Clinical trial results:
A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Study Evaluating the Efficacy and Safety of Remdesivir in Participants with Severely Reduced Kidney Function who are Hospitalized for COVID-19

Summary

EudraCT number	2020-005416-22
Trial protocol	PT ES
Global end of trial date	24 May 2022

Results information

Result version number	v1 (current)
This version publication date	28 May 2023
First version publication date	28 May 2023

Trial information

Trial identification

Sponsor protocol code	GS-US-540-5912

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04745351
WHO universal trial number (UTN)	-
Other trial identifiers	South African Clinical Trials Register: DOH-27-012022-4779

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2022
Global end of trial reached?	Yes
Global end of trial date	24 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate whether remdesivir (RDV, GS-5734™) reduces the composite risk of death or invasive mechanical ventilation (IMV) through Day 29 in participants with severely reduced kidney function who are hospitalized for coronavirus disease 2019 (COVID-19).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

For studies with data uploaded using XML, this information will be populated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Portugal: 20
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United States: 184
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Brazil: 1
Worldwide total number of subjects	249
EEA total number of subjects	60

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	96
From 65 to 84 years	121
85 years and over	32

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Brazil, Portugal, Spain, the United Kingdom, and the United States.

Pre-assignment

Screening details:

258 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Remdesivir

Arm description:

Participants received continued Standard of Care (SOC) therapy together with RDV 200 mg intravenous (IV) infusion on Day 1 followed by RDV 100 mg IV infusion from Day 2 up to Day 5.

Arm type	Experimental
Investigational medicinal product name	Remdesivir
Investigational medicinal product code	
Other name	GS-5734™, Veklury®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg administered on Day 1 followed by 100 mg on Days 2-5.

Investigational medicinal product name	Standard of care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Infusion

Dosage and administration details:

Standard of Care treatment for COVID-19 infection was determined by the investigator and included various routes of administration and pharmaceutical forms.

Arm title	Placebo

Arm description:

Participants received continued SOC therapy together with RDV matching placebo IV saline on Day 1 followed by RDV matching placebo IV saline from Day 2 up to Day 5.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

RDV matching placebo IV saline administered on Days 1-5.

Investigational medicinal product name	Standard of care
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Infusion

Dosage and administration details:

Standard of Care treatment for COVID-19 infection was determined by the investigator and included various routes of administration and pharmaceutical forms.

Number of subjects in period 1[1]	Remdesivir	Placebo
Started	163	80
Completed	95	50
Not completed	68	30
Protocol violation	1	-
Death	51	25
Adverse event	4	-
Lost to follow-up	9	3
Withdrew consent	1	2
Investigator's discretion	2	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 6 participants who were randomised but not treated were not included in the Safety Analysis Set for the overall study period reported in subject disposition section.

Baseline characteristics

Reporting groups	
Reporting group title	Remdesivir
Reporting group description:	
Participants received continued Standard of Care (SOC) therapy together with RDV 200 mg intravenous (IV) infusion on Day 1 followed by RDV 100 mg IV infusion from Day 2 up to Day 5.	
Reporting group title	Placebo
Reporting group description:	
Participants received continued SOC therapy together with RDV matching placebo IV saline on Day 1 followed by RDV matching placebo IV saline from Day 2 up to Day 5.	

Reporting group values	Remdesivir	Placebo	Total
Number of subjects	163	80	243
Age categorical Units: Subjects			
< 18 Years	0	0	0
>= 18 to < 65 Years	70	22	92
>= 65 Years	93	58	151
Age continuous Units: years			
arithmetic mean	68	71	
standard deviation	± 14.1	± 13.0	-
Gender categorical Units: Subjects			
Female	71	33	104
Male	92	47	139
Ethnicity Units: Subjects			
Hispanic or Latino	23	8	31
Not Hispanic or Latino	135	72	207
Unknown or Not Reported	5	0	5
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	4	2	6
Black	43	18	61
Native Hawaiian or Pacific Islander	1	0	1
White	104	55	159
Other	8	3	11
Unknown or Not Reported	2	2	4
Clinical Status (8-point Ordinal Scale)			
The 8-point Ordinal scale assesses the clinical status of participants:1.Not hospitalized, no limitations on activities;2.Not hospitalized, limitation on activities/requiring home oxygen;3.Hospitalized,not requiring supplemental oxygen,no longer require ongoing medical care; 4.Hospitalized,not requiring supplemental oxygen-require ongoing medical care for COVID-19−specific medical care;5.Hospitalized,supplemental oxygen;6.Hospitalized,on noninvasive ventilation or highflow oxygen devices;7.Hospitalized,on invasive mechanical ventilation (IMV)/extracorporeal membrane oxygenation (ECMO);8.Death.			
Units: Subjects			
Score: 1	0	0	0
Score: 2	0	0	0

Score: 3	0	0	0
Score: 4	36	18	54
Score: 5	97	47	144
Score: 6	30	15	45
Score: 7	0	0	0
Score: 8	0	0	0

End points

End points reporting groups

Reporting group title	Remdesivir
Reporting group description:	
Participants received continued Standard of Care (SOC) therapy together with RDV 200 mg intravenous (IV) infusion on Day 1 followed by RDV 100 mg IV infusion from Day 2 up to Day 5.	
Reporting group title	Placebo
Reporting group description:	
Participants received continued SOC therapy together with RDV matching placebo IV saline on Day 1 followed by RDV matching placebo IV saline from Day 2 up to Day 5.	

Primary: Percentage of Participants With All-cause Death or Invasive Mechanical Ventilation (IMV) Through Day 29

End point title	Percentage of Participants With All-cause Death or Invasive Mechanical Ventilation (IMV) Through Day 29
End point description:	
This is the combined endpoint reporting the percentage of participants with all-cause death or IMV through Day 29. Full Analysis Set included all participants who were randomised into the study and had received at least 1 dose of study drug. The reported percentage was from the Kaplan-Meier estimate.	
End point type	Primary
End point timeframe:	
First dose date up to Day 29	

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	30.2	33.5		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6132 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.816

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.504
upper limit	1.321

Notes:

[1] - P-value was calculated from stratified log-rank test, stratified by the baseline stratification factors.

Secondary: All-cause Mortality Through Day 29

End point title	All-cause Mortality Through Day 29

End point description:

The reported percentage was from the Kaplan-Meier estimate. Participants in the Full Analysis Set were analysed.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	25.9	29.7		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3881 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.497
upper limit	1.388

Notes:

[2] - P-value was calculated from stratified log-rank test stratified by the baseline stratification factors.

Secondary: Percentage of Participants With Initiation of IMV Through Day 29

End point title	Percentage of Participants With Initiation of IMV Through Day 29

End point description:

The reported percentage was the cumulative-incidence estimate. Participants in the Full Analysis Set were analysed.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	13.8	12.8		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9116 [3]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.043
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.493
upper limit	2.207

Notes:

[3] - The treatment effect p-value was calculated using Cox model with death as the competing risk and baseline stratification factors as covariates.

Secondary: Time to Recovery Without Subsequent Worsening (Defined as an Ordinal Scale Score of > 4) by Day 29

End point title	Time to Recovery Without Subsequent Worsening (Defined as an Ordinal Scale Score of > 4) by Day 29

End point description:

Time to recovery is the time from first dose to recovery. Recovery is defined as the first day on which the participant with a baseline score ≥ 4, satisfies categories 1, 2, or 3 from the 8-point ordinal scale: 1) Non-hospitalized, no limitations on activities; 2) Non-hospitalized, limitations on activities/requiring home oxygen; 3) Hospitalized, not requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19; 5) Hospitalized, supplemental oxygen; 6) Hospitalized, on noninvasive ventilation; 7) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 8) Death. Cumulative incidence was reported. Participants in Full Analysis Set were analysed. 9999=Q3 was not estimable due to <75% of participants with recovery by Day 29.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: days				
median (inter-quartile range (Q1-Q3))	20 (7 to 9999)	19 (7 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recovery Independent of Further Worsening by Day 29

End point title	Time to Recovery Independent of Further Worsening by Day 29

End point description:

Time to recovery is the time from first dose to recovery. Recovery is defined as the first day on which the participant with a baseline score ≥ 4, satisfies categories 1, 2, or 3 from the 8-point ordinal scale: 1) Non-hospitalized, no limitations on activities; 2) Non-hospitalized, limitations on activities/requiring home oxygen; 3) Hospitalized, not requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19; 5) Hospitalized, supplemental oxygen; 6) Hospitalized, on noninvasive ventilation; 7) Hospitalized, on invasive mechanical ventilation or ECMO; 8) Death. Cumulative incidence was reported. Participants in Full Analysis Set were analysed. 9999=Q3 was not estimable due to the <75% of participants with recovery by Day 29.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: days				
median (inter-quartile range (Q1-Q3))	10 (6 to 9999)	13 (6 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Within Each Clinical Status Category as Assessed by an 8-Point Ordinal Scale on Day 15

End point title	Percentage of Participants Within Each Clinical Status Category as Assessed by an 8-Point Ordinal Scale on Day 15

End point description:

Clinical status is derived from death, hospital discharge, and the ordinal scale. Each day, the worst (highest) score from the previous day was recorded. The 8-point Ordinal scale is as follows: 1. Not hospitalized, no limitations on activities; 2. Not hospitalized, limitation on activities and/or requiring home oxygen; 3. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care (other than per-protocol RDV/saline as placebo administration); 4. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19–specific medical care (other than per-protocol RDV administration); 5. Hospitalized, supplemental oxygen; 6. Hospitalized, on noninvasive ventilation or high-flow oxygen devices; 7. Hospitalized, on IMV or ECMO; and 8. Death. Higher scores indicate worse clinical status. Participants in the Full Analysis Set were analysed.

End point type	Secondary

End point timeframe:

Day 15

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)				
Score: 1	0	0		
Score: 2	48.5	48.8		
Score: 3	5.5	2.5		
Score: 4	9.2	7.5		
Score: 5	6.1	11.3		
Score: 6	8.0	5.0		
Score: 7	4.9	6.3		
Score: 8	17.8	18.8		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8541 [4]
Method	Proportional odds model

Notes:

[4] - P-value was analysed from proportional odds model including treatment as the independent variable.

Secondary: Percentage of Participants Within Each Clinical Status Category as Assessed by an 8-Point Ordinal Scale on Day 29

End point title	Percentage of Participants Within Each Clinical Status Category as Assessed by an 8-Point Ordinal Scale on Day 29

End point description:

Clinical status is derived from death, hospital discharge, and the ordinal scale. Each day, the worst (highest) score from the previous day was recorded. The 8-point Ordinal scale is as follows: 1. Not hospitalized, no limitations on activities; 2. Not hospitalized, limitation on activities and/or requiring home oxygen; 3. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical

care (other than per-protocol RDV/saline as placebo administration); 4. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19-specific medical care (other than per-protocol RDV administration); 5. Hospitalized, supplemental oxygen; 6. Hospitalized, on noninvasive ventilation or high-flow oxygen devices; 7. Hospitalized, on IMV or ECMO; and 8. Death. Higher scores indicate worse clinical status. Participants in the Full Analysis Set were analysed.

End point type	Secondary

End point timeframe:

Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)				
Score: 1	11.7	16.3		
Score: 2	42.9	45.0		
Score: 3	3.1	2.5		
Score: 4	4.3	1.3		
Score: 5	9.2	2.5		
Score: 6	1.8	1.3		
Score: 7	1.8	2.5		
Score: 8	25.2	28.8		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4974 [5]
Method	Proportional odds model

Notes:

[5] - P-value was analysed from proportional odds model including treatment as the independent variable.

Secondary: Renal Replacement Therapy (RRT)-Free Days (Among Those Without End-Stage Kidney Disease [ESKD] at Baseline) Through Day 29

End point title	Renal Replacement Therapy (RRT)-Free Days (Among Those Without End-Stage Kidney Disease [ESKD] at Baseline) Through Day 29

End point description:

The number of RRT free days were calculated as the number of full days from Day 1 to Day 29 on which the participant was alive and did not receive RRT. Participants without ESKD at baseline in the Full Analysis Set with available data were analysed.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	50		
Units: days				
median (full range (min-max))	29 (1 to 29)	29 (4 to 29)		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4283 [6]
Method	Wilcoxon (Mann-Whitney)

Notes:

[6] - P-value was calculated based on Wilcoxon rank sum test.

Secondary: Percentage of Participants With Recovery Without Subsequent Worsening (Defined as an Ordinal Scale Score of > 4) Through Day 29

End point title	Percentage of Participants With Recovery Without Subsequent Worsening (Defined as an Ordinal Scale Score of > 4) Through Day 29

End point description:

Recovery is defined as the first day on which the participant with a baseline score >= 4, satisfies categories 1, 2, or 3 from the 8-point ordinal scale including: 1) Non-hospitalized, no limitations on activities; 2) Non-hospitalized, limitations on activities/requiring home oxygen; 3) Hospitalized, not requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19; 5) Hospitalized, supplemental oxygen; 6) Hospitalized, on noninvasive ventilation; 7) Hospitalized, on IMV or ECMO; 8) Death.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	57.7	63.8		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2773 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.731
upper limit	1.091

Notes:

[7] - The treatment effect p-value was calculated using Cochran-Mantel-Haenszel (CMH) analysis including baseline stratification factors.

Secondary: Percentage of Participants With Recovery Independent of Further Worsening Through Day 29

End point title	Percentage of Participants With Recovery Independent of Further Worsening Through Day 29

End point description:

Recovery is defined as the first day on which the participant with a baseline score >= 4, satisfies categories 1, 2, or 3 from the 8-point ordinal scale including: 1) Non-hospitalized, no limitations on activities; 2) Non-hospitalized, limitations on activities/requiring home oxygen; 3) Hospitalized, not requiring supplemental oxygen; 4) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care for COVID-19; 5) Hospitalized, supplemental oxygen; 6) Hospitalized, on noninvasive ventilation; 7) Hospitalized, on IMV or ECMO; 8) Death.

End point type	Secondary

End point timeframe:

First dose date up to Day 29

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	66.3	67.5		

Statistical analyses

Statistical analysis title	Statistical Analysis: Remdesivir vs Placebo
Comparison groups	Remdesivir v Placebo

Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7538 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.819
upper limit	1.155

Notes:

[8] - The treatment effect p-value was calculated using CMH analysis including baseline stratification factors.

Secondary: Percentage of Participants Experiencing Serious Adverse Events (SAEs)

End point title	Percentage of Participants Experiencing Serious Adverse Events (SAEs)

End point description:

An SAE was defined as an event that, at any dose, results in the following: Death, a life-threatening situation, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, a congenital anomaly/birth defect, a medically important event or reaction which may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require intervention to prevent one of the other outcomes constituting SAEs. Safety Analysis Set included all participants who were randomised into the study and had received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

First dose date up to last dose date (Maximum: 5 days) plus 30 days

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	50.3	50.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Permanently Discontinued Investigational Drug Due to Adverse Events (AEs)

End point title	Percentage of Participants Who Permanently Discontinued Investigational Drug Due to Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a clinical study participant administered an investigational drug, which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of an investigational drug, whether or not the AE is considered related to the investigational drug. Participants

in the Safety Analysis Set were analysed.

End point type	Secondary

End point timeframe:

First dose date up to last dose date (Maximum: 5 days)

End point values	Remdesivir	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	80		
Units: percentage of participants				
number (not applicable)	4.9	1.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Randomisation up to last follow-up visit (maximum of 15 weeks); Adverse Events: First dose date up to last dose date (maximum: 5 days) plus 30 days

Adverse event reporting additional description:

All-Cause Mortality: All Randomised Analysis Set included all participants who were randomised in the study.
Adverse Events: Safety Analysis Set included all participants who were randomised into the study and had received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Remdesivir

Reporting group description:

Participants received continued SOC therapy together with RDV 200 mg IV infusion on Day 1 followed by RDV 100 mg IV infusion from Day 2 up to Day 5.

Reporting group title	Placebo

Reporting group description:

Participants received continued SOC therapy together with RDV matching placebo IV saline on Day 1 followed by RDV matching placebo IV saline from Day 2 up to Day 5.

Serious adverse events	Remdesivir	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	82 / 163 (50.31%)	40 / 80 (50.00%)	
number of deaths (all causes)	55	26	
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	7 / 163 (4.29%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shock			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic stenosis			

subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Shock haemorrhagic			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	4 / 163 (2.45%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 4	0 / 1	
Death			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General physical health ~ deterioration			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	7 / 163 (4.29%)	10 / 80 (12.50%)	
occurrences causally related to treatment / all	0 / 8	0 / 10	
deaths causally related to treatment / all	0 / 5	0 / 7	
Acute respiratory failure			
subjects affected / exposed	10 / 163 (6.13%)	4 / 80 (5.00%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 6	0 / 1	
Hypoxia			
subjects affected / exposed	6 / 163 (3.68%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 1	
Pneumothorax			
subjects affected / exposed	2 / 163 (1.23%)	3 / 80 (3.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory distress			
subjects affected / exposed	3 / 163 (1.84%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute pulmonary oedema			

subjects affected / exposed	1 / 163 (0.61%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 163 (0.61%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumomediastinum			
subjects affected / exposed	0 / 163 (0.00%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	0 / 163 (0.00%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoptysis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Glomerular filtration rate abnormal			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dialysis related complication			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fall			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wound haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	8 / 163 (4.91%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 7	0 / 1	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 163 (1.23%)	3 / 80 (3.75%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Atrial fibrillation			
subjects affected / exposed	3 / 163 (1.84%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	2 / 163 (1.23%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	3 / 163 (1.84%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Bradycardia			

subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dementia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 163 (1.23%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Large intestinal haemorrhage			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic ischaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	5 / 163 (3.07%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
End stage renal disease			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal impairment			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 163 (0.61%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			
subjects affected / exposed	6 / 163 (3.68%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 4	0 / 2	
Sepsis			

subjects affected / exposed	5 / 163 (3.07%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Covid-19			
subjects affected / exposed	2 / 163 (1.23%)	3 / 80 (3.75%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Covid-19 pneumonia			
subjects affected / exposed	3 / 163 (1.84%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Bacteraemia			
subjects affected / exposed	3 / 163 (1.84%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	2 / 163 (1.23%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cytomegalovirus infection ~ reactivation			
subjects affected / exposed	1 / 163 (0.61%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	2 / 163 (1.23%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bacteroides bacteraemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related bacteraemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gangrene			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii infection			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection bacterial			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	1 / 163 (0.61%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 163 (0.00%)	2 / 80 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			

subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipasaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 163 (0.61%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Remdesivir	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 163 (36.81%)	34 / 80 (42.50%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	12 / 163 (7.36%)	4 / 80 (5.00%)	
occurrences (all)	12	5	
Hypertension			
subjects affected / exposed	4 / 163 (2.45%)	6 / 80 (7.50%)	
occurrences (all)	4	7	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	7 / 163 (4.29%)	4 / 80 (5.00%)	
occurrences (all)	7	4	
Nervous system disorders			
Headache			

subjects affected / exposed	3 / 163 (1.84%)	4 / 80 (5.00%)	
occurrences (all)	3	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 163 (6.13%)	1 / 80 (1.25%)	
occurrences (all)	13	3	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	12 / 163 (7.36%)	7 / 80 (8.75%)	
occurrences (all)	12	7	
Nausea			
subjects affected / exposed	12 / 163 (7.36%)	3 / 80 (3.75%)	
occurrences (all)	13	4	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 163 (3.07%)	7 / 80 (8.75%)	
occurrences (all)	6	7	
Agitation			
subjects affected / exposed	5 / 163 (3.07%)	4 / 80 (5.00%)	
occurrences (all)	5	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 163 (1.23%)	4 / 80 (5.00%)	
occurrences (all)	2	4	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	13 / 163 (7.98%)	1 / 80 (1.25%)	
occurrences (all)	14	1	
Hyperglycaemia			
subjects affected / exposed	7 / 163 (4.29%)	5 / 80 (6.25%)	
occurrences (all)	8	5	
Hypoglycaemia			
subjects affected / exposed	8 / 163 (4.91%)	4 / 80 (5.00%)	
occurrences (all)	8	4	
Hypokalaemia			

subjects affected / exposed	5 / 163 (3.07%)	7 / 80 (8.75%)	
occurrences (all)	5	10	
Hypomagnesaemia			
subjects affected / exposed	3 / 163 (1.84%)	4 / 80 (5.00%)	
occurrences (all)	3	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 January 2021	• Clarified study rationale to revise amount of sulfobutylether β-cyclodextrin sodium (SBECD) in 5-day course of RDV • Text was added to provide rationale for why dose adjustment was not appropriate due to metabolic pathways of RDV, and that RDV should be administered before hemodialysis if both fall on same day • Updated risk/benefit assessment to describe risk-benefit specific to study participants with severely reduced renal function who were hospitalized with COVID-19 • Primary objective was revised from all-cause death through Day 29, to a composite risk of IMV/death through Day 29 and endpoints were revised to reflect these changes • Amendments were made to descriptions of packaging, labeling for RDV and saline • Text was added to provide clear directions for concomitant medications use, to clarify personnel responsibilities for study drug accountability and handling of unused study drug, to further clarify management of clinically significant laboratory abnormalities, AEs • Updated study procedures sections and table • Numbers of participants from whom PK samples would be collected for intensive PK substudy and hemodialysis substudy were increased • Text was added to clarify details of first DMC meeting to review safety data and sample size re-estimation at second DMC meeting was removed so as not to enroll additional participants • An interim efficacy analysis was added per health authority recommendation so that study could be halted early due to either efficacy or futility • Updated statistical methods to reflect updated primary endpoint, to state that primary endpoint and key α-controlled secondary endpoint would be analysed at interim analysis, to clarify that their assessment would be based on interim analysis results and adjustments for multiplicity were added • Ratio for randomisation to RDV arm to placebo arm was changed from 1:1 to 2:1 to provide RDV to more participants, placebo to fewer participants per health authority feedback.
02 August 2021	• Increased the number of planned study centers to 150 • Expanded inclusion criteria to include participants with acute kidney injury (AKI) • Provided clarity on concomitant medications that are prohibited and allowed during the study, and account for current and future drug authorisations and approvals • Updated study procedures to capture vaccination status of participants • Provided clarity on conduction of sparse plasma PK assessments • Added IMV to follow-up visit in the study procedure table.
27 August 2021	• Clarified the inclusion criteria for AKI to specify that the increase in serum creatinine (SCr) should be sustained on repeat measurement • Clarified that urinalysis is not required in oliguric participants • Updated study procedures table to align with protocol changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated due to study enrollment feasibility. This decision was not based on efficacy or safety concerns.

Notes: