Remdesivir Trials in Participants with Severe COVID-19

1) A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants with Severe COVID-19

2) A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants with Moderate COVID-19 Compared to Standard of Care Treatment

Study 5773: Severe Infection

- Mechanically Ventilated participants who meet all eligibility criteria may be randomized into one of the following treatment groups:
  - **Treatment Group 1:** continued standard of care therapy together with IV RDV200 mg on Day 1 followed by IV RDV 100 mg on Days 2, 3, 4, and 5
  - **Treatment Group 2:** continued standard of care therapy together with IV RDV200 mg on Day 1 followed by IV RDV 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10

OBJECTIVES

- The primary objective of this study is as follows:
  - To evaluate the efficacy of 2 RDV regimens with respect to the normalization of temperature and oxygen saturation through Day 14
- The secondary objective of this study is as follows:
  - To evaluate the safety and tolerability of RDV

Endpoint of the study

1. Primary endpoint of this study is:
    1. The proportion of participants in each group with normalization of fever and oxygen saturation [criteria for normalization: temperature < 36.6°C armpit, < 37.2°C oral, < 37.8°Crectal; and SpO_2 > 94%, sustained for at least 24 hours] through Day 14
2. The secondary endpoint of this study is:
    - The proportion of participants with treatment emergent adverse events leading to study drug discontinuation
3. Other endpoints of interest are:
    1. Time to SpO2 > 94% on room air
    2. Time to first fever normalization (criteria for normalization: temperature < 36.6°C armpit, < 37.2°C oral, < 37.8°C rectal)
    3. Time to first negative SARS-CoV-2 polymerase chain reaction (PCR)
    4. Duration of oxygen therapy
    5. Duration of hospitalization (days)
    6. All cause mortality at Day 28
    7. Time to clinical improvement (days): Clinical improvement is defined using a 6-point ordinal scale at Day 1 status dropped by 2 points or discharge

5573 Severe

Inclusion

- Informed consent/legal representative
- ≥ 18 years of age
- SARS-CoV-2 confirmed by PCR ≤ 4 days before randomization
- Currently hospitalized
- **mechanically ventilated**
- Radiological evidence of pulmonary infiltrates
- Men and woman of childbearing potential who engage in heterosexual intercourse must agree to use protocol specified methods of contraception

Exclusion

- Participation in any other clinical trial or experimental treatment for COVID-19
- Concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 < 24 hours prior to study drug dosing (discontinue other agents at minimum 24 hours prior to receiving first dose of RDV)
- Evidence if multiorgan failure
- Mechanically ventilated (including V-V ECMO) ≥ 5 days, or any duration of V-A ECMO
- ALT or AST > 5 x ULN
- Creatinine clearance < 50 mL/min using the Cockcroft-Gault formula
- Positive pregnancy test
- Breastfeeding
- Known hypersensitivity to the study drug, the metabolites, or formulation excipient

Study 5774: Moderate Infection

- Approximately 600 participants who meet all eligibility criteria may be randomized in 1:1:1 ratio into one of the following treatment groups:
  - **Treatment Group 1:** continued SOC therapy together with intravenous (IV) RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2, 3, 4, and 5
  - **Treatment Group 2:** continued SOC therapy together with IV RDV 200 mg on Day 1 followed by IV RDV 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10
  - **Treatment Group 3:** continued SOC therapy

OBJECTIVES

- The primary objective of this study is as follows:
  - To evaluate the efficacy of 2 RDV regimens compared to standard of care (SOC), with respect to the time to discharge
- The secondary objective of this study is as follows:
  - To evaluate the safety and tolerability of RDV

Endpoint of the study

1. Primary endpoint of this study is:
    1. The proportion of participants discharged by Day 14
2. The secondary endpoint of this study is:
    - The proportion of participants with treatment emergent adverse events leading to study drug discontinuation
3. Other endpoints of interest are:
    1. Time to first fever normalization (criteria for normalization: temperature < 36.6°C armpit, < 37.2°C oral, < 37.8°C rectal)
    2. Time to first negative SARS-CoV-2 polymerase chain reaction (PCR)
    3. Duration of oxygen therapy
    4. Duration of hospitalization (days)
    5. All cause mortality at Day 28
    6. Time to clinical improvement (days): Clinical improvement is defined using a 6-point ordinal scale at Day 1 status dropped by 2 points or discharge

5774 Moderate:

Inclusion

- Informed consent
- ≥18 years of age
- SARS-CoV-2 confirmed by PCR ≤ 4 days before randomization
- Currently hospitalized and requiring medical care for COVID
- SpO2 > 94% on room air at screening
- Radiologic evidence of pulmonary infiltrates
- Men and woman of childbearing potential who engage in heterosexual intercourse must agree to use protocol specified methods of contraception

Exclusion

- Participation in any other clinical trial or experimental treatment for COVID-19
- Concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 < 24 hours prior to study drug dosing (discontinue other agents at minimum 24 hours prior to receiving first dose of RDV)
- Requiring mechanical ventilation at screening
- ALT or AST > 5 x ULN
- Creatinine clearance < 50 mL/min using the Cockcroft-Gault formula
- Positive pregnancy test
- Breastfeeding
- Known hypersensitivity to the study drug, the metabolites, or formulation excipient

Required Labs

- Screening
  - CBC w/ diff
  - CMP
  - Pregnancy test for women
- Daily
  - CBC w/ diff
  - CMP

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