



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

| | | | |
|-----------------------------|-----------------|----------------|--|
| 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 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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: