Remdesivir reduces mortality in immunocompromised patients hospitalised for COVID-19 across the pandemic and endemic eras

Poster #P0354

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Conclusions

- RDV continues to demonstrate significant mortality reduction among immunocompromised patients hospitalized with a primary diagnosis of COVID-19 across variant of concern periods across patients with all supplemental oxygen requirements
- The findings from this study provide additional evidence that the effectiveness of RDV continues through April 2023 in immunocompromised individuals and also validates prior research showing benefit for RDV, across all predominant variants from Dec 2020 to Apr 2022[11]
- This study provides additional evidence in support of the NIH guideline-recommended treatment of immunocompromised COVID-19 patients with remdesivir [6]
- In this study of vulnerable patients with immunocompromised conditions, RDV remains an optimal therapeutic choice

Background

- Remdesivir (RDV) is associated with a reduction in time to recovery and improvement in clinical outcomes for patients with COVID-19 in several randomized controlled trials;[1,2] and real-world studies[3-5]
- NIH guidelines recommend administration of RDV in immunocompromised patients with COVID-19, who are at high risk of severe disease or hospitalization[6]
- Immunocompromised patients remain at high risk of hospitalizations, complications, and mortality due to COVID-19[7-10]
- Further, prior research has demonstrated that RDV is associated with lower risk of mortality in immunocompromised patients hospitalized for COVID-19 until the early Omicron period till April 2022 [11]
  - In this study, we build upon this prior research by extending the Omicron era to cover 1 more year of data through April 2023
- The objective of this study was to compare inpatient all-cause mortality in immunocompromised patients hospitalized for COVID-19 between December 2020 to April 2023 who were administered RDV in the first two days of hospitalization vs. those not administered RDV during the hospitalization

Methods

Study Design

- Comparative Effectiveness Retrospective cohort study (**Table 1**)
- Data source: PINC AI Healthcare Database (formerly Premier Healthcare Database)
  - U.S. 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 and activities for each day of the hospitalization
- Baseline was defined as the first two days of hospitalization
- **Primary Endpoints:** 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 logistic regression models.
- 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)
- PS-Matching was conducted as specified in **Figure 1**
- 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

Table 1. Study design

Inclusion criteria	✓ First admission to the hospital Dec 1, 2020-Apr 30, 2023 ✓ Age ≥18 years old ✓ ***Primary* discharge diagnosis of COVID-19** (ICD-10-CM: U07.1) flagged for being "present-on-admission" ✓ **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 ✕ Had incomplete/erroneous data fields ✕ Transferred from another hospital or hospice ✕ Transferred to another hospital ✕ Admitted for elective procedures ✕ 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

Figure 1. PS Matching approach

Matching conducted separately for different baseline supplemental oxygen requirements using:

1:1 Preferential Same-Hospital Matching with replacement

1. PS-matching (caliper = 0.2x s.d. of the logit of the PS) for patients with same age group, same supplemental oxygenation, same two/three-month blocks of admission month within the same hospital
   ↓ If unmatched in step 1
2. PS-matching (caliper = 0.2x s.d. of the logit of the PS) for patients with same age group, same supplemental oxygenation, same two/three-month blocks of admission month within another RDV-using hospital of same bed size

Matched patients were not discharged within 3 days of RDV initiation to emulate ACTT-1 exclusion (which excludes anticipated discharges/transfers within 72 hrs)

Matching with replacement: allowed for majority of the patients treated with RDV to be matched and included in the analysis despite a restricted matching criteria and higher % of RDV use in the study cohort; hence conclusions made are applicable to majority of the RDV patients.

Results

Study Population

- After applying inclusion/exclusion criteria, 53,829 immunocompromised patients were included in the analysis:
  - 33,089 patients were treated with RDV in the first two days of hospitalization
  - 20,740 patients were not treated with RDV during the hospitalization
- After 1:1 matching with replacement:
  - 24,081 RDV-treated patients were matched to 9,607 unique non-RDV patients (equivalent to 24,081 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, except for admission month with a standardized difference absolute value of 0.26 (this covariate was adjusted for in the Cox proportional hazards model)
- In the matched cohort: 66% were age 65 years or older, 44% with NSOc, and 56% with any supplemental oxygen charges at baseline (**Table 2**)

Unadjusted Analysis (PS-matched cohort)

- Between December 2020 – April 2023, a *lower mortality rate* was observed among immunocompromised RDV treated patients vs. non-RDV treated patients overall and by supplemental oxygen requirements:

	14-day mortality		28-day mortality	
	RDV	**Non-RDV**	**RDV**	**Non-RDV**
Overall	11.1%	14.9%	16.9%	21.3%
NSOc	7.6%	11.0%	11.3%	15.4%
Any Supp. O2	13.9%	18.0%	21.4%	26.0%

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

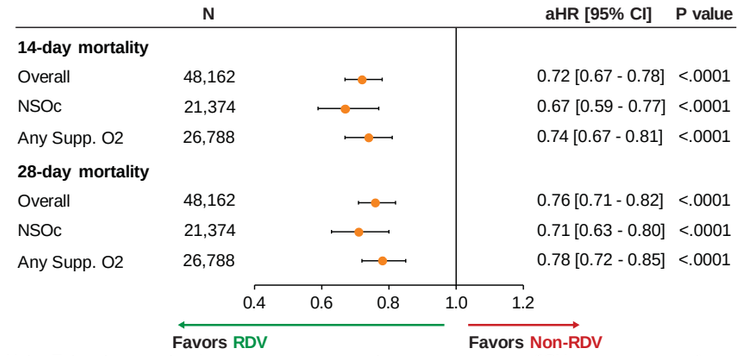
- At 28 days, after adjusting for baseline and clinical covariates, RDV was associated with significantly lower mortality risk compared to non-RDV overall (adjusted hazard ratio [95% CI]: 0.76 [0.71-0.82]), in immunocompromised patients with NSOc (0.71 [0.63-0.80]) and in patients with any supplemental oxygen requirement (0.78 [0.72-0.85]) (**Figure 2**)
- At 14-days, a similar benefit for RDV vs. non-RDV was observed. RDV was associated with a significantly lower mortality risk compared to non-RDV overall (0.72 [0.67-0.78]), in immunocompromised patients with NSOc (0.67 [0.59-0.77]) and in patients with any supplemental oxygen requirement (0.74 [0.67-0.81]) (**Figure 2**)

Table 2: Baseline characteristics before and after matching

		Before matching		After matching	
		Non-RDV	**RDV**	**Non-RDV**	**RDV**
		n=20,740	**n=33,089**	**n=24,081**	**n=24,081**
Age group, years	18-49	10.0%	11.7%	9.2%	9.2%
	50-64	23.8%	26.5%	25.0%	25.0%
	65+	66.2%	61.8%	65.7%	65.7%
Gender	Female	49.9%	50.6%	51.2%	50.6%
Race	White	72.9%	75.4%	76.4%	76.2%
	Black	18.3%	14.3%	14.0%	14.5%
	Asian	1.4%	1.4%	1.7%	1.8%
	Other	7.3%	7.3%	7.9%	7.6%
Ethnicity	Hispanic	9.0%	12.9%	10.7%	11.4%
	Non-Hispanic	82.0%	79.2%	81.7%	80.5%
	Unknown	8.9%	7.8%	7.6%	8.1%
Primary payor	Commercial	15.8%	20.9%	19.2%	19.2%
	Medicare	71.3%	65.6%	68.4%	68.7%
	Medicaid	8.3%	8.7%	7.8%	7.7%
	Other	4.6%	4.7%	4.5%	4.5%
Admission source	Transfer from SNF or ICF	2.2%	1.9%	2.1%	2.1%
Hospital size, no. of beds	<100	6.3%	6.8%	6.4%	6.3%
	100-199	14.5%	16.6%	15.4%	15.4%
	200-299	20.1%	17.9%	18.6%	18.6%
	300-399	19.3%	17.2%	18.1%	18.5%
	400-499	11.6%	9.9%	10.5%	10.2%
	500+	28.3%	31.5%	30.9%	30.9%
Comorbidities	Obesity	26.3%	31.1%	31.2%	31.1%
	COPD	33.4%	36.8%	37.1%	36.9%
	Cardiovascular disease	87.8%	84.1%	85.6%	85.8%
	Diabetes mellitus	39.7%	38.2%	39.4%	39.0%
	Renal disease	39.9%	26.8%	29.8%	28.3%
	Cancer	39.1%	37.4%	37.6%	38.1%
Hospital ward upon admission	General ward	82.6%	81.3%	81.8%	82.2%
	ICU	17.4%	18.7%	18.2%	17.8%
Other treatments at baseline	Anticoagulants	69.6%	79.2%	79.3%	79.5%
	Corticosteroids	72.1%	91.0%	91.8%	91.6%
	Convalescent plasma	1.7%	6.0%	3.9%	3.6%
	Tocilizumab	2.8%	4.9%	4.8%	4.7%
	Baricitinib	3.7%	4.6%	4.9%	5.3%
Baseline supplemental oxygen requirements	NSOc	54.3%	43.9%	44.4%	44.4%
	LFO	28.4%	34.8%	35.2%	35.2%
	HFO/NIV	14.0%	19.1%	18.8%	18.8%
	IMV/ECMO	3.4%	2.3%	1.6%	1.6%

Note: Baseline was defined as the first two days of the hospitalization
ICU: Intensive 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, remdesivir; SNF, skilled nursing facility; ICF, intermediate care facility

Figure 2. 14- and 28-day mortality in immunocompromised patients hospitalized for COVID-19 from December 2020 to April 2023 (Cox Proportional Hazards Model)



Note: Estimates adjusted for age, admission month, admission venue (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; CI, Confidence interval; NSOc, no supplemental oxygen charges; RDV, remdesivir

Any Supp. O2 includes low-flow oxygen, high-flow oxygen/non-invasive ventilation and invasive mechanical ventilation/extracorporeal membrane oxygenation;

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