Clinical trial results:
A Phase 3 Randomized, Double-Blind Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Remdesivir (GS-5734™) Treatment of COVID-19 in an Outpatient Setting

Summary

EudraCT number	2020-003510-12
Trial protocol	DK GB PT
Global end of trial date	06 May 2021

Results information

Result version number	v1 (current)
This version publication date	20 November 2021
First version publication date	20 November 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-540-9012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04501952
WHO universal trial number (UTN)	-

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 May 2021
Global end of trial reached?	Yes
Global end of trial date	06 May 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the efficacy of remdesivir (RDV) in reducing the rate of of coronavirus disease 2019 (COVID-19) related hospitalization or all-cause death in non-hospitalized participants with early stage COVID-19 and to evaluate the safety of RDV administered in an outpatient setting.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2020
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	Spain: 17
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	United States: 552
Worldwide total number of subjects	584
EEA total number of subjects	27

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	8
Adults (18-64 years)	479
From 65 to 84 years	93
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe and the United States. The first participant was screened on 18 September 2020. The last study visit occurred on 06 May 2021.

Pre-assignment

Screening details:

630 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 (RDV)

Arm description:

Participants received a single dose of intravenous (IV) RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2 and 3.

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 and 3

Arm title	Placebo

Arm description:

Participants received IV placebo to match (PTM) RDV on Days 1 to 3.

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

Dosage and administration details:

PTM RDV on Days 1 to 3

Number of subjects in period 1[1]	Remdesivir (RDV)	Placebo
Started	279	283
Completed	266	272
Not completed	13	11
Withdrew Consent	5	4
Adverse Event	-	3
Investigator's Discretion	-	1
Protocol Violation	1	1
Lost to follow-up	7	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: Thirteen participants in Remdesivir group and nine participants in the Placebo group were randomized but did not receive the study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Remdesivir (RDV)
Reporting group description:	
Participants received a single dose of intravenous (IV) RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2 and 3.	
Reporting group title	Placebo
Reporting group description:	
Participants received IV placebo to match (PTM) RDV on Days 1 to 3.	

Reporting group values	Remdesivir (RDV)	Placebo	Total
Number of subjects	279	283	562
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	50	51	
standard deviation	± 15.3	± 14.8	-
Gender categorical			
Units: Subjects			
Female	131	138	269
Male	148	145	293
Race			
Not Permitted means local regulators did not allow collection of race information.			
Units: Subjects			
American Indian or Alaska Native	15	21	36
Asian	6	7	13
Black	20	22	42
Native Hawaiian or Pacific Islander	1	0	1
White	228	224	452
Other	3	2	5
Not Permitted	6	7	13
Ethnicity			
Not Permitted means local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	123	112	235
Not Hispanic or Latino	146	158	304
Not Permitted	10	13	23

End points

End points reporting groups

Reporting group title	Remdesivir (RDV)
Reporting group description:	
Participants received a single dose of intravenous (IV) RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2 and 3.	
Reporting group title	Placebo
Reporting group description:	
Participants received IV placebo to match (PTM) RDV on Days 1 to 3.	

Primary: Percentage of Participants With Coronavirus Disease 2019 (COVID-19) Related Hospitalization (Defined as at Least 24 Hours of Acute Care) or All-cause Death by Day 28

End point title	Percentage of Participants With Coronavirus Disease 2019 (COVID-19) Related Hospitalization (Defined as at Least 24 Hours of Acute Care) or All-cause Death by Day 28
End point description:	
The composite outcome of COVID-19 related hospitalization (defined as at least 24 hours of acute care) or all-cause death by Day 28 was derived by combining the available all-cause death and COVID-19 related hospitalization reported by the site. The first COVID-19 related hospitalization was used for the percentage of COVID-19 related hospitalization or all-cause death. The percentage of the composite outcome was from the Kaplan-Meier estimate. Full Analysis Set included all participants who were randomized into the study and received at least 1 dose of study treatment.	
End point type	Primary
End point timeframe:	
Randomization up to Day 28	

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	283		
Units: percentage of participants				
number (not applicable)	0.7	5.4		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	562
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0076 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.134

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.031
upper limit	0.586

Notes:

[1] - Hazard ratio and two-sided 95% confidence interval (CI) were estimated using the Cox regression with baseline stratification factors as covariates.

[2] - p-value were estimated using the Cox regression with baseline stratification factors as covariates.

Primary: Percentage of Participants Who Experienced Treatment-Emergent Adverse Events (TEAEs)

End point title	Percentage of Participants Who Experienced Treatment-Emergent Adverse Events (TEAEs)[3]

End point description:

TEAEs were defined as any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug and/or any AEs leading to premature discontinuation of study drug. Safety Analysis Set included all participants who were randomized into the study and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

First dose date up to last dose date (maximum: 3 days) plus 30 days

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	283		
Units: percentage of participants				
number (not applicable)	42.3	46.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19 Related Medical Visits Attended in Person by the Participant and a Health Care Professional (MAVs) or All-Cause Death by Day 28

End point title	Percentage of Participants With COVID-19 Related Medical Visits Attended in Person by the Participant and a Health Care Professional (MAVs) or All-Cause Death by Day 28

End point description:

The composite outcome of COVID-19 related MAVs or all-cause death by Day 28 was derived by combining the available all-cause death and COVID-19 related MAVs reported by the site. The percentage of the composite outcome was from the Kaplan-Meier estimate. Modified Full Analysis Set included all participants who were randomized into the study, and received at least 1 dose of study treatment, and enrolled under protocol amendment 2 or later.

End point type	Secondary

End point timeframe:

Randomization up to Day 28

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	252		
Units: percentage of participants				
number (not applicable)	1.7	8.5		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0024 [5]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.191
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.065
upper limit	0.555

Notes:

[4] - Hazard ratio and two-sided 95% CI were estimated using the Cox regression with baseline stratification factors as covariates.

[5] - p-value were estimated using the Cox regression with baseline stratification factors as covariates.

Secondary: Percentage of Participants Who Died by Day 28

End point title	Percentage of Participants Who Died by Day 28

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Randomization up to Day 28

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	274		
Units: percentage of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19 Related Hospitalization at Day 28

End point title	Percentage of Participants With COVID-19 Related Hospitalization at Day 28

End point description:

COVID-19 related hospitalization is defined as at least 24 hours of acute care derived by COVID-19 related hospitalization reported by the site. The percentage of the outcome and the corresponding 95% confidence interval were from Kaplan-Meier estimate. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Randomization up to Day 28

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	283		
Units: percentage of participants				
number (confidence interval 95%)	0.7 (0.2 to 2.9)	5.4 (3.3 to 8.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With COVID-19 Related Hospitalization or All-cause Death by Day 14

End point title	Percentage of Participants With COVID-19 Related Hospitalization or All-cause Death by Day 14

End point description:

The composite outcome of COVID-19 related hospitalization (defined as at least 24 hours of acute care) or all-cause death by Day 14 was derived by combining the available all-cause death and COVID-19 related hospitalization reported by the site. The first COVID-19 related hospitalization was used for the percentage of COVID-19 related hospitalization or all-cause death. The percentage of the composite outcome was from the Kaplan-Meier estimate. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Randomization up to Day 14

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	283		
Units: percentage of participants				
number (not applicable)	0.7	5.4		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Placebo v Remdesivir (RDV)
Number of subjects included in analysis	562
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.0076 [7]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.134
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.031
upper limit	0.586

Notes:

[6] - Hazard ratio and two-sided 95% CI were estimated using the Cox regression with baseline stratification factors as covariates.

[7] - p-value were estimated using the Cox regression with baseline stratification factors as covariates.

Secondary: Percentage of Participants With COVID-19 Related MAVs or All-cause Death by Day 14

End point title	Percentage of Participants With COVID-19 Related MAVs or All-cause Death by Day 14

End point description:

The composite outcome of COVID-19 related MAVs or all-cause death by Day 14 was derived by combining the available all-cause death and COVID-19 related MAVs reported by the site. The percentage of the composite outcome was from the Kaplan-Meier estimate. Participants in the modified Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Randomization up to Day 14

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	252		
Units: percentage of participants				
number (not applicable)	0.8	8.0		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	498
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.0019 [9]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.023
upper limit	0.43

Notes:

[8] - Hazard ratio and two-sided 95% CI were estimated using the Cox regression with baseline stratification factors as covariates.

[9] - p-value were estimated using the Cox regression with baseline stratification factors as covariates.

Secondary: Time-Weighted Average Change in Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Viral Load From Baseline to Day 7

End point title	Time-Weighted Average Change in Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Viral Load From Baseline to Day 7

End point description:

The time-weighted average change from baseline to study Day 7 (DAVG7) in SARS-CoV-2 viral load is defined as the time-weighted average between the first postbaseline value through the last available value up to Day 7 minus the baseline value in SARS-CoV-2 viral load (log10 copies/mL). DAVG7 is calculated using the trapezoidal rule and the area under the curve (AUC). For participants with data through days prior to Day 7, the time-weighted average change used data up to last available timepoint. If there was no postbaseline data, the participant was excluded from the analysis. Participants in the Virology Analysis Set (all the participants who were randomized into the study, received at least 1 dose of study treatment, and had positive SARS-CoV-2 viral load at baseline) with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline up to Day 7

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	208		
Units: log10 copies/mililiter (mL)				
arithmetic mean (standard deviation)	-1.24 (± 1.123)	-1.14 (± 1.099)		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.4318
Method	ANCOVA
Parameter estimate	Least Squares Mean
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[10] - Least squares Mean (LSM), standard error (SE) and 95% CI were from an ANCOVA model with baseline viral load as a covariate.

Secondary: Time to Alleviation (Mild or Absent) of Baseline COVID-19 Symptoms as Reported on the COVID-19-adapted Influenza Patient-Reported Outcome Plus Questionnaire (FLU-PRO Plus)

End point title	Time to Alleviation (Mild or Absent) of Baseline COVID-19 Symptoms as Reported on the COVID-19-adapted Influenza Patient-Reported Outcome Plus Questionnaire (FLU-PRO Plus)

End point description:

The COVID-19-adapted FLU-PRO Plus is a questionnaire that assesses the severity of symptoms in participants with COVID-19 across six body systems: nose, throat, eyes, chest/respiratory, gastrointestinal, and body/systemic. Each domain scores range from 0 (symptom free) to 4 (very severe symptoms). A higher score indicates increased symptom severity. Alleviation is defined as symptom scores of 0 (absent) or 1 (mild). Time to alleviation of baseline COVID-19 symptoms is defined (in days) as: First Date of the two consecutive dates achieving alleviation - First dose Date + 1. If a participant had not achieved symptom alleviation at last FLU-PRO Plus assessment or early discontinuation of study, the participant was censored at last FLU-PRO Plus assessment date. Participants in the Full Analysis Set with available data were analyzed. 99999 indicates that not enough event to estimate Median and Inter-Quartile Range.

End point type	Secondary

End point timeframe:

First Dose Date up to Day 14

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	60		
Units: days				
median (inter-quartile range (Q1-Q3))	99999 (10.0 to 99999)	99999 (13.0 to 99999)		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2987 [11]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.405
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.733
upper limit	2.693

Notes:

[11] - p-value was based on stratified log-rank test with baseline stratification factor as strata.

Secondary: Percentage of Participants With Worsening After Alleviation of Baseline COVID-19 Symptoms as Reported on the COVID-19-adapted FLU-PRO Plus Questinnaire

End point title	Percentage of Participants With Worsening After Alleviation of Baseline COVID-19 Symptoms as Reported on the COVID-19-adapted FLU-PRO Plus Questinnaire

End point description:

The worsening after alleviation of baseline COVID-19 symptoms is defined as for a participant who has achieved alleviation of baseline COVID-19 symptoms, if symptoms scored as 2 or higher at baseline is scored as 2 or higher postbaseline after achieved alleviation, or symptoms scored as 1 at baseline are scored as 1 or higher postbaseline after achieved alleviation. The COVID-19-adapted FLU-PRO Plus was used. It is a questionnaire that assesses the severity of symptoms in participants with COVID-19 across six body systems: nose, throat, eyes, chest/respiratory, gastrointestinal, and body/systemic. Each domain scores range from 0 (symptom free) to 4 (very severe symptoms). A higher score indicates increased symptom severity. Alleviation is defined as symptom scores of 0 (absent) or 1 (mild). Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

First dose date up to Day 28

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	15		
Units: percentage of participants				
number (not applicable)	30.4	13.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Required Oxygen Supplementation by Day 28

End point title	Percentage of Participants Who Required Oxygen Supplementation by Day 28
End point description:	
Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe:	
Randomization up to Day 28	

End point values	Remdesivir (RDV)	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	283		
Units: percentage of participants				
number (not applicable)	0.4	1.8		

Statistical analyses

Statistical analysis title	Remdesivir vs Placebo
Comparison groups	Remdesivir (RDV) v Placebo
Number of subjects included in analysis	562
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2163
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to 3 days plus 30 days; All-Cause Mortality: Randomization to the end of study (maximum: 59 days)

Adverse event reporting additional description:

Adverse Events: Safety Analysis Set included all participants who were randomized into the study and received at least 1 dose of study treatment; All-Cause Mortality: All Randomized Analysis Set included all participants who were randomized in the study (i.e. participants exposed, Remdesivir=292, Placebo=292).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Remdesivir (RDV)

Reporting group description:

Participants received a single dose of intravenous (IV) RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2 and 3.

Reporting group title	Placebo

Reporting group description:

Patients who received Placebo

Serious adverse events	Remdesivir (RDV)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 279 (1.79%)	19 / 283 (6.71%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Blood pressure inadequately controlled			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 279 (0.72%)	0 / 283 (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	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve prolapse			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			

subjects affected / exposed	0 / 279 (0.00%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 279 (0.36%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
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	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 283 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19 pneumonia			
subjects affected / exposed	0 / 279 (0.00%)	7 / 283 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 279 (0.72%)	3 / 283 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Covid-19			
subjects affected / exposed	1 / 279 (0.36%)	2 / 283 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Viral myocarditis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 283 (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 (RDV)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 279 (17.20%)	49 / 283 (17.31%)	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 279 (5.73%)	17 / 283 (6.01%)	
occurrences (all)	16	17	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	30 / 279 (10.75%)	21 / 283 (7.42%)	
occurrences (all)	31	21	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 279 (3.58%)	18 / 283 (6.36%)	
occurrences (all)	10	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2020	• Added ClinicalTrials.gov identifier • Increased the number of planned study centers to 150 to help complete enrollment within planned timelines • Removed restriction on percentage of participants that may be enrolled from skilled nursing facilities • Decreased minimum age to include adolescent participants ages ≥ 12 • Modified inclusion and exclusion criteria • Added sputum samples for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quantitative reverse transcriptase polymerase chain reaction (RT- qPCR) viral load testing and possible resistance testing • Added study drug administration instructions • Revised Adverse Events • Removed Appendix Pandemic Risk Assessment and Mitigation Plan as it was not applicable for this study
06 November 2020	• Updates to endpoints in the study made in response to evolving treatment paradigms and understanding of COVID-19 • Updated General Information section to refer to the latest investigator brochure (IB))• Addition of coagulation panel • Clarification and/or update of inclusion and exclusion criteria • Addition of complete physical examination requirements section
12 November 2020	• The secondary endpoint of time to alleviation of COVID-19 symptoms was returned back to secondary from exploratory after further consideration.
14 January 2021	• Updated primary and secondary study objectives to align with updated study endpoints • Updated primary and secondary study endpoints to address US regulatory agency comments • Updated exclusion criterion to clarify exclusion of COVID-19 vaccines • Updated study drugs' storage and handling requirement • Updated statistical methods

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 April 2021	In April 2021, the study was terminated due to study enrollment feasibility and changing needs of non-hospitalized participants. This decision is not based on efficacy or safety concerns.	-

Notes:

Limitations and caveats

None reported