# Remdesivir Reduces Mortality in Immunocompromised Patients Hospitalised for COVID-19 During Omicron

Poster #664

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## Conclusions

- RDV continues demonstrating significant mortality reduction among immunocompromised patients hospitalized with a primary diagnosis of COVID-19 in the more recent Omicron period, irrespective of the supplemental oxygen requirements
- These consistent findings through the Omicron period provides additional evidence to prior research showing benefit for RDV across all pre-dominant variants from December 2020 to April 2022[13]
- In this study cohort of vulnerable patients with immunocompromised conditions, RDV remains an optimal therapy of choice

## Background

- Remdesivir (RDV) reduced time to recovery and improved clinical outcomes for COVID-19 patients in several randomized controlled trials;[1-2] with additional evidence on effectiveness through real-world studies[3-5]
- NIH, IDSA and WHO guidelines recommend RDV to be initiated within seven days of symptom onset in patients with high-risk for progression to severe disease, including immunocompromised patients[6-8]
- Immunocompromised patients remain at high risk of hospitalizations, complications, and mortality due to COVID-19[9-12]
- Prior research has documented the effectiveness of RDV in reducing mortality among immunocompromised patients hospitalized for COVID-19[13]
- Building upon prior research with more recent data, the objective of this study was to compare inpatient all-cause mortality in patients who were administered RDV in the first two days of hospitalization vs. those not administered RDV during the hospitalization during Omicron predominant era (Dec 2021 – Apr 2023)

**References**

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**Disclosures**: **EM, MB**: employee and shareholder (Gilead Sciences, Inc.); **AC**: employee of Certara (contracted by Gilead Sciences, Inc. to conduct the study); **RLG**: advisor (AbbVie, Gilead Sciences, Inc., Eli Lilly, Roche, Johnson & Johnson ), consultant (Eli Lilly, Gilead Sciences, Inc., Johnson & Johnson , Kinevant Sciences, Roche), de minimis investment (AbCellera), research contracts (Eli Lilly, Gilead Sciences, Inc., Johnson & Johnson, Pfizer), speaker's bureau (Pfizer); **CCM**: advisor (AstraZeneca, Gilead Sciences, Inc.), speaker's bureau (AstraZeneca, Boehringer Ingelheim), consultant (Gilead Sciences, Inc.); **ANA**: principal investigator or co-investigator (clinical trials sponsored by NIH/NIAID, NeuroRx Pharma, Pulmotect, Blade Therapeutics, Novartis, Takeda, Humanigen, Eli Lilly, PTC Therapeutics, OctaPharma, Fulcrum Therapeutics, Alexion), speaker and/or consultant (Pfizer, Salix, Alexion, AstraZeneca, Bayer, Ferring, Seres, Spero, Eli Lilly, Nova Nordisk, Gilead, Renibus, GSK, Dexcom, Reprieve, HeartRite, Aspetiscope)- these relationships are unrelated to the current work; **TW**: received grants (DFG, BMBF, EU, WHO), fees for lectures (AstraZeneca, Bayer, Biontech, Boehringer, Berlin Chemie GSK, MSD, Novartis, Pfizer, Roche, Sanofi Aventis), served on Advisory Boards (AstraZeneca, Bayer, Boehringer, GSK, Novartis, Pfizer, Roche, Sanofi Aventis); **PES:** study investigator (Gilead Sciences, ViiV), advisor or review panel member (Gilead Sciences, ViiV, Janssen, Merck)-all of these relationships are unrelated to COVID-19; **ACK**: investigator (National Institutes of Health Adaptive COVID-19 Treatment Trial).

## Methods

### Study Design

- Comparative Effectiveness Retrospective cohort study (**Table 1**)
- Data source: PINC AI Healthcare Database (formerly Premier Healthcare Database)
  - US hospital-based, service-level, all-payer (Commercial, Medicare, Medicaid, others) database
  - Covers ~25% of all US hospitalizations from 48 states
  - Includes information on billed services for each day of hospitalization

**Table 1. Study design**

| | |
|---|---|
| **Inclusion criteria** | ✓ First admission to the hospital Dec 1, 2021-Apr 30, 2023<br>✓ Age ≥18 years old<br>✓ ***Primary* discharge diagnosis of COVID-19** (ICD-10-CM: U07.1) flagged for being "present-on-admission"<br>✓ **Diagnosed with an immunocompromised condition:** cancer, transplant, hematologic malignancies, immunosuppressive medications, toxic effects of antineoplastics, primary immunodeficiencies, severe combined immunodeficiencies, asplenia, bone marrow failure/aplastic anaemia, or HIV |
| **Exclusion criteria** | ✕ Pregnant<br>✕ Had incomplete/erroneous data fields<br>✕ Transferred from another hospital or hospice<br>✕ Transferred to another hospital<br>✕ Admitted for elective procedures<br>✕ Discharged or died during the baseline period (first two days of hospitalization) |
| | **RDV** / **Non-RDV** |
| **Treatment** | RDV treatment within 2 days of admission / Patients not receiving RDV during the hospitalization |

- All baseline variables (supplemental oxygenation, concomitant medications) were examined within the first two days of hospitalization
- **Primary End Points:** 14-day and 28-day all-cause inpatient mortality (defined as a discharge status of "expired" or "hospice")

### Statistical analysis

- Analyses were stratified by no supplemental oxygen charges (NSOc) and any supplemental oxygen requirements upon admission
- Propensity scores (PS) were estimated using separate logistic regression models for NSOc / any supplemental oxygenation at baseline
- Covariates used in PS calculation: baseline demographics (age, gender, race, ethnicity, primary payor), comorbidities (obesity, COPD, diabetes mellitus, renal disease, cardiovascular disease, cancer, immunocompromised condition), hospital characteristics (bed size, urban/rural, teaching, region of the hospital), admission month, admission from skilled nursing facility (SNF), intensive care unit (ICU)/General ward at baseline, other indicators of severity based on admit diagnoses (respiratory failure, hypoxemia, sepsis, pneumonia), concomitant medications at baseline (corticosteroids, convalescent plasma, anticoagulants, tocilizumab, baricitinib)
- Cox Proportional Hazards Model (adjusting for hospital-level random effects and key clinical covariates) was used to examine time to 14- and 28-day mortality overall
- Patients who did not have the outcome of interest or were discharged alive were censored at 14 and 28 days in the analyses

## Results

### Study population

- After applying inclusion/exclusion criteria, 26,770 patients were included in the analysis:
  - 15,257 patients were treated with RDV in the first two days of hospitalization and
  - 11,513 patients were not treated with RDV
- After 1:1 matching with replacement:
  - 10,687 RDV-treated patients were matched to 4,989 unique non-RDV patients (equivalent to 10,687 non-RDV patients based on matching with replacement)
- Post-matching balance was achieved across groups with different baseline supplemental oxygen and VOC periods with all covariates with a standardized difference absolute value of <0.15
- In the matched cohort: 74% were 65 years or older, 49% with NSOc, and 51% with any supplemental oxygen charges at baseline (**Table 2**)

### Unadjusted analysis (PS-matched cohort)

- During Dec 2021 – Apr2023, a lower mortality rate was consistently observed overall and by supplemental oxygen requirements in the overall study period:

| | 28-day mortality | | 14-day mortality | |
|---|---|---|---|---|
| | **RDV** | **Non-RDV** | **RDV** | **Non-RDV** |
| **Omicron period** | 10.3% | 13.7% | 15.0% | 19.2% |
| **NSOc** | 7.0% | 9.9% | 10.7% | 17.3% |
| **Any Supp. O2** | 13.5% | 17.3% | 19.7% | 24.5% |

Note: RDV, remdesivir, NSOc, no supplementary oxygen charges

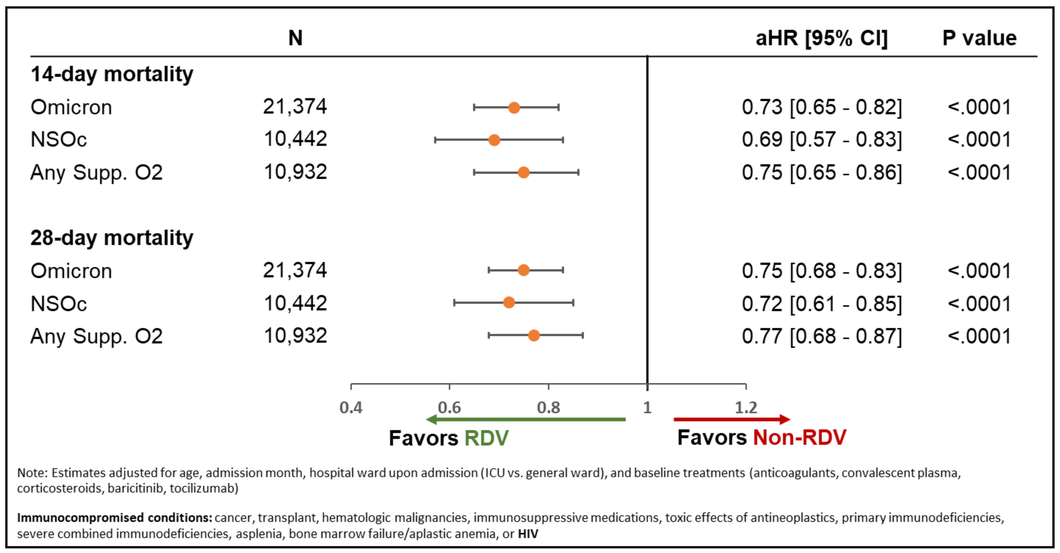
- After adjusting for baseline and clinical covariates, RDV was associated with a significantly lower mortality risk compared to non-RDV overall (adjusted hazard ratio [95% CI]: 0.75 [0.68-0.83]) in patients with NSOc (0.72 [0.61-0.85]) and in patients with any supplemental oxygen requirement (0.77[0.68-0.87]) at 28 days
- A similar benefit for RDV vs. non-RDV was observed for 14-day mortality overall (0.73 [0.65-0.82]) in patients with NSOc (0.69 [0.57-0.83]) and in patients with any supplemental oxygen requirement (0.75 [0.65-0.86]) (**Figure 1**)

**Table 2. Baseline characteristics before and after matching**

| | | Unmatched cohort | | Matched cohort | |
|---|---|---|---|---|---|
| | | No RDV | RDV | No RDV | RDV |
| | | n= 11,513 | n= 15,257 | n= 10,687 | n= 10,687 |
| **Age group** | 18-49 | 7.4% | 7.8% | 5.4% | 5.4% |
| | 50-64 | 21.3% | 22.7% | 20.8% | 20.8% |
| | 65+ | 71.2% | 69.5% | 73.9% | 73.9% |
| **Gender** | Female | 49.9% | 51.1% | 52.0% | 50.9% |
| **Race** | White | 74.8% | 75.8% | 78.0% | 76.6% |
| | Black | 17.0% | 14.4% | 13.7% | 14.6% |
| | Asian | 1.5% | 2.2% | 1.7% | 1.9% |
| | Other | 6.7% | 7.6% | 6.6% | 6.9% |
| **Ethnicity** | Hispanic | 8.5% | 11.4% | 9.7% | 9.7% |
| | Non-Hispanic | 83.7% | 82.7% | 83.9% | 84.0% |
| | Unknown | 7.8% | 5.9% | 6.4% | 6.4% |
| **Primary payor** | Commercial | 13.1% | 15.3% | 13.8% | 76.1% |
| | Medicare | 75.3% | 73.0% | 75.7% | 7.0% |
| | Medicaid | 7.8% | 8.4% | 7.2% | 3.2% |
| | Other | 3.8% | 3.4% | 3.4% | 76.1% |
| **Bed size** | <100 | 6.6% | 6.4% | 6.1% | 6.0% |
| | 100-199 | 14.8% | 15.5% | 14.8% | 14.9% |
| | 200-299 | 20.4% | 18.6% | 18.6% | 19.4% |
| | 300-399 | 19.7% | 16.2% | 18.4% | 17.6% |
| | 400-499 | 11.6% | 10.4% | 10.5% | 10.4% |
| | 500+ | 26.8% | 32.9% | 31.7% | 31.7% |
| **Comorbidities** | Obesity | 24.1% | 26.0% | 26.7% | 26.4% |
| | COPD | 36.2% | 41.2% | 41.3% | 41.0% |
| | Cardiovascular disease | 89.6% | 87.8% | 88.4% | 89.6% |
| | Diabetes mellitus | 39.1% | 37.4% | 38.0% | 38.1% |
| | Renal disease | 40.7% | 30.8% | 32.4% | 32.8% |
| | Cancer | 42.0% | 42.2% | 42.0% | 43.2% |
| **Hospital ward upon admission** | General Ward | 83.4% | 81.1% | 82.7% | 82.1% |
| | ICU | 16.6% | 18.9% | 17.3% | 17.9% |
| **Other treatments at baseline** | Anticoagulants | 66.7% | 74.7% | 74.3% | 75.0% |
| | Corticosteroids | 0.1% | 0.2% | 0.1% | 0.1% |
| | Convalescent plasma | 69.2% | 86.8% | 88.1% | 88.1% |
| | Tocilizumab | 4.2% | 4.3% | 6.2% | 5.1% |
| | Baricitinib | 2.4% | 3.8% | 3.8% | 3.9% |
| **Baseline oxygenation** | NSOc | 56.8% | 49.1% | 48.9% | 48.9% |
| | LFO | 26.4% | 30.6% | 31.0% | 31.0% |
| | HFO/NIV | 13.7% | 18.0% | 18.5% | 18.5% |
| | IMV/ECMO | 3.2% | 2.2% | 1.6% | 1.6% |

Note: Baseline was assessed as the worst status in the first two days of the hospitalization
ICU: Intermediate Care Unit; COPD: Chronic Obstructive Pulmonary Disorder; NSOc: No supplementary oxygen charges; LFO: Low-Flow Oxygen; HFO/NIV: High-Flow Oxygen/Non-invasive ventilation; IMV/ECMO: Invasive Mechanical Ventilation/ Extracorporeal Membrane Oxygenation; RDV, remdesivir1

**Figure 1. 14- and 28- day mortality for RDV vs. Non-RDV immunocompromised patients with COVID-19 during Omicron period (adjusted Cox Proportional Hazards model)**




Note: Estimates adjusted for age, admission month, hospital ward upon admission (ICU vs. general ward), and baseline treatments (anticoagulants, convalescent plasma, corticosteroids, baricitinib, tocilizumab)

**Immunocompromised conditions:** cancer, transplant, hematologic malignancies, immunosuppressive medications, toxic effects of antineoplastics, primary immunodeficiencies, severe combined immunodeficiencies, asplenia, bone marrow failure/aplastic anemia, or **HIV**

aHR=adjusted hazard ratio; Any Supp. O2= low-flow oxygen, high-flow oxygen/non-invasive ventilation and invasive mechanical ventilation/extracorporeal membrane oxygenation; CI=confidence interval; NSOc=no supplemental oxygen charges; RDV=remdesivir