Poster #LB074

Remdesivir is associated with lower mortality in cancer patients hospitalized for COVID-19 across emerging variants

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Introduction

- 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]
- Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths[6]
- However, there is limited information on effectiveness of COVID-19 therapies in cancer patients, who are at higher risk of hospitalizations, complications, and mortality due to COVID-19 due to their immunocompromised status[7-10]

Objective

- The objective of this study, focused on routine clinical practice, was to examine hospital all-cause mortality for RDV use vs. no RDV use among cancer patients with COVID-19 across dominant variants of concern (VOC) periods: Pre-Delta (Dec'20-Apr'21), Delta (May-Nov'21) and Omicron (Dec'21-Apr'22)

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
  - 21,136 hospitalizations with a primary diagnosis of COVID-19 and a cancer diagnosis from 796 hospitals during the study period

Table 1. Study design

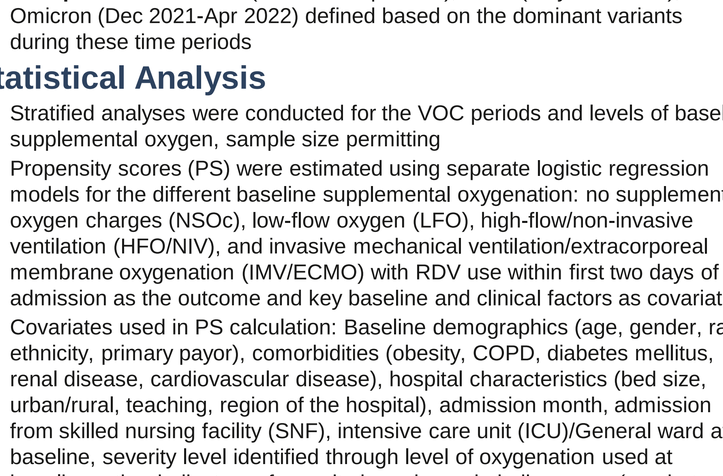
Inclusion criteria	✓ First admission to the hospital Dec 1, 2020-Apr 30, 2022 ✓ Age ≥18 years old ✓ **Primary discharge diagnosis of COVID-19** (ICD-10-CM: U07.1) flagged for being "present-on-admission" ✓ **Cancer diagnosis: ICD-10-CM codes C00.x- C96.x**	
Exclusion criteria	✕ Pregnant ✕ Had incomplete/erroneous 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

- All baseline variables (supplemental oxygenation, concomitant medications) were examined within the first two days of hospitalization
- **Primary Endpoints**: 14-day and 28-day all-cause hospital mortality (defined as a discharge status of "expired" or "hospice")
- **VOC periods**: Pre-Delta (Dec 2020-Apr 2021), Delta (May-Nov 2021), Omicron (Dec 2021-Apr 2022) defined based on the dominant variants during these time periods

Statistical Analysis

- Stratified analyses were conducted for the VOC periods and levels of baseline supplemental oxygen, sample size permitting
- Propensity scores (PS) were estimated using separate logistic regression models for the different baseline supplemental oxygenation: no supplemental oxygen charges (NSOc), low-flow oxygen (LFO), high-flow/non-invasive ventilation (HFO/NIV), and invasive mechanical ventilation/extracorporeal membrane oxygenation (IMV/ECMO) with RDV use within first two days of admission as the outcome and key baseline and clinical factors as covariates
- Covariates used in PS calculation: Baseline demographics (age, gender, race, ethnicity, primary payor), comorbidities (obesity, COPD, diabetes mellitus, renal disease, cardiovascular disease), 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, severity level identified through level of oxygenation used 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
- Patients who did not have the outcome of interest or were discharged alive were censored at 14 and 28 days in the analyses

Figure 1. PS matching approach



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

- Source: 21,136 adults with cancer hospitalized in 796 hospitals with a primary discharge diagnosis of COVID-19 during Dec 2020-Apr 2022
- After applying inclusion/exclusion criteria, 13,323 patients from 702 hospitals included in the analysis:
  - 7,482 patients were treated with RDV in the first two days of hospitalization and
  - 4,802 patients were not treated with RDV
  - 1,039 patients were treated with RDV after the first two days of hospitalization and were not included in further analysis

- After 1:1 matching with replacement (**Figure 1**):
  - 4,937 RDV patients were matched to 2,088 unique non-RDV patients (equivalent to 4,937 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: 80% were 65 years or older, 43% with no supplementary oxygen charges, 39.5% received LFO, 15.8% received HFO/NIV and 1.7% IMV/ECMO at baseline (**Table 2**)

Table 2: Baseline characteristics before and after matching

		Unmatched cohort		Matched cohort	
		RDV	Non-RDV	RDV	Non-RDV
		n=7,482	n=4,802	n=4,937	n=4,937
Age group	18-49	5%	5%	2%	2%
	50-64	24%	21%	18%	18%
	65+	71%	74%	80%	80%
Gender	Female	47%	46%	46%	47%
Race	White	79%	75%	80%	80%
	Black	12%	18%	12%	12%
	Asian	2%	1%	1%	2%
	Other	7%	6%	7%	6%
Ethnicity	Hispanic	11%	8%	9%	8%
	Non-Hispanic	80%	82%	82%	82%
	Unknown	9%	10%	9%	10%
Primary payor	Commercial	18%	14%	15%	14%
	Medicare	71%	75%	77%	77%
	Medicaid	7%	7%	5%	6%
	Other	4%	4%	3%	3%
VOC period	Pre-delta	35%	33%	34%	34%
	Delta	33%	27%	30%	30%
	Omicron	32%	40%	36%	36%
Bed size	<100	6%	5%	5%	5%
	100-599	63%	65%	64%	64%
	500+	31%	30%	31%	31%
Comorbidities	Obesity	25%	23%	24%	23%
	COPD	33%	31%	34%	35%
	Cardiovascular disease	86%	88%	88%	89%
	Diabetes mellitus	36%	37%	37%	37%
	Renal disease	22%	34%	24%	25%
Hospital ward upon admission	General Ward	81%	82%	82%	82%
	ICU	19%	18%	18%	18%
Other treatments at baseline	Anticoagulants	26%	34%	28%	28%
	Corticosteroids	93%	70%	93%	94%
	Convalescent plasma	8%	2%	4%	5%
	Tocilizumab	4%	3%	4%	4%
	Baricitinib	5%	4%	5%	5%
Baseline oxygenation	NSOc	40%	53%	43%	43%
	LFO	39%	31%	39%	39%
	HFO/NIV	18%	13%	16%	16%
	IMV/ECMO	3%	3%	2%	2%

Note: Baseline was assessed as the worst status in the first two days of the hospitalization
SNF: Skilled Nursing Facility; ICF: Intermediate Care Facility; COPD: Chronic Obstructive Pulmonary Disorder; ICU: Intensive Care Unit; 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

Unadjusted analysis (PS-matched cohort)

- During Dec 2020-Apr 2022, unadjusted mortality rate was significantly lower for RDV patients at 14 days (16% vs 25%; p<0.0001) and 28 days (23% vs 31.5%; p<0.0001) compared to patients that did not receive RDV (log-rank test for 28-day mortality: p<0.0001) (**Figure 2**)
- Lower mortality rate observed across all VOC periods (log-rank test for 28-day mortality: p<0.0001) (**Figure 2**):

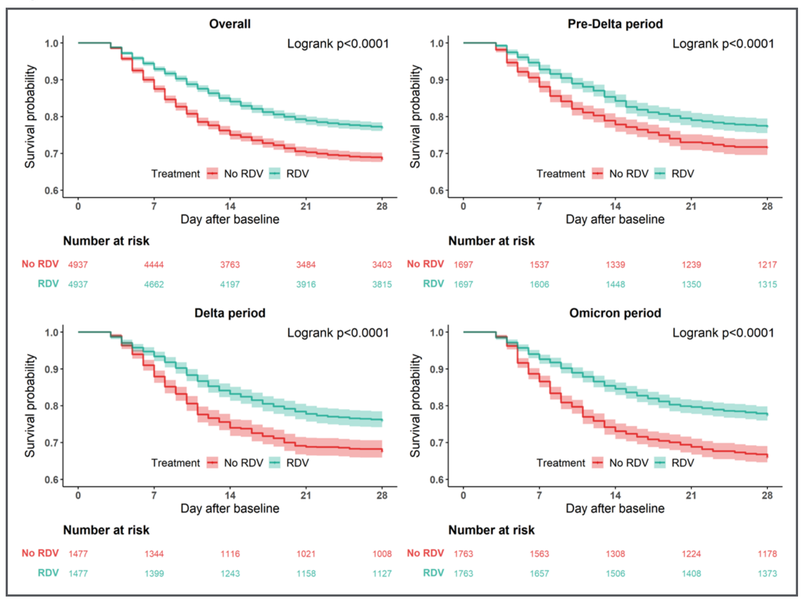
	14-day mortality		28-day mortality	
	RDV	Non-RDV	RDV	Non-RDV
Overall	15.9%	25.0%	23.0%	31.5%
Pre-Delta	15.7%	22.2%	22.6%	28.3%
Delta	16.8%	26.0%	24.0%	32.4%
Omicron	15.4%	26.9%	22.5%	33.9%

- Lower mortality rates were also observed for patients with NSOc and across all baseline supplemental oxygen requirements:

	14-day mortality		28-day mortality	
	RDV	Non-RDV	RDV	Non-RDV
NSOc	11.3%	17.7%	16.2%	22.8%
LFO	14.1%	25.9%	21.2%	31.2%
HFO/NIV	30.1%	40.0%	41.9%	51.2%
IMV/ECMO	45.8%	50.6%	59.0%	78.3%

NSOc: No supplemental oxygen charges; LFO: Low-Flow Oxygen; HFO/NIV: High-Flow Oxygen/Non-invasive ventilation; IMV/ECMO: Invasive Mechanical Ventilation/Extracorporeal Membrane Oxygenation

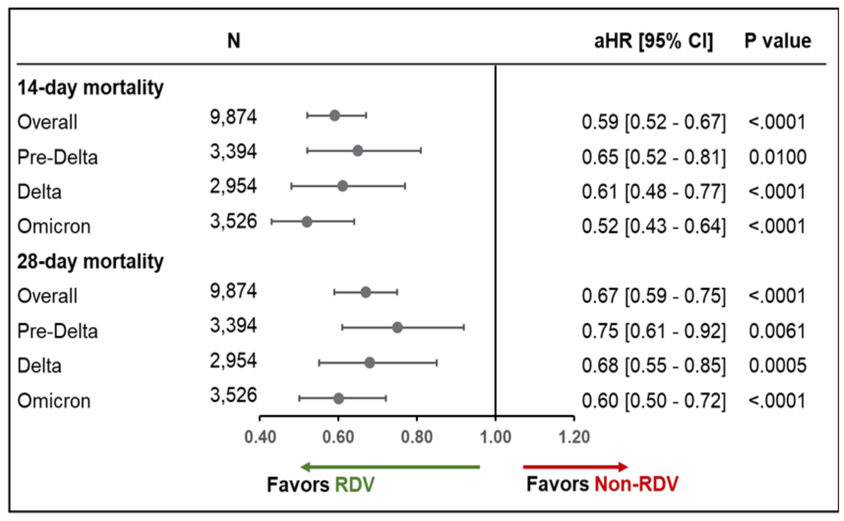
Figure 2. Kaplan-Meier curves



Adjusted analysis (PS-matched cohort)

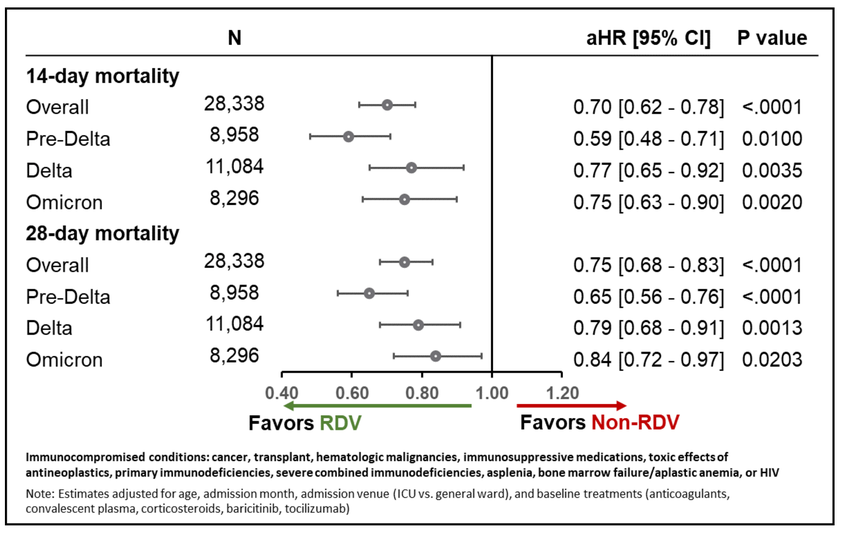
- After adjusting for baseline and clinical covariates, 14-day results showed that RDV had statistically significantly lower mortality risk compared to non-RDV across all VOC periods: overall (41% lower risk), Pre-Delta (35%), Delta (39%), Omicron (48%) (**Figure 3**)
- Similarly, 28-day results showed that RDV had statistically significantly lower mortality risk compared to non-RDV across all VOC periods: overall (33% lower risk), Pre-Delta (25%), Delta (32%), Omicron (40%) (**Figure 3**)
- RDV had statistically significant lower mortality risk compared to non-RDV in subgroups of patients on NSOc and those on LFO or HFO/NIV, as sufficient sample size was available
  - Sample sizes in the IMV/ECMO (n=166) subgroup was not sufficient to warrant statistical analysis
- In previously presented analysis on a broader cohort of immunocompromised patients hospitalized with COVID-19, lower mortality risk associated with RDV vs. non-RDV was also consistently observed across all VOC periods (**Figure 4**)[11]

Figure 3. 14- and 28- day mortality in cancer patients across the COVID-19 variant periods (adjusted 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)
aHR: Adjusted Hazard Ratio; 95% CI: 95% Confidence Interval; RDV: remdesivir; ICU: intensive care unit

Figure 4. 14- and 28- day mortality in immunocompromised patients across the COVID-19 variant periods (adjusted Cox Proportional Hazards model), previously presented[11]



Note: Estimates adjusted for age, admission month, admission venue (ICU vs. general ward), and baseline treatments (anticoagulants, convalescent plasma, corticosteroids, baricitinib, tocilizumab)
aHR: Adjusted Hazard Ratio; 95% CI: 95% Confidence Interval; RDV: remdesivir; ICU: intensive care unit

Conclusions

- Given the high mortality rates across all baseline supplemental oxygen requirements, there is a need for effective therapies in this vulnerable group of patients with cancer hospitalized for COVID-19
- In this study of cancer patients hospitalized for COVID-19 in routine clinical practice in the US, RDV initiation within the first two days of hospital admission was associated with statistically significant reductions in mortality at 14- and 28- days
- This significant reduction in mortality was consistently observed across all VOC periods through the period of time examined (prior to emergence of BA4/5 that was not yet assessed)
- Initiation of antiviral therapy upon admission could save significant number of lives of cancer patients admitted for COVID-19

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Disclosures:
EM, CDT, LD, RG, MB: employee and shareholder (Gilead Sciences, Inc.); **ACK**: investigator for the National Institutes of Health Adaptive COVID-19 Treatment Trial; **CCM**: advisor (AstraZeneca, Gilead Sciences, Inc.), speaker's bureau (AstraZeneca, Boehringer Ingelheim), consultant (Gilead Sciences, Inc.); **AC, SHR**: 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)

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