Table 2a. Remdesivir: Selected Clinical Data

Last Updated: February 24, 2022

The clinical trials described in this table do not represent all the trials that the Panel reviewed while developing the recommendations for RDV. The studies summarized below are the randomized controlled trials that have had the greatest impact on the Panel’s recommendations. Studies of hospitalized patients are listed first, followed by studies of nonhospitalized patients.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Results</th>
<th>Limitations and Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACTT-1</strong>: Multinational, Placebo-Controlled, Double-Blind RCT of Remdesivir in Hospitalized Patients With COVID-19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key Inclusion Criteria:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Laboratory-confirmed SARS-CoV-2 infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ≥1 of the following criteria:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pulmonary infiltrates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• $\text{SpO}_2 \leq 94%$ on room air</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Need for supplemental oxygen, high-flow oxygen, NIV, MV, or ECMO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key Exclusion Criteria:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ALT or AST &gt;5 times ULN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• eGFR &lt;30 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pregnancy or breastfeeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RDV 200 mg IV on Day 1, then RDV 100 mg daily for up to 9 more days (n = 541)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Placebo for up to 10 days (n = 521)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Endpoint:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Time to clinical recovery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key Secondary Endpoints:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Clinical status at Day 15, as measured by an OS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mortality by Day 29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Occurrence of SAEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant Characteristics:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mean age 58.9 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 53.3% White, 21.3% Black, 12.7% Asian, 23.5% Hispanic/Latinx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Coexisting conditions: 26.2% with 1; 55.2% with ≥2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 13.0% not on oxygen; 41.0% on supplemental oxygen; 18.2% on high-flow oxygen or NIV; 26.8% on MV or ECMO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Median time from symptom onset to randomization: 9 days (IQR 6–12 days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Received corticosteroids during study: 21.6% in RDV arm; 24.4% in placebo arm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Outcomes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Time to clinical recovery: 10 days in RDV arm vs. 15 days in placebo arm (rate ratio for recovery 1.29; 95% CI, 1.12–1.49; $P &lt; 0.001$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Benefit of RDV greatest in patients randomized during first 10 days after symptom onset and those who required supplemental oxygenation at enrollment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No difference in time to recovery for patients on high-flow oxygen, NIV, MV, or ECMO at enrollment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary Outcomes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Clinical status at Day 15: improvement more likely in RDV arm (OR 1.5; 95% CI, 1.2–1.9; $P &lt; 0.001$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mortality by Day 29: no difference between arms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Proportion of patients with SAEs: similar between arms (25% vs. 32%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key Limitations:

• Wide range of disease severity among patients; study not powered to detect differences within subgroups
• Powered to detect differences in clinical improvement, not mortality
• No data on longer-term morbidity

Interpretation:

• In patients with severe COVID-19, RDV reduced time to clinical recovery.
• The benefit was most apparent in hospitalized patients who were receiving supplemental oxygen.
• There was no observed benefit in those on high-flow oxygen, NIV, MV, or ECMO, but study was not powered to detect differences within subgroups.
### DisCoVeRy: Open-Label, Adaptive RCT of Remdesivir in Hospitalized Patients With Moderate or Severe COVID-19 in Europe

**Key Inclusion Criteria:**
- Laboratory-confirmed SARS-CoV-2 infection
- Illness of any duration
- \( \text{SpO}_2 \leq 94\% \) on room air or use of supplemental oxygen, high-flow oxygen devices, NIV, or MV

**Key Exclusion Criteria:**
- ALT or AST >5 times ULN
- Severe chronic kidney disease

**Interventions:**
- RDV 200 mg IV on Day 1, then RDV 100 mg IV once daily for up to 9 days (n = 429)
- SOC (n = 428)

**Primary Endpoint:**
- Clinical status at Day 15, as measured by an OS

**Key Secondary Endpoints:**
- Mortality at Day 29
- Occurrence of SAEs

**Participant Characteristics:**
- Median age 64 years; 70% men; 69% White
- 74% with \( \geq 1 \) coexisting condition
- 40% received corticosteroids during study
- Median days from symptom onset to randomization: 9 days in both arms
- 61% with moderate disease; 39% with severe disease

**Primary Outcomes:**
- Clinical status at Day 15: no difference between arms (OR 0.98; 95% CI, 0.77–1.25; \( P = 0.85 \))
- A prespecified subgroup analysis based on duration of symptoms found no significant difference in clinical status between arms.

**Secondary Outcomes:**
- Mortality: no difference between arms (8% in RDV arm vs. 9% in SOC arm)
- Proportion of patients with SAEs: no difference between arms (33% in RDV arm vs. 31% in SOC arm; \( P = 0.48 \))

**Key Limitations:**
- Open-label study
- 440 participants in this study also enrolled in the WHO Solidarity trial.

**Interpretation:**
- There was no clinical benefit of RDV in hospitalized patients who were symptomatic for \( >7 \) days and who required supplemental oxygen.

### WHO Solidarity Trial: Multinational, Open-Label, Adaptive RCT of Repurposed Drugs in Hospitalized Patients With COVID-19

**Key Inclusion Criteria:**
- Aged \( \geq 18 \) years
- Not known to have received any study drug
- Not expected to be transferred elsewhere within 72 hours

**Interventions:**
- RDV 200 mg IV on Day 0, then RDV 100 mg IV on Days 1–9 (n = 2,743)
- Local SOC (n = 2,708)

**Primary Endpoint:**
- In-hospital mortality

**Key Secondary Endpoint:**
- Initiation of MV

**Participant Characteristics:**
- 47% aged 50–69 years; 18% aged \( \geq 70 \) years
- At entry: 67% on supplemental oxygen; 9% on MV
- Rates of comorbidities similar between arms
- 48% in both arms received corticosteroids during study

**Primary Outcome:**
- In-hospital mortality: 11.0% in RDV arm vs. 11.2% in SOC arm (rate ratio 0.95; 95% CI, 0.81–1.11)

**Secondary Outcome:**
- Initiation of MV: 10.8% in RDV arm vs. 10.5% in SOC arm

**Key Limitations:**
- Open-label design limits ability to assess time to recovery, as RDV may have been continued even if patient improved.
- No data on time from symptom onset to enrollment
- No assessment of outcomes post hospital discharge

**Interpretation:**
- RDV did not decrease in-hospital mortality or the need for MV compared to SOC.
**Methods**

**GS-US-540-5774 Study:** Multinational, Open-Label RCT of 10 Days or 5 Days of Remdesivir Compared With Standard of Care in Hospitalized Patients With Moderate COVID-19

**Key Inclusion Criteria:**
- Laboratory-confirmed SARS-CoV-2 infection
- Pulmonary infiltrates
- \( \text{SpO}_2 \) >94% on room air

**Key Exclusion Criteria:**
- ALT or AST >5 times ULN
- CrCl <50 mL/min

**Interventions:**
- RDV 200 mg IV on Day 1, then RDV 100 mg daily for 9 days (n = 193)
- RDV 200 mg IV on Day 1, then RDV 100 mg daily for 4 days (n = 191)
- Local SOC (n = 200)

**Primary Endpoint:**
- Clinical status at Day 11, as measured by an OS

**Participant Characteristics:**
- Demographic and baseline disease characteristics similar across arms
- Ranges for participant characteristics across the 3 arms:
  - Median age 56–58 years
  - Men: 60% to 63%
  - 81% to 87% required no supplemental oxygen; 12% to 18% required low-flow oxygen; 1% required high-flow oxygen or NIV
- Concomitant medication use in the 10-day RDV, 5-day RDV, and SOC arms:
  - Steroids: 15%, 17%, 19%
  - Tocilizumab: 1%, 1%, 5%
  - HCQ/CQ: 11%, 8%, 45%
  - LPV/RTV: 6%, 5%, 22%
  - AZM: 21%, 18%, 31%
- Median length of therapy: 6 days in 10-day RDV arm; 5 days in 5-day RDV arm

**Primary Outcomes:**
- Clinical status at Day 11:
  - Significantly better in 5-day RDV arm than in SOC arm (OR 1.65; 95% CI, 1.09–2.48; \( P = 0.02 \))
  - No difference in clinical status at Day 11 between 10-day RDV arm and SOC arm (\( P = 0.18 \))

**Limitations and Interpretation**

**Key Limitations:**
- Open-label design may have affected decisions on concomitant medications (e.g., more patients in the SOC arm received AZM, HCQ or CQ, and LPV/RTV) and time of hospital discharge.
- No data on time to return to activity for discharged patients

**Interpretation:**
- Hospitalized patients with moderate COVID-19 who received 5 days of RDV had better clinical status at Day 11 than those who received SOC.
- There was no difference in the clinical status at Day 11 between patients who received 10 days of RDV and those who received SOC.
### Methods

**GS-US-540-5773 Study**: Multinational, Open-Label RCT of 10 Days or 5 Days of Remdesivir Compared with Standard of Care in Hospitalized Patients With Moderate COVID-19

### Results

#### Key Inclusion Criteria:
- Laboratory-confirmed SARS-CoV-2 infection
- Pulmonary infiltrates and $\text{SpO}_2 \leq 94\%$ on room air or receipt of supplemental oxygen

#### Key Exclusion Criteria:
- Need for MV or ECMO
- Multiorgan failure
- ALT or AST >5 times ULN
- Estimated CrCl <50 mL/min

#### Interventions:
- RDV 200 mg IV on Day 1, then RDV 100 mg daily for 4 days ($n = 200$)
- RDV 200 mg IV on Day 1, then RDV 100 mg daily for 9 days ($n = 197$)

#### Participant Characteristics:
- Median age 61 years in 5-day arm; 62 years in 10-day arm
- 60% men in 5-day arm; 68% men in 10-day arm
- Oxygen requirements at baseline for the 5-day and 10-day arms:
  - None: 17%, 11%
  - Low-flow supplemental oxygen: 56%, 54%
  - High-flow oxygen or NIV: 24%, 30%
  - MV or ECMO: 2%, 5%
- Baseline clinical status: worse in 10-day arm than in 5-day arm ($P = 0.02$)

#### Primary Endpoint:
- Clinical status at Day 14, as measured by an OS

#### Key Secondary Endpoints:
- Time to clinical improvement
- Time to recovery

#### Primary Outcome:
- Day 14 distribution in clinical status after adjusting for baseline clinical status: similar between arms ($P = 0.14$)

#### Secondary Outcomes:
- Time to clinical improvement: similar between arms (10 days in 5-day arm vs. 11 days in 10-day arm)
- Time to recovery: Median hospitalization duration for patients discharged on or before Day 14: similar between arms (7 days in 5-day arm vs. 8 days in 10-day arm)

### Limitations and Interpretation

#### Key Limitations:
- Open-label trial
- Baseline imbalances in clinical status of patients in 5-day and 10-day arms

#### Interpretation:
- In hospitalized patients with severe COVID-19 who were not receiving MV or ECMO, using RDV for 5 or 10 days had similar clinical benefits.
<table>
<thead>
<tr>
<th>Methods</th>
<th>Results</th>
<th>Limitations and Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PINETREE</strong>: Double-Blind, Placebo-Controlled RCT of Remdesivir for 3 Days in Nonhospitalized Patients With COVID-19 at High Risk for Disease Progression</td>
<td><strong>Participant Characteristics:</strong>&lt;br&gt;- Mean age 50 years; 30.2% aged ≥60 years; 52.1% men&lt;br&gt;- 80.4% White, 7.5% Black, 41.8% Hispanic/Latinx&lt;br&gt;- 61.6% with DM; 55.2% with obesity; 47.4% with HTN&lt;br&gt;- Median duration of symptoms before first infusion: 5 days (IQR 3–6 days)&lt;br&gt;- Median time from RT-PCR confirmation: 2 days (IQR 1–4 days)</td>
<td><strong>Key Limitations:</strong>&lt;br&gt;- Study halted early due to administrative issues.&lt;br&gt;- Vaccinated individuals were excluded. <strong>Interpretation:</strong>&lt;br&gt;- Three consecutive days of IV RDV resulted in an 87% relative reduction in the risk of hospitalization or death when compared to placebo.</td>
</tr>
<tr>
<td><strong>Key Inclusion Criteria:</strong>&lt;br&gt;- Laboratory-confirmed SARS-CoV-2 infection ≤4 days from screening&lt;br&gt;- Aged ≥12 years&lt;br&gt;- ≥1 risk factor for disease progression&lt;br&gt;- Symptom onset ≤7 days from randomization&lt;br&gt;- ≥1 ongoing COVID-19 symptom</td>
<td><strong>Primary Outcomes:</strong>&lt;br&gt;- COVID-19-related hospitalization or death from any cause by Day 28: 2 (0.7%) in RDV arm vs. 15 (5.3%) in placebo arm (HR 0.13; 95% CI, 0.03–0.59; P = 0.008)&lt;br&gt;- AEs: 42.3% in RDV arm vs. 46.3% in placebo arm</td>
<td>&lt;br&gt;<strong>Secondary Outcome:</strong>&lt;br&gt;- COVID-19-related medically attended visit or death from any cause by Day 28: 4 (1.6%) in RDV arm vs. 2 (8.3%) in placebo arm (HR 0.19; 95% CI, 0.07–0.56)</td>
</tr>
<tr>
<td><strong>Key Exclusion Criteria:</strong>&lt;br&gt;- COVID-19 vaccination&lt;br&gt;- Supplemental oxygen&lt;br&gt;- Previous hospitalization or treatment for COVID-19</td>
<td><strong>Key Secondary Endpoints:</strong>&lt;br&gt;- COVID-19-related, medically attended visit or death from any cause by Day 28</td>
<td>&lt;br&gt;- Any AE</td>
</tr>
<tr>
<td><strong>Interventions:</strong>&lt;br&gt;- RDV 200 mg IV on Day 1, then RDV 100 mg daily on Days 2 and 3 (n = 279)&lt;br&gt;- Placebo (n = 283)</td>
<td><strong>Key Limitations:</strong>&lt;br&gt;- Study halted early due to administrative issues.&lt;br&gt;- Vaccinated individuals were excluded. <strong>Interpretation:</strong>&lt;br&gt;- Three consecutive days of IV RDV resulted in an 87% relative reduction in the risk of hospitalization or death when compared to placebo.</td>
<td></td>
</tr>
<tr>
<td><strong>Primary Endpoints:</strong>&lt;br&gt;- COVID-19-related hospitalizations or death from any cause by Day 28</td>
<td><strong>Secondary Outcome:</strong>&lt;br&gt;- COVID-19-related medically attended visit or death from any cause by Day 28: 4 (1.6%) in RDV arm vs. 2 (8.3%) in placebo arm (HR 0.19; 95% CI, 0.07–0.56)</td>
<td>&lt;br&gt;- Any AE</td>
</tr>
<tr>
<td><strong>Key Secondary Endpoints:</strong>&lt;br&gt;- COVID-19-related, medically attended visit or death from any cause by Day 28</td>
<td><strong>Secondary Outcome:</strong>&lt;br&gt;- COVID-19-related medically attended visit or death from any cause by Day 28: 4 (1.6%) in RDV arm vs. 2 (8.3%) in placebo arm (HR 0.19; 95% CI, 0.07–0.56)</td>
<td>&lt;br&gt;- Any AE</td>
</tr>
</tbody>
</table>

**Key:** AE: adverse event; ALT = alanine transaminase; AST = aspartate aminotransferase; AZM = azithromycin; CQ = chloroquine; CrCl = creatinine clearance; DM = diabetes mellitus; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; HCQ = hydroxychloroquine; HTN = hypertension; IV = intravenous; LPV/RTV = lopinavir/ritonavir; MV = mechanical ventilation; NIV = noninvasive ventilation; OS = ordinal scale; the Panel = the COVID-19 Treatment Guidelines Panel; RCT = randomized controlled trial; RDV = remdesivir; RT-PCR = reverse transcription polymerase chain reaction; SAE = serious adverse event; SOC = standard of care; SpO₂ = oxygen saturation; ULN = upper limit of normal; WHO = World Health Organization
References


