



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 standard deviation | 50 ± 15.3 | 51 ± 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 | <ul style="list-style-type: none">Added ClinicalTrials.gov identifierIncreased the number of planned study centers to 150 to help complete enrollment within planned timelinesRemoved restriction on percentage of participants that may be enrolled from skilled nursing facilitiesDecreased minimum age to include adolescent participants ages ≥ 12Modified inclusion and exclusion criteriaAdded 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 testingAdded study drug administration instructionsRevised Adverse EventsRemoved Appendix Pandemic Risk Assessment and Mitigation Plan as it was not applicable for this study |
| 06 November 2020 | <ul style="list-style-type: none">Updates to endpoints in the study made in response to evolving treatment paradigms and understanding of COVID-19Updated General Information section to refer to the latest investigator brochure (IB)Addition of coagulation panelClarification and/or update of inclusion and exclusion criteriaAddition of complete physical examination requirements section |
| 12 November 2020 | <ul style="list-style-type: none">The secondary endpoint of time to alleviation of COVID-19 symptoms was returned back to secondary from exploratory after further consideration. |
| 14 January 2021 | <ul style="list-style-type: none">Updated primary and secondary study objectives to align with updated study endpointsUpdated primary and secondary study endpoints to address US regulatory agency commentsUpdated exclusion criterion to clarify exclusion of COVID-19 vaccinesUpdated study drugs' storage and handling requirementUpdated 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