



Clinical trial results:

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of GS-5245 for the Treatment of COVID-19 in Participants With High-Risk for Disease Progression Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2022-002741-18 |
| Trial protocol | FR HU ES BG IT |
| Global end of trial date | 07 November 2023 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 13 November 2024 |
| First version publication date | 13 November 2024 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-611-6273 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05603143 |
| 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? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 November 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 07 November 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The goal of this clinical study was to test how well the study drug, obeldesivir (GS-5245), worked and how safe it was in treating coronavirus disease 2019 (COVID-19) in participants that have a higher risk of getting a serious illness.

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 | 05 November 2022 |
| 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 | Brazil: 8 |
| Country: Number of subjects enrolled | Bulgaria: 196 |
| Country: Number of subjects enrolled | Canada: 18 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Japan: 5 |
| Country: Number of subjects enrolled | Mexico: 48 |
| Country: Number of subjects enrolled | Poland: 19 |
| Country: Number of subjects enrolled | Romania: 53 |
| Country: Number of subjects enrolled | Singapore: 1 |
| Country: Number of subjects enrolled | South Africa: 31 |
| Country: Number of subjects enrolled | Korea, Republic of: 3 |
| Country: Number of subjects enrolled | Spain: 23 |
| Country: Number of subjects enrolled | Taiwan: 40 |
| Country: Number of subjects enrolled | Türkiye: 2 |

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | Portugal: 9 |
| Worldwide total number of subjects | 468 |
| EEA total number of subjects | 304 |

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) | 0 |
| Adults (18-64 years) | 332 |
| From 65 to 84 years | 130 |
| 85 years and over | 6 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the South America, Europe, North America, Africa and Asia.

Pre-assignment

Screening details:

515 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 | Obeldesivir |

Arm description:

Participants received obeldesivir 350 mg orally twice daily for 5 days.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Obeldesivir |
| Investigational medicinal product code | |
| Other name | GS-5245 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Tablets administered orally without regard to food.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Participants received placebo-to-match obeldesivir orally twice daily for 5 days.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo tablets administered orally without regard to food.

| Number of subjects in period 1 | Obeldesivir | Placebo |
|---------------------------------------|-------------|---------|
| Started | 233 | 235 |
| Completed | 224 | 227 |
| Not completed | 9 | 8 |
| Adverse event, non-fatal | 2 | - |

| | | |
|------------------------------|---|---|
| Death | - | 1 |
| Withdrew consent | 6 | 2 |
| Investigator's discretion | 1 | - |
| Randomized but never treated | - | 3 |
| Lost to follow-up | - | 1 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-------------|
| Reporting group title | Obeldesivir |
| Reporting group description: | |
| Participants received obeldesivir 350 mg orally twice daily for 5 days. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo-to-match obeldesivir orally twice daily for 5 days. | |

| Reporting group values | Obeldesivir | Placebo | Total |
|--|-------------|---------|-------|
| Number of subjects | 233 | 235 | 468 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18 – 64 Years) | 159 | 173 | 332 |
| Geriatrics (65 – 84 Years) | 71 | 59 | 130 |
| Geriatrics (85 Years and Over) | 3 | 3 | 6 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 57 | 53 | |
| standard deviation | ± 14.9 | ± 16.6 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 147 | 117 | 264 |
| Male | 86 | 118 | 204 |
| Race | | | |
| Units: Subjects | | | |
| White | 178 | 168 | 346 |
| Asian | 24 | 32 | 56 |
| American Indian or Alaska Native | 21 | 19 | 40 |
| Black or African American | 9 | 10 | 19 |
| Other or More Than One Race | 1 | 4 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | 2 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 36 | 43 | 79 |
| Not Hispanic or Latino | 197 | 192 | 389 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Baseline Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Nasal Swab Viral Load | | | |
| The Safety Analysis Set included all participants who received at least 1 dose of study drug with data available were analyzed. One participant randomized to placebo arm received obeldesivir and was counted in obeldesivir group for the analysis of this baseline measure. For obeldesivir arm N=218, placebo arm N=215. | | | |
| Units: log10 copies/mL | | | |
| arithmetic mean | 6.15 | 6.15 | |
| standard deviation | ± 1.629 | ± 1.622 | - |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | Obeldesivir |
| Reporting group description: | |
| Participants received obeldesivir 350 mg orally twice daily for 5 days. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo-to-match obeldesivir orally twice daily for 5 days. | |

Primary: Percentage of Participants With Coronavirus Disease 2019 (COVID-19) Related Hospitalization or All-Cause Death by Day 29

| | |
|--|--|
| End point title | Percentage of Participants With Coronavirus Disease 2019 (COVID-19) Related Hospitalization or All-Cause Death by Day 29 |
| End point description: | |
| COVID-19-related hospitalization was defined as ≥ 24 hours of acute care for a reason related to COVID-19, in a hospital or similar acute care facility, including emergency rooms or temporary facilities instituted to address medical needs of those with COVID-19. This included specialized acute medical care units within an assisted living facility or nursing home. This did not include hospitalization for the purposes of public health and/or clinical trial execution. The date and duration of hospital admission, and primary reason for hospitalization (including if the hospitalization was related to COVID-19) were recorded. | |
| Full Analysis Positive Set included all randomized participants who received at least 1 dose of study drug and were SARS-CoV-2 positive at baseline as confirmed by cepheid's xpert xpress coronavirus-2/flu/respiratory syncytial virus plus test or SARS-CoV-2 reverse transcriptase quantitative polymerase chain reaction test from the central laboratory. | |
| End point type | Primary |
| End point timeframe: | |
| Up to Day 29 | |

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 207 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0.5 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
| Comparison groups | Obeldesivir v Placebo |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3161 ^[1] |
| Method | Logrank |

Notes:

[1] - PLACEHOLDER1

Secondary: Percentage of Participants With Treatment-Emergent Adverse Events

| | |
|-----------------|---|
| End point title | Percentage of Participants With Treatment-Emergent Adverse Events |
|-----------------|---|

End point description:

TEAEs were defined as 1 or both of the following:

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. Any AEs leading to premature discontinuation of study drug. Percentages were rounded off.

Analysis Population Description: The Safety Analysis Set included all participants who received at least 1 dose of study drug. One participant randomized to placebo arm received obeldesivir and was counted in obeldesivir group for the analysis of this endpoint

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

First dose date up to 5 Days plus 30 Days

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 233 ^[2] | 231 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 22.2 | 20.8 | | |

Notes:

[2] - N=234, one participant in placebo group received obeldesivir and was counted in obeldesivir group.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Laboratory Abnormalities

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing Laboratory Abnormalities |
|-----------------|--|

End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study drug plus 30 days. Percentages were rounded off.

Analysis Population Description: Participants in the Safety Analysis Set were analyzed. One participant randomized to placebo arm received obeldesivir and was counted in obeldesivir group for the analysis of this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

First dose date up to 5 Days plus 30 Days

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 219 | 223 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Any grade | 56.1 | 61.7 | | |
| Grade 3 or 4 | 6.5 | 4.8 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Serious Adverse Events (SAEs) and Adverse Events (AEs) Leading to Study Drug Discontinuation

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing Serious Adverse Events (SAEs) and Adverse Events (AEs) Leading to Study Drug Discontinuation |
|-----------------|--|

End point description:

A treatment emergent AE is defined as an AE that occurs or worsens in severity on or after the date of the first dose of study drug but no later than 30 days after the permanent discontinuation of study drug or an AE leading to discontinuation of study drug. A SAE is defined as an event that, at any dose, resulted in any of the following: death, life-threatening, in-patient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapacity, a congenital anomaly/birth defect, or a medically important event or reaction. Percentages were rounded off.

Analysis Population Description: Participants in the Safety Analysis Set were analyzed. One participant randomized to placebo arm received obeldesivir and was counted in obeldesivir group for the analysis of this endpoint.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

First dose date up to 5 Days plus 30 Days

| End point values | Obeldesivir | Placebo | | |
|--|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 233 ^[3] | 231 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| AEs Leading to Study Drug Discontinuation | 1.7 | 0.9 | | |
| SAEs Leading to Study Drug Discontinuation | 0.9 | 0.9 | | |

Notes:

[3] - One participant randomized to placebo arm received ODV and was counted in ODV group for the analysis

Statistical analyses

Secondary: Percentage of Participants With All-Cause Hospitalization by Day 29

| | |
|-----------------|---|
| End point title | Percentage of Participants With All-Cause Hospitalization by Day 29 |
|-----------------|---|

End point description:

All-cause hospitalization was defined as ≥ 24 hours of acute care, in a hospital or similar acute care facility, including emergency rooms or temporary facilities instituted to address medical needs of those with COVID-19. This includes specialized acute medical care units within an assisted living facility or nursing home. This does not include hospitalization for the purposes of public health and/or clinical study execution. The date and duration of hospital admission, and primary reason for hospitalization (including if the hospitalization is related to COVID-19) were recorded. Percentages were rounded off. Analysis Population Description: Participants in the Full Analysis Positive Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Day 29

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 207 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0.5 | 0 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3219 |
| Method | Logrank |

Secondary: Percentage of Participants With COVID-19–Related Medically Attended Visits (MAVs) or All-Cause Death by Day 29

| | |
|-----------------|--|
| End point title | Percentage of Participants With COVID-19–Related Medically Attended Visits (MAVs) or All-Cause Death by Day 29 |
|-----------------|--|

End point description:

Medically attended visits were defined as interactions with health care professionals other than study staff or designees including hospitalization; in-person emergency, urgent, or primary care visits; or any other in-person visit attended by the participant and a health care professional. The nature and cause of the visit were identified. KM estimates were used in the outcome measure analysis. Percentages were rounded off.

Analysis Population Description: Participants in the Full Analysis Positive Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Day 29

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 207 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 1.0 | 1.0 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
|---|---|
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6568 ^[4] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.496 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 8.952 |

Notes:

[4] - Hazard ratio and two-sided 95% CI for hazard ratio were estimated using the Cox regression.

Secondary: Percentage of Participants With COVID-19–Related MAVs by Day 29

| | |
|-----------------|---|
| End point title | Percentage of Participants With COVID-19–Related MAVs by Day 29 |
|-----------------|---|

End point description:

Medically attended visits were defined as interactions with health care professionals other than study staff or designees including hospitalization; in-person emergency, urgent, or primary care visits; or any other in-person visit attended by the participant and a health care professional. The nature and cause of the visit were identified. KM estimates were used in the outcome measure analysis. Percentages were rounded off.

Analysis Population Description: Participants in the Full Analysis Positive Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Day 29

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 207 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 1 | 0.5 | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
|---|---|
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.319 ^[5] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 2.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.311 |
| upper limit | 28.74 |

Notes:

[5] - Hazard ratio and two-sided 95% CI for hazard ratio were estimated using the Cox regression.

Secondary: Percentage of Participants With All-cause Death by Day 29

| End point title | Percentage of Participants With All-cause Death by Day 29 |
|--|---|
| End point description: | |
| Percentages were rounded off. Analysis Population Description: Participants in the Full Analysis Positive Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 29 | |

| End point values | Obeldesivir | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 207 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 0.5 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 418 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3161 |
| Method | Logrank |

Secondary: Time to COVID-19 Symptom Alleviation by Day 15

| | |
|-----------------|--|
| End point title | Time to COVID-19 Symptom Alleviation by Day 15 |
|-----------------|--|

End point description:

Time to COVID-19 symptom alleviation was calculated as symptom alleviation date/time minus the first dose date/time. Symptom alleviation was evaluated for the 15 targeted symptoms using symptoms of infection with coronavirus-19 (SIC) questionnaire. The SIC questionnaire assessed all targeted symptoms, alleviation was defined as the SIC rating of 0, or at least 3 points decrease in rating from baseline, or an answer "No" to the question for at least 48 consecutive hours.

Analysis Population Description: Participants in the Full Analysis Positive Set with Covid19 symptoms who completed Symptoms of Infection With Coronavirus-19 at baseline were analyzed.

1111: Upper limit of CI did not reach due to low number of participants with events.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Day 15

| | | | | |
|----------------------------------|------------------|-------------------|--|--|
| End point values | Obeldesivir | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 78 | | |
| Units: Days | | | | |
| median (confidence interval 95%) | 7.3 (5.4 to 9.4) | 9.3 (6.5 to 1111) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 162 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0859 ^[6] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.425 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.961 |
| upper limit | 2.112 |

Notes:

[6] - P-value was based on stratified Log-rank test with randomization stratification factors as the strata.

Secondary: Change from Baseline in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Nasal Swab Viral Load at Day 5

| | |
|-----------------|---|
| End point title | Change from Baseline in Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Nasal Swab Viral Load at Day 5 |
|-----------------|---|

End point description:

The mixed model for repeated measures (MMRM) was used for analysis.. Analysis Population Description: Virology Analysis Set included all randomized participants who received at least 1 dose of study drug and had baseline SARS-CoV-2 viral load greater than or equal to lower limit of quantitation.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 5

| End point values | Obeldesivir | Placebo | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 193 | 192 | | |
| Units: log10 copies/mL | | | | |
| least squares mean (standard error) | -2.80 (± 0.092) | -2.22 (± 0.092) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis Obeldesivir vs Placebo |
| Comparison groups | Obeldesivir v Placebo |
| Number of subjects included in analysis | 385 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[7] |
| P-value | < 0.0001 |
| Method | Mixed Models Analysis |
| Parameter estimate | Treatment Difference (vs Placebo) |
| Point estimate | -0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.83 |
| upper limit | -0.33 |

Notes:

[7] - Least-squares mean (SE), 95% CI and P value were from MMRM with baseline viral load and randomization strata as covariates.

Secondary: Plasma Concentrations of GS-441524 (Metabolite of Obeldesivir)

| | |
|-----------------|---|
| End point title | Plasma Concentrations of GS-441524 (Metabolite of Obeldesivir) ^[8] |
|-----------------|---|

End point description:

Pharmacokinetic Analysis Set included all randomized participants who received at least 1 dose of study drug and had at least 1 non missing concentration value reported by the PK laboratory with available data were analyzed .

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1, 0.75 and 2 hours postdose and Day 5 predose and 0.75 hours postdose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical comparison was planned or performed.

| End point values | Obeldesivir | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 224 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| D 1, 0.75 h N=216 | 2330.42 (± 1709.560) | | | |
| D 1, 2 h N=95 | 2535.84 (± 1370.131) | | | |
| D 5, Predose N=170 | 1116.81 (± 1101.371) | | | |
| D 5, 0.75 h N=174 | 3089.09 (± 1839.992) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All-cause mortality, AE's: First dose date up to 5 Days plus 30 Days

Adverse event reporting additional description:

All-cause mortality: All Randomized Analysis Set; Adverse events: Safety Analysis Set. 1 participant randomized to placebo arm accidentally received obeldesivir and was counted in obeldesivir arm for the analysis of all-cause mortality and adverse events.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Patients who received Placebo

| | |
|-----------------------|-------------|
| Reporting group title | Obeldesivir |
|-----------------------|-------------|

Reporting group description:

Patients who received ODV

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The participants did not experience any non-serious adverse events.

| Serious adverse events | Placebo | Obeldesivir | |
|--|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 2 / 234 (0.85%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 234 (0.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 234 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 234 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 234 (0.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo | Obeldesivir | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 234 (0.00%) | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 29 March 2023 | Key changes included in Amendment 1 were the addition and modification of risk factors and targeted signs and symptoms of COVID-19 to the inclusion criteria, aligning with the Centers for Disease Control and Prevention. Additional relevant nonclinical toxicology, pharmacology, and PK language were included based on Phase 1 drug-drug interactions and radiolabeled ADME. Consequently, restrictions on the coadministration of acid-reducing agents were removed, hormonal contraceptive measures were amended, and phototoxicity results demonstrating that GS-5245 was not considered a photosafety risk were incorporated. Updates to secondary and exploratory objectives and endpoints were made to capture omissions (PK) and reflect additional analyses (PROs, viral titer, and coinfections).. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported