placebo – ITT Population

		Odds Ratio		
Analysis/Subgroup	**Treatment Group**	**Estimate**	**95% CI**	**P-value**
Analysis of Key Secondary Endpoint[a], Full ITT Population	Remdesivir (N=541)	1.6	1.3, 1.9	<0.001
	Placebo (N=521)			
Geographic region (US Site)	Remdesivir (N=427)	1.6	1.3, 2.0	<0.001
	Placebo (N=410)			
Geographic region (Non-US Site)	Remdesivir (N=114)	1.3	0.8, 2.1	0.233
	Placebo (N=111)			
Geographic region (North America)	Remdesivir (N=431)	1.6	1.3, 2.0	<0.001
	Placebo (N=416)			
Geographic region (Asia)	Remdesivir (N=26)	1.3	0.5, 3.5	0.592
	Placebo (N=26)			
Geographic region (Europe)	Remdesivir (N=84)	1.4	0.8, 2.4	0.246
	Placebo (N=79)			
Duration of symptoms prior to enrollment (First Quartile (≤ 6 Days))	Remdesivir (N=158)	2.7	1.8, 4.2	<0.001
	Placebo (N=124)			
Duration of symptoms prior to enrollment (Second Quartile (7 to ≤ 9 Days))	Remdesivir (N=148)	1.1	0.8, 1.7	0.573
	Placebo (N=152)			
Duration of symptoms prior to enrollment (Third Quartile (10 to ≤ 12 Days))	Remdesivir (N=113)	1.4	0.9, 2.3	0.150
	Placebo (N=108)			
Duration of symptoms prior to enrollment (Fourth Quartile (13+ Days))	Remdesivir (N=121)	1.3	0.9, 2.1	0.186
	Placebo (N=135)			
Duration of symptoms prior to enrollment (≤ 10 Days)	Remdesivir (N=356)	1.7	1.3, 2.2	<0.001
	Placebo (N=320)			
Duration of symptoms prior to enrollment (> 10 Days)	Remdesivir (N=184)	1.3	0.9, 1.9	0.125
	Placebo (N=199)			
Duration of symptoms prior to enrollment (≤ Median (9 Days))	Remdesivir (N=306)	1.7	1.2, 2.2	0.001
	Placebo (N=276)			
Duration of symptoms prior to enrollment (> Median (9 Days))	Remdesivir (N=234)	1.4	1.0, 1.9	0.042
	Placebo (N=243)			
Race (White)	Remdesivir (N=279)	1.6	1.2, 2.1	0.002
	Placebo (N=287)			

		Odds Ratio		
Analysis/Subgroup	**Treatment Group**	**Estimate**	**95% CI**	**P-value**
Race (Black or African American)	Remdesivir (N=109)	1.2	0.7, 1.9	0.470
	Placebo (N=117)			
Race (Asian)	Remdesivir (N=79)	1.1	0.6, 2.0	0.739
	Placebo (N=56)			
Race (Other)	Remdesivir (N=74)	2.9	1.6, 5.5	0.001
	Placebo (N=61)			
Comorbidities (No Comorbidities)	Remdesivir (N=97)	1.5	0.9, 2.5	0.125
	Placebo (N=97)			
Comorbidities (Any Comorbidities)	Remdesivir (N=435)	1.6	1.3, 2.1	<0.001
	Placebo (N=422)			
Comorbidities (None)	Remdesivir (N=97)	1.5	0.9, 2.5	0.125
	Placebo (N=97)			
Comorbidities (One)	Remdesivir (N=138)	1.8	1.2, 2.8	0.005
	Placebo (N=137)			
Comorbidities (Two or More)	Remdesivir (N=296)	1.5	1.1, 2.0	0.004
	Placebo (N=283)			
Obesity (Obese)	Remdesivir (N=242)	1.6	1.2, 2.2	0.004
	Placebo (N=234)			
Obesity (Non-Obese)	Remdesivir (N=289)	1.6	1.2, 2.1	0.003
	Placebo (N=284)			
Age (<40)	Remdesivir (N=59)	2.8	1.4, 5.4	0.003
	Placebo (N=60)			
Age (40-64)	Remdesivir (N=295)	1.3	1.0, 1.8	0.059
	Placebo (N=264)			
Age (>=65)	Remdesivir (N=187)	1.5	1.1, 2.1	0.023
	Placebo (N=197)			
Sex (Female)	Remdesivir (N=189)	1.6	1.1, 2.3	0.009
	Placebo (N=189)			
Sex (Male)	Remdesivir (N=352)	1.5	1.1, 1.9	0.003
	Placebo (N=332)			
Severity of disease (Randomization stratification: Mild-Moderate Disease)	Remdesivir (N=82)	1.2	0.7, 2.2	0.475
	Placebo (N=77)			
Severity of disease (Randomization stratification: Severe Disease)	Remdesivir (N=459)	1.6	1.3, 2.0	<0.001
	Placebo (N=444)			

		Odds Ratio		
Analysis/Subgroup	**Treatment Group**	**Estimate**	**95% CI**	**P-value**
Severity of disease (Actual disease severity at baseline: Mild-Moderate Disease)	Remdesivir (N=55)	1.5	0.7, 3.0	0.302
	Placebo (N=50)			
Severity of disease (Actual disease severity at baseline: Severe Disease)	Remdesivir (N=486)	1.6	1.2, 1.9	<0.001
	Placebo (N=471)			
Severity of disease (Baseline ordinal scale category: 4)	Remdesivir (N=75)	1.5	0.8, 2.7	0.234
	Placebo (N=63)			
Severity of disease (Baseline ordinal scale category: 5)	Remdesivir (N=232)	1.6	1.2, 2.3	0.004
	Placebo (N=203)			
Severity of disease (Baseline ordinal scale category: 6)	Remdesivir (N=95)	1.4	0.9, 2.3	0.186
	Placebo (N=98)			
Severity of disease (Baseline ordinal scale category: 7)	Remdesivir (N=131)	1.2	0.8, 1.9	0.369
	Placebo (N=154)			
[a] Analysis of key secondary endpoint using the full ITT population with disease severity as a model covariate.				

Table S15. Summary of NEWS by Treatment Group and Study Visit – ITT Population

Study Visit	Statistic	Remdesivir (N=541)	Placebo (N=521)	All Subjects (N=1062)
Baseline	n	531	514	1045
	Mean (SD)	5.7 (3.2)	6.1 (3.2)	5.9 (3.2)
	Median	5.0	6.0	6.0
	Range (Min, Max)	(0, 16)	(0, 15)	(0, 16)
Day 3	n	503	501	1004
	Mean (SD)	5.5 (3.5)	6.1 (3.5)	5.8 (3.5)
	Median	5.0	6.0	5.0
	Range (Min, Max)	(0, 18)	(0, 15)	(0, 18)
	n[a]	502	499	1001
	Change from Baseline Mean (SD)	-0.3 (2.6)	0.1 (2.8)	-0.1 (2.7)
Day 5	n	439	449	888
	Mean (SD)	5.6 (3.8)	6.6 (3.9)	6.1 (3.9)
	Median	5.0	7.0	6.0
	Range (Min, Max)	(0, 16)	(0, 17)	(0, 17)
	n[a]	438	447	885
	Change from Baseline Mean (SD)	-0.4 (2.9)	0.3 (3.3)	0.0 (3.2)
Day 8	n	322	351	673
	Mean (SD)	6.0 (3.8)	6.5 (3.9)	6.3 (3.9)
	Median	5.5	7.0	6.0
	Range (Min, Max)	(0, 14)	(0, 18)	(0, 18)
	n[a]	321	348	669
	Change from Baseline Mean (SD)	-0.5 (3.2)	-0.3 (3.8)	-0.3 (3.5)
Day 11	n	255	293	548
	Mean (SD)	6.3 (3.9)	6.6 (4.0)	6.5 (3.9)
	Median	6.0	7.0	6.0
	Range (Min, Max)	(0, 17)	(0, 17)	(0, 17)
	n[a]	254	291	545
	Change from Baseline Mean (SD)	-0.5 (3.5)	-0.3 (4.1)	-0.4 (3.9)
Day 15	n	302	293	595
	Mean (SD)	4.4 (4.1)	5.4 (4.0)	4.8 (4.1)
	Median	3.0	5.0	4.0

Study Visit	Statistic	Remdesivir (N=541)	Placebo (N=521)	All Subjects (N=1062)
	Range (Min, Max)	(0, 14)	(0, 16)	(0, 16)
	n[a]	301	290	591
	Change from Baseline Mean (SD)	-1.7 (3.6)	-1.4 (4.2)	-1.5 (3.9)
Day 22	n	121	152	273
	Mean (SD)	5.6 (4.1)	6.0 (3.7)	5.8 (3.9)
	Median	5.0	7.0	6.0
	Range (Min, Max)	(0, 16)	(0, 14)	(0, 16)
	n[a]	120	151	271
	Change from Baseline Mean (SD)	-1.7 (4.1)	-1.4 (4.0)	-1.5 (4.1)
Day 29	n	252	223	475
	Mean (SD)	2.3 (2.9)	3.1 (3.5)	2.6 (3.3)
	Median	1.0	2.0	1.0
	Range (Min, Max)	(0, 14)	(0, 20)	(0, 20)
	n[a]	251	221	472
	Change from Baseline Mean (SD)	-3.3 (3.2)	-3.2 (4.0)	-3.3 (3.6)

N = Number of subjects in the ITT Population.
SD = Standard deviation.
n = Number of subjects with an assessment at the time point being summarized.
n[a] = Number of subjects with an assessment at both baseline and the time point being summarized.

Table S16. Summary of Change from Baseline in NEWS by Treatment Group and Study Visit – ITT Population

Study Visit	All Subjects (N=1062)	Remdesivir (N=541)	Placebo (N=521)	Difference[a]
Change from Baseline NEWS – Mean Change (Standard Deviation)				
Day 3	0.0 (3.0)	-0.2 (2.9)	0.3 (3.1)	0.4 (3.0)
Day 5	0.1 (3.6)	-0.2 (3.4)	0.4 (3.7)	0.7 (3.6)
Day 8	-0.1 (4.4)	-0.5 (3.9)	0.3 (4.9)	0.8 (4.4)
Day 11	-0.3 (4.8)	-0.7 (4.2)	0.1 (5.3)	0.8 (4.8)
Day 15	-0.6 (5.4)	-1.1 (4.8)	-0.1 (6.0)	1.0 (5.4)
Day 29	-1.1 (6.3)	-1.4 (5.8)	-0.9 (6.7)	0.5 (6.3)

N = Number of subjects in the ITT Population.
NEWS = National Early Warning Score.
[a] Defined as the difference in mean change from baseline between Remdesivir and Placebo.

Table S17. Overall Summary of Adverse Events – As Treated Population

	Remdesivir (N=532)						Placebo (N=516)						All Participants (N=1048)					
	Mild-Moderate (N=55)		Severe (N=477)		Any Severity (N=532)		Mild-Moderate (N=49)		Severe (N=467)		Any Severity (N=516)		Mild-Moderate (N=104)		Severe (N=944)		Any Severity (N=1048)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event	17	31	288	60	305	57	14	29	309	66	323	63	31	30	597	63	628	60
At least one related adverse event	2	4	39	8	41	8	-	-	47	10	47	9	2	2	86	9	88	8
Moderate (Grade 2)	-	-	-	-	-	-	-	-	1	<1	1	<1	-	-	1	<1	1	<1
Severe (Grade 3)	2	4	34	7	36	7	-	-	39	8	39	8	2	2	73	8	75	7
Life-threatening (Grade 4)	-	-	7	1	7	1	-	-	13	3	13	3	-	-	20	2	20	2
Death (Grade 5)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
At least one serious adverse event[b]	5	9	126	26	131	25	8	16	155	33	163	32	13	13	281	30	294	28
At least one related serious adverse event	-	-	2	<1	2	<1	-	-	3	1	3	1	-	-	5	1	5	<1
At least one adverse event leading to early termination[c]	2	4	43	9	45	8	2	4	57	12	59	11	4	4	100	11	104	10
At least one adverse event leading to treatment discontinuation[c]	3	5	54	11	57	11	1	2	76	16	77	15	4	4	130	14	134	13
At least one unanticipated problem	-	-	1	<1	1	<1	-	-	1	<1	1	<1	-	-	2	<1	2	<1

N= Number of participants in the As Treated Population.
[a]Participants are counted once for each category regardless of the number of events.
[b] One SAE occurred after Day 29 (and is not reported on Table S17
[c]The number of participants with adverse events leading to discontinuation of treatment or early termination from the study are based on the data collected on the adverse event eCRF.
All Grade 3 and 4 AEs are captured as AEs. In addition, any Grade 2 or higher suspected drug-related hypersensitivity reaction is reported as an AE.

Table S18. Participants Experiencing Grade 3 or 4 AEs and SAEs through Day 29 by Treatment Group– As Treated Population

	Remdesivir (N=532)			Placebo (N=516)			
Safety Event Outcome	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**P-value**
Grade 3 or 4 AE	273	51	47.0, 55.6	295	57	52.8, 61.5	0.058
SAE	130	24	20.9, 28.3	163	32	27.7, 35.7	0.010

N = Number of participants in the Treated Population.
n = Number of participants in a given treatment group who experienced the specified safety event outcome.
95% CI calculated using C-P/Blaker method.
P-value calculated using Two-Sided Barnard's Exact Test.

Table S19. Serious Adverse Events Occurring in 5 or More Participants in Any Preferred Term by Treatment Group

MedDRA System Organ Class	Preferred Term	Remdesivir (N = 532) No.(%)	Placebo (N = 516) No.(%)
Any System Organ Class	Any Preferred Term	131 (24.6)	163 (31.6)
Cardiac disorders	Cardiac arrest	10 (1.9)	7 (1.4)
	Atrial fibrillation	5 (0.9)	1 (0.2)
General disorders and administration site conditions	Multiple organ dysfunction syndrome	5 (0.9)	3 (0.6)
Infections and infestations	Septic shock	8 (1.5)	15 (2.9)
	COVID-19	2 (0.4)	5 (1.0)
Investigations	Glomerular filtration rate decreased[a]	5 (0.9)	2 (0.4)
Renal and urinary disorders	Acute kidney injury[a]	7 (1.3)	12 (2.3)
	Renal failure[a]	2 (0.4)	5 (1.0)
Respiratory, thoracic and mediastinal disorders	Respiratory failure[b]	39 (7.3)	66 (12.8)
	Acute respiratory failure[b]	8 (1.5)	14 (2.7)
	Respiratory distress[c]	6 (1.1)	11 (2.1)
	Acute respiratory distress syndrome	7 (1.3)	5 (1.0)
	Pneumothorax	5 (0.9)	5 (1.0)
	Pulmonary embolism	5 (0.9)	4 (0.8)
	Hypoxia[c]	4 (0.8)	4 (0.8)
	Pneumonia aspiration	4 (0.8)	2 (0.4)
Vascular disorders	Hypotension	4 (0.8)	7 (1.4)
	Shock	5 (0.9)	4 (0.8)

No. = number of subjects reporting at least one event.
[a] The combined number of subjects with glomerular filtration rate decreased,acute kidney injury or renal failure are 14 for Remdesivir and 17 for Placebo.
[b] The combined number of subjects with respiratory failure or acute respiratory failure is 47 for Remdesivir and 80 for Placebo.
Endotracheal intubations serious adverse events without a respiratory serious adverse event are summarized as respir atory failures.
[c] The combined number of subjects with hypoxia or respiratory distress are 10 for Remdesivir and 15 for Placebo.

Table S20. Non-Serious Adverse Events Occurring in 5 or More Participants in Any Preferred Term by Treatment Group

MedDRA System Organ Class	Preferred Term	Remdesivir (N = 532) No.(%)	Placebo (N = 516) No.(%)
Any System Organ Class	Any Preferred Term	276 (51.9)	295 (57.2)
Blood and lymphatic system disorders	Anaemia[a]	42 (7.9)	52 (10.1)
	Lymphopenia[b]	13 (2.4)	30 (5.8)
Cardiac disorders	Atrial fibrillation	5 (0.9)	10 (1.9)
	Arrhythmia	4 (0.8)	1 (0.2)
	Supraventricular tachycardia	3 (0.6)	2 (0.4)
General disorders and administration site conditions	Pyrexia	38 (7.1)	32 (6.2)
Hepatobiliary disorders	Hyperbilirubinaemia	2 (0.4)	3 (0.6)
Infections and infestations	Pneumonia	12 (2.3)	6 (1.2)
	Bacteraemia	0 (-)	10 (1.9)
	Sepsis	4 (0.8)	4 (0.8)
	Pneumonia bacterial	4 (0.8)	3 (0.6)
	Pneumonia staphylococcal	3 (0.6)	4 (0.8)
	Septic shock	3 (0.6)	3 (0.6)
Investigations	Glomerular filtration rate decreased[c]	55 (10.3)	74 (14.3)
	Haemoglobin decreased[a]	48 (9.0)	62 (12.0)
	Lymphocyte count decreased[b]	44 (8.3)	54 (10.5)
	Blood creatinine increased[c]	31 (5.8)	36 (7.0)
	Blood glucose increased[e]	39 (7.3)	27 (5.2)
	Aspartate aminotransferase increased[d]	18 (3.4)	33 (6.4)
	Alanine aminotransferase increased[d]	12 (2.3)	24 (4.7)
	Prothrombin time prolonged	26 (4.9)	8 (1.6)
	Blood bilirubin increased	9 (1.7)	16 (3.1)
	Transaminases increased[d]	7 (1.3)	11 (2.1)
	Blood albumin decreased	7 (1.3)	4 (0.8)
	Creatinine renal clearance decreased[c]	4 (0.8)	6 (1.2)
	Oxygen saturation decreased	4 (0.8)	5 (1.0)
	Platelet count decreased	6 (1.1)	2 (0.4)
	Electrocardiogram QT prolonged	2 (0.4)	5 (1.0)
	Liver function test increased	3 (0.6)	3 (0.6)
	Troponin increased	1 (0.2)	5 (1.0)

MedDRA System Organ Class	Preferred Term	Remdesivir (N = 532) No.(%)	Placebo (N = 516) No.(%)
	Blood creatine phosphokinase increased	2 (0.4)	3 (0.6)
Metabolism and nutrition disorders	Hyperglycaemia[e]	34 (6.4)	34 (6.6)
	Acidosis	8 (1.5)	5 (1.0)
	Hypoalbuminaemia	6 (1.1)	7 (1.4)
	Hypernatraemia	4 (0.8)	4 (0.8)
	Alkalosis	3 (0.6)	3 (0.6)
	Hypocalcaemia	3 (0.6)	2 (0.4)
Musculoskeletal and connective tissue disorders	Muscular weakness	3 (0.6)	2 (0.4)
Psychiatric disorders	Delirium	10 (1.9)	8 (1.6)
	Mental status changes	2 (0.4)	4 (0.8)
Renal and urinary disorders	Acute kidney injury[c]	21 (3.9)	21 (4.1)
Respiratory, thoracic and mediastinal disorders	Respiratory distress[f]	12 (2.3)	16 (3.1)
	Hypoxia[f]	10 (1.9)	13 (2.5)
	Dyspnea[f]	9 (1.7)	6 (1.2)
Vascular disorders	Hypertension	23 (4.3)	20 (3.9)
	Hypotension	14 (2.6)	11 (2.1)
	Deep vein thrombosis	8 (1.5)	14 (2.7)
	Thrombosis	3 (0.6)	4 (0.8)

No. = number of participants reporting at least one event.
[a] The combined number of participants with anaemia or haemoglobin decreased are 88 for Remdesivir and 112 for Placebo.
[b] The combined number of participants with lymphopenia or lymphocyte count decreased are 56 for Remdesivir and 84 for Pla cebo.
[c] The combined number of participants with glomerular filtration rate decreased, acute kidney injury, blood creatinine increased or creatinine renal clearance decreased are 85 for Remdesivir and 105 for Placebo.
[d] The combined number of participants with transaminases increased, aspartate aminotransferase increased or alanine aminotransferase increased are 32 for Remdesivir and 55 for Placebo.
[e] The combined number of participants with hyperglycaemia or blood glucose increased are 73 for Remdesivir and 61 for Place bo.
[f] The combined number of participants with hypoxia, dyspnea or respiratory distress are 30 for Remdesivir and 34 for Placebo.

Figure S1. Day 15 outcomes by baseline ordinal scale in the intent-to-treat population.
Bar plots are shifted to compare improvement versus no improvement / worsening compared to the baseline ordinal score category (i.e., the "Enrollment Score"). Movement to the right of the enrollment score line reflect improvement by Day 15. Movement to the left of the enrollment line reflect no change in ordinal status or worsening by Day 15.

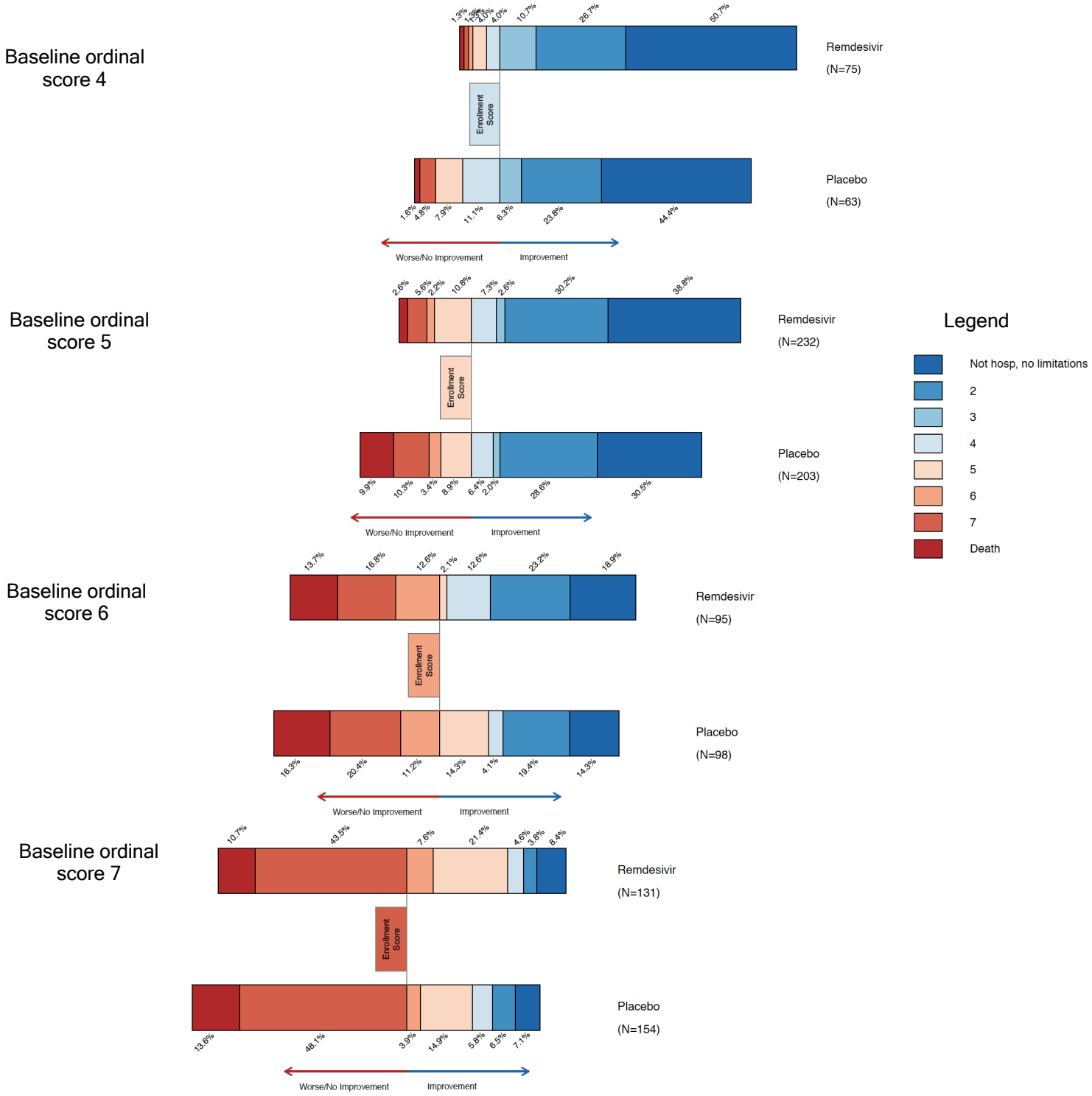


Figure S2. Distribution of Ordinal Scale by Treatment by Day.

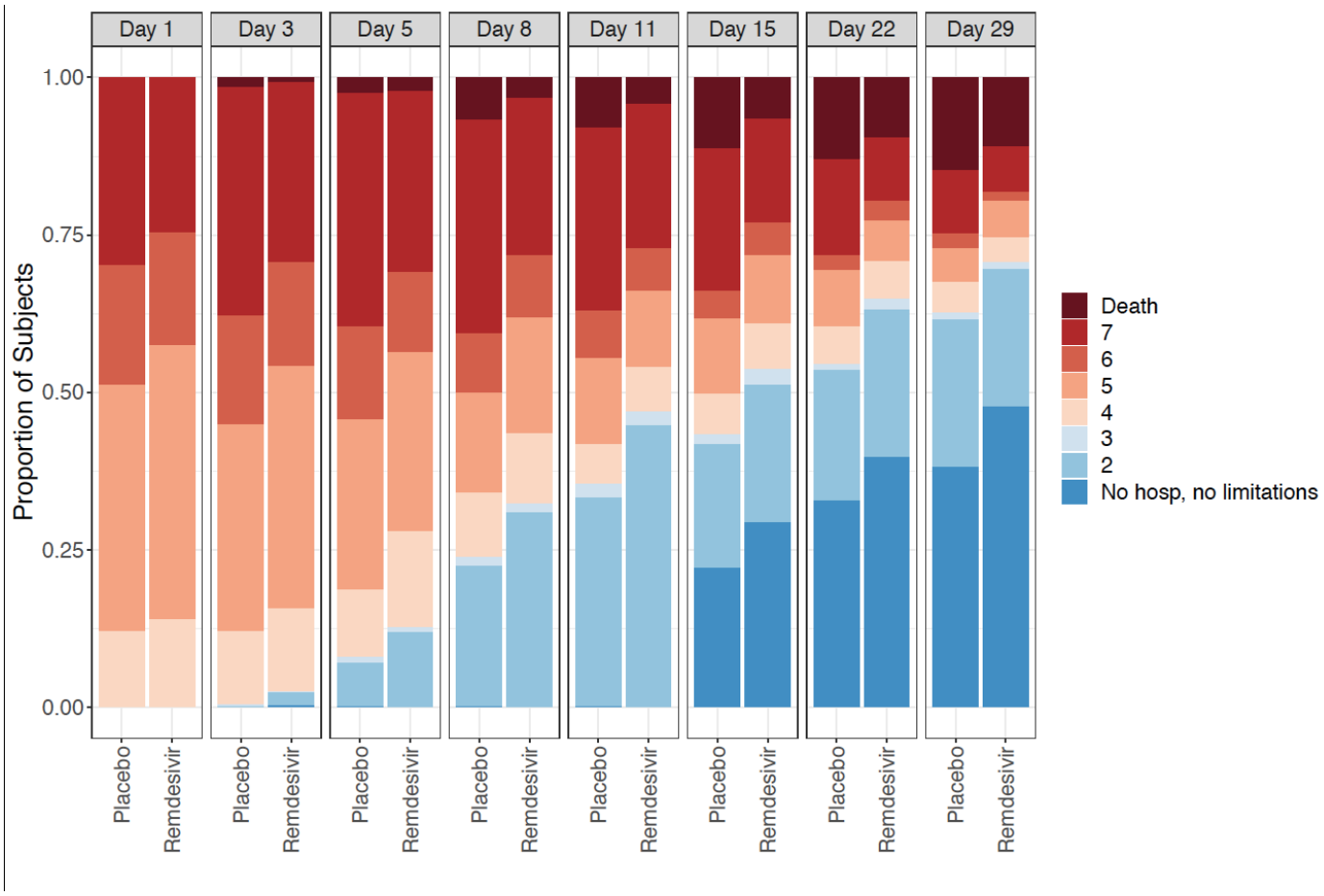


Figure S3. Distribution of Ordinal Scale by Treatment by Day by Baseline score.

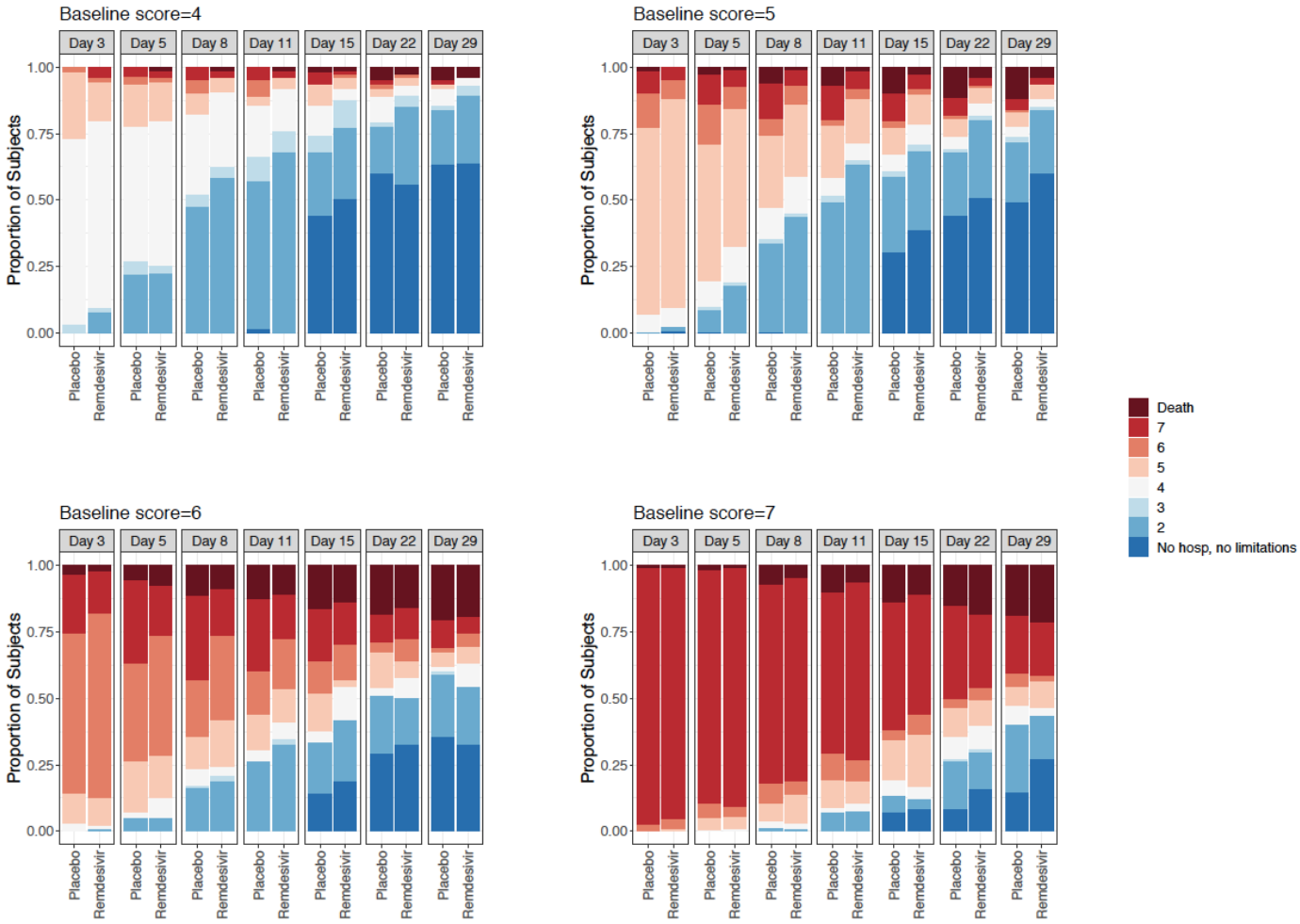
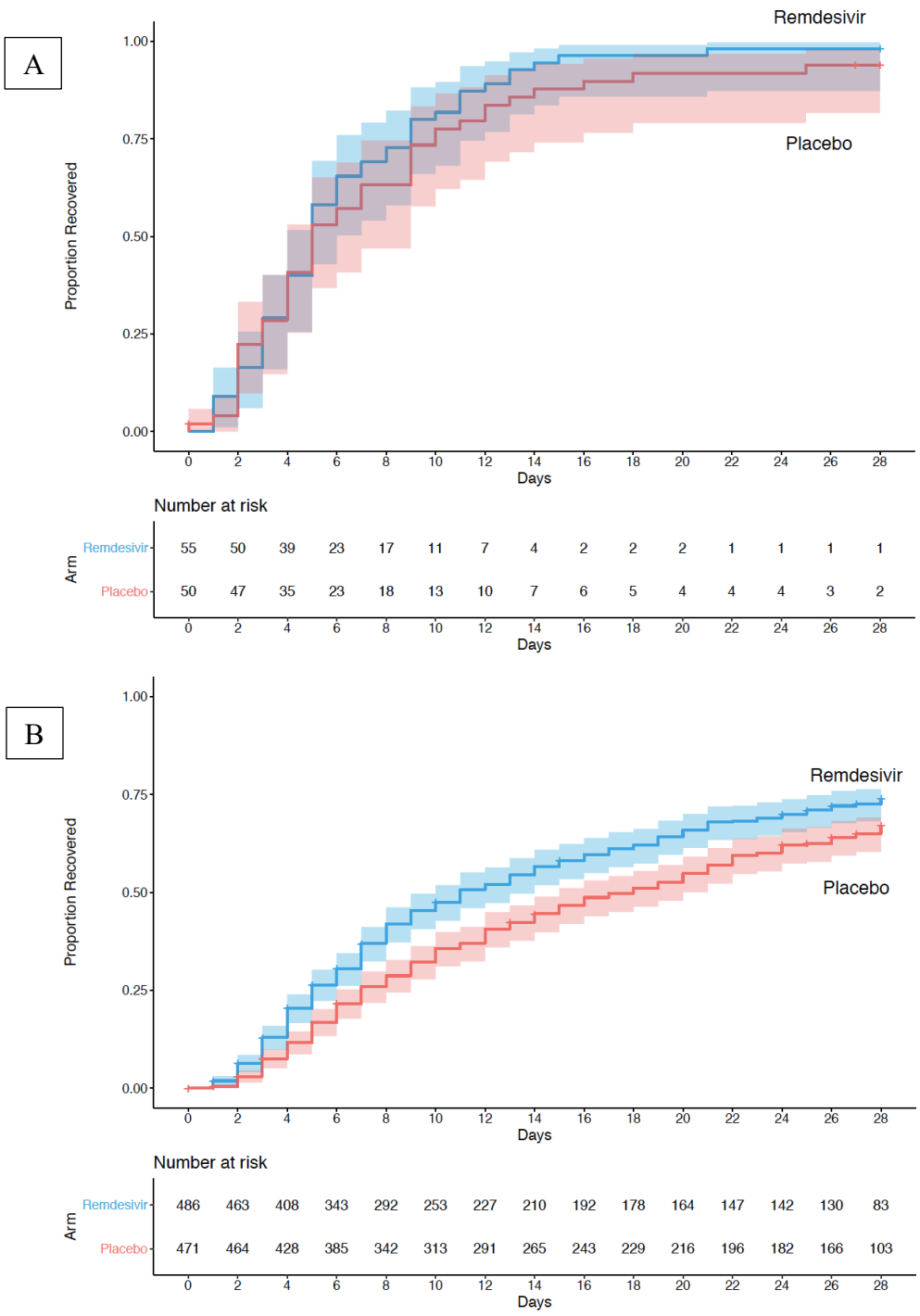
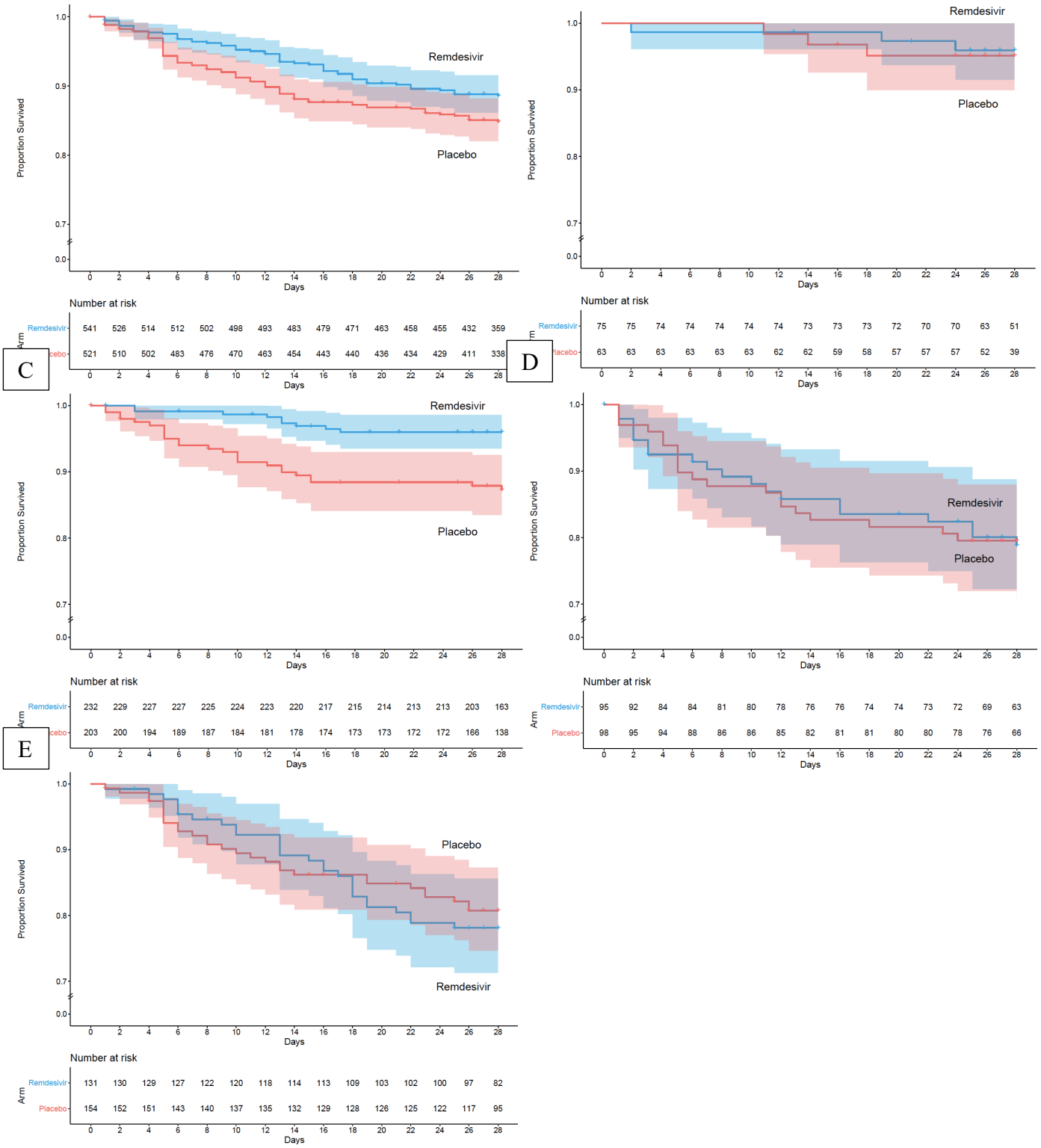


Figure S4. Kaplan–Meier Estimates of the Cumulative Recoveries by Baseline Disease Severity. Panel A shows the estimates (and 95% confidence bands) in patients with mild-moderate disease, and Panel B in patients with severe disease.



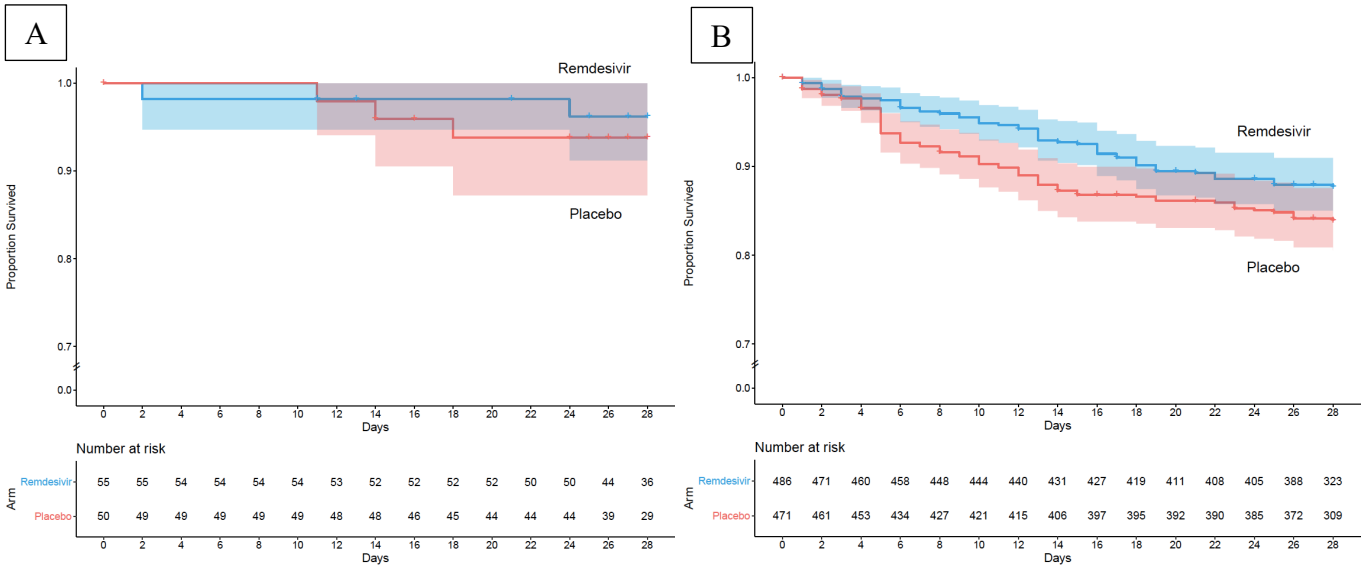
Note: the widths of confidence intervals have not been adjusted for multiplicity and cannot be used to infer treatment effects.

Figure S5. Kaplan–Meier Estimates of Survival by Baseline Ordinal Scale.
Panel A shows the estimates (and 95% confidence bands) in the overall population, Panel B in those with baseline ordinal e = 4, Panel C in those with baseline ordinal scale = 5, l D in those with baseline ordinal scale = 6, and Panel E in e with baseline ordinal scale = 7.



Note: the widths of confidence intervals have not been adjusted for multiplicity and cannot be used to infer treatment effects.

Figure S6. Kaplan–Meier Estimates of Survival by Disease Severity.
Panel A shows the estimates (and 95% confidence bands) in patients with mild-moderate disease, and Panel B in patients with severe disease.



Note: the widths of confidence intervals have not been adjusted for multiplicity and cannot be used to infer treatment effects.

Figure S7. Histogram of ordinal scores at Day 15 by treatment arm

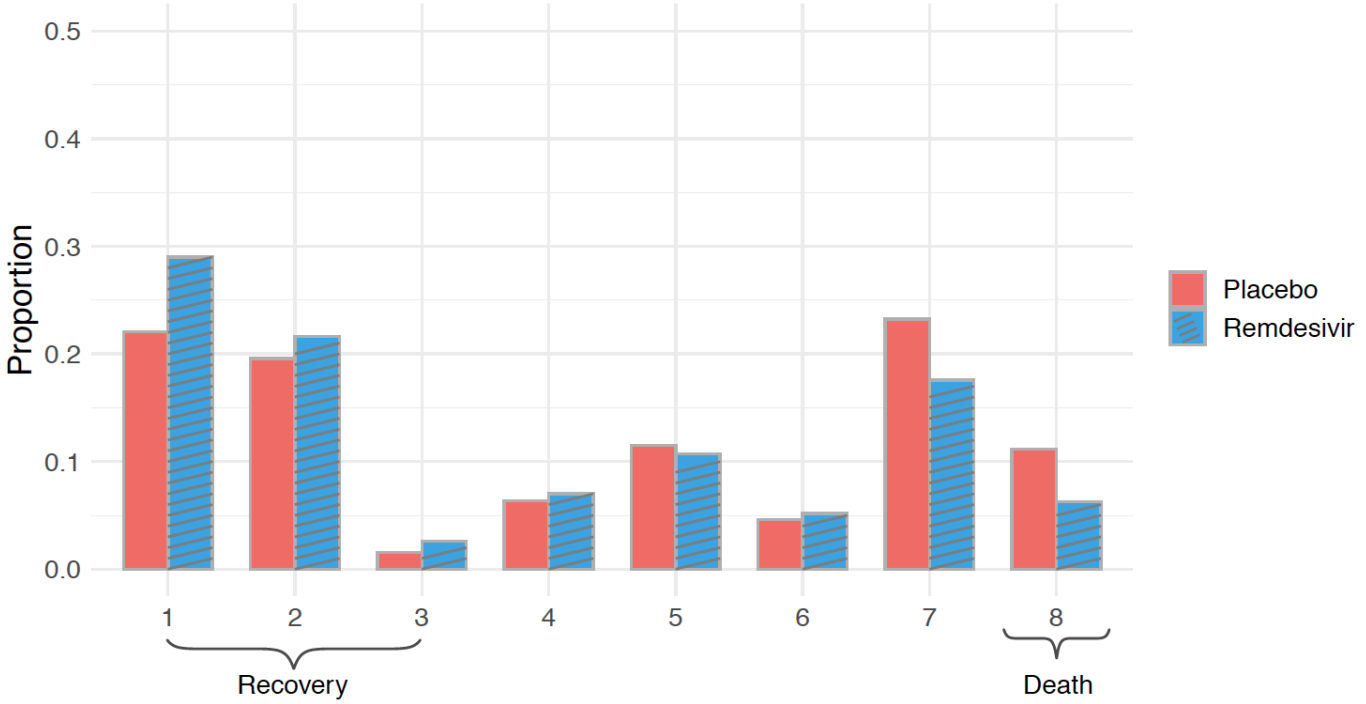
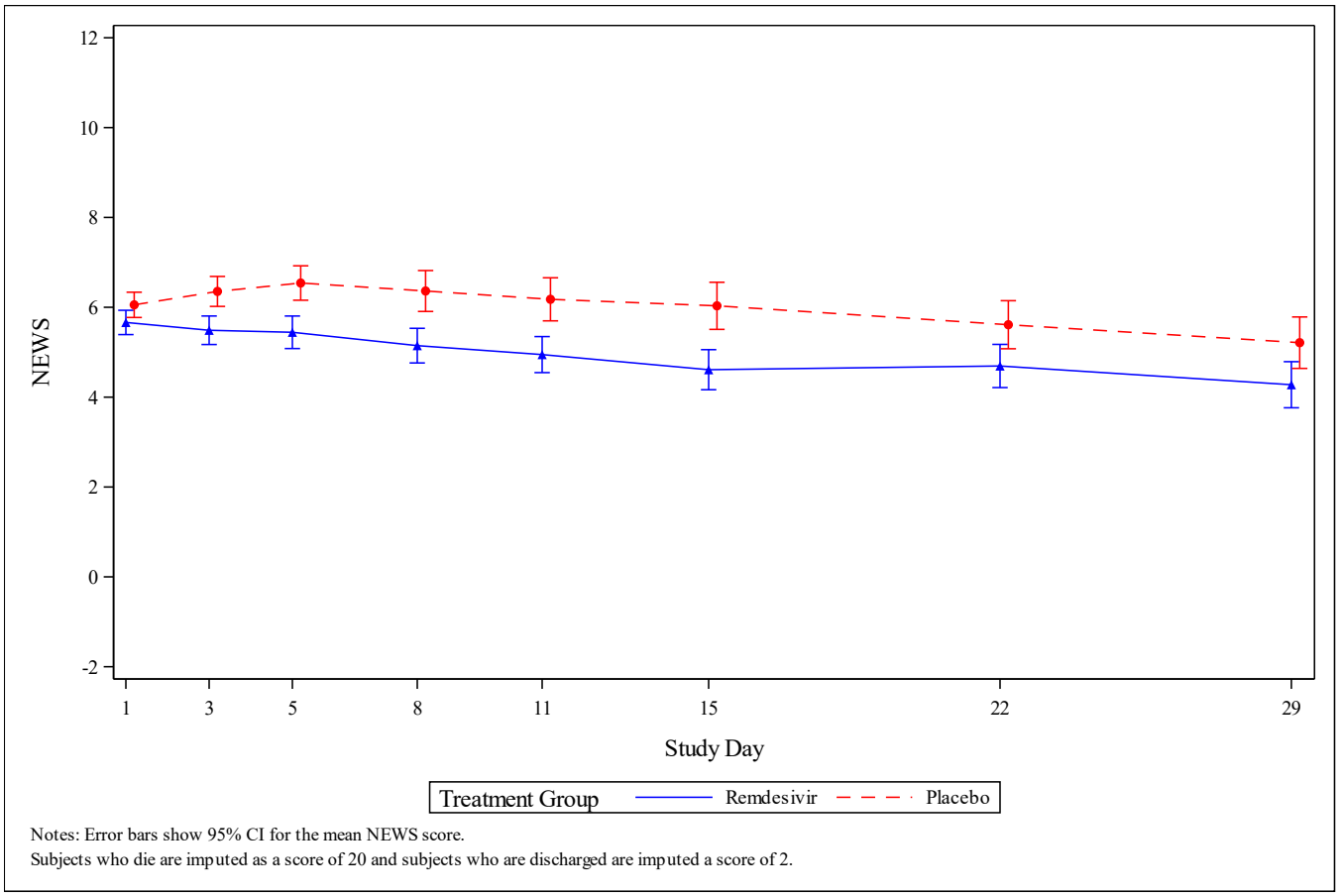


Figure S8. Mean NEWS by Day and Treatment Group – ITT Population



Notes: Error bars show 95% CI for the mean NEWS score.
Subjects who die are imputed as a score of 20 and subjects who are discharged are imputed a score of 2.

References:

1. 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.
2. Royal College of Physicians. National Early Warning Score (NEWS) 2 2017 [Available from: https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news-2.
3. King JC, Beigel JH, Ison MG, Rothman RE, Uyeki TM, Walker RE, et al. Clinical Development of Therapeutic Agents for Hospitalized Patients With Influenza: Challenges and Innovations. Open Forum Infect Dis. 2019;6(4):ofz137.