RISK OF DEATH IN REMDESIVIR TREATED AND UNTREATED PATIENTS WITH COVID-19 INFECTION

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Background

- Remdesivir inhibits SARS-CoV-2 in vitro, and early treatment with remdesivir in nonhuman primates with MERS-CoV is associated with reduced lung virus levels and reduced lung damage.
- In a randomized, open-label phase 3 study, 397 patients with pneumonia on chest X-ray and oxygen saturation of <94% at room air, a 2-point improvement in oxygen-support status was achieved in 64% of those receiving 5 days and 54% of those receiving 10 day of remdesivir. (Goldman et al. NEJM 2020)
- In a double-blind, randomized, placebo-controlled trial of hospitalized patients with Covid-19 with lower respiratory tract infection (ACTT-1 study), 541 were assigned to 10 days of remdesivir and 521 to placebo. (Biegel et al. NEJM 2020)
- Remdesivir group had a median recovery time of 10 days (95% CI, 9,11), vs. 15 days (95% CI, 13,18) for placebo recipients (rate ratio for recovery, 1.29; 95% CI, 1.12,1.49; P<0.001, by a log-rank test).
- Remdesivir recipients were more likely to have clinical improvement at day 15 (OR, 1.5; 95% CI, 1.2 to 1.9, after adjustment for actual disease severity).
- Remdesivir is approved for use in adults and pediatric patients (> 28 days old; > 3kg) who are hospitalized, or have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19
- Real-world evidence of the impact of remdesivir upon clinical outcomes in high-risk populations is limited.

OBJECTIVES

- To determine the role of remdesivir in reducing short-term mortality in a national cohort of patients who were hospitalized with COVID-19.

METHODS

- We used the Department of Veterans Affairs' (VA) national COVID-19 Shared Data Resource database for the current study.
- Among Veterans with confirmed COVID-19 between Jul 1, 2020 and Dec 31, 2021, we identified those hospitalized within 28 days of their positive test.
- We excluded those who were hospitalized within the previous 28 days of the positive test; those who had received any remdesivir prior to the hospital admission; those who died or were discharged from the hospital within 3 days of admission and those who remained hospitalized for >60 days.
- For each remdesivir recipient identified, we identified a propensity-score matched person who had not received remdesivir.
- Matching was done on demographics, comorbidities, severity of illness at presentation, use of other COVID-19 therapeutics, month of admission, and geographical location.
- Our primary outcome of interest was 28-day mortality. Time at risk began after the third day of admission (to account for critically ill patients at admission).

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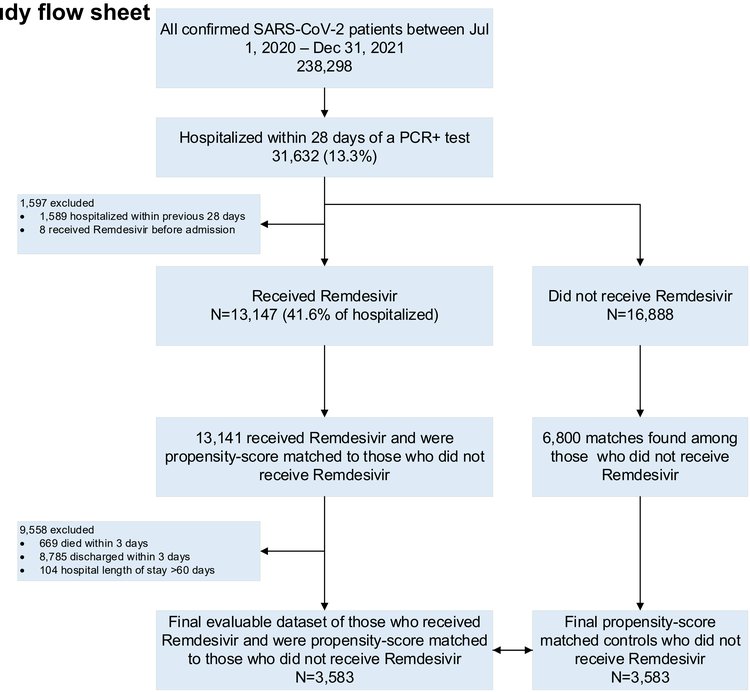
RESULTS

Study flow sheet

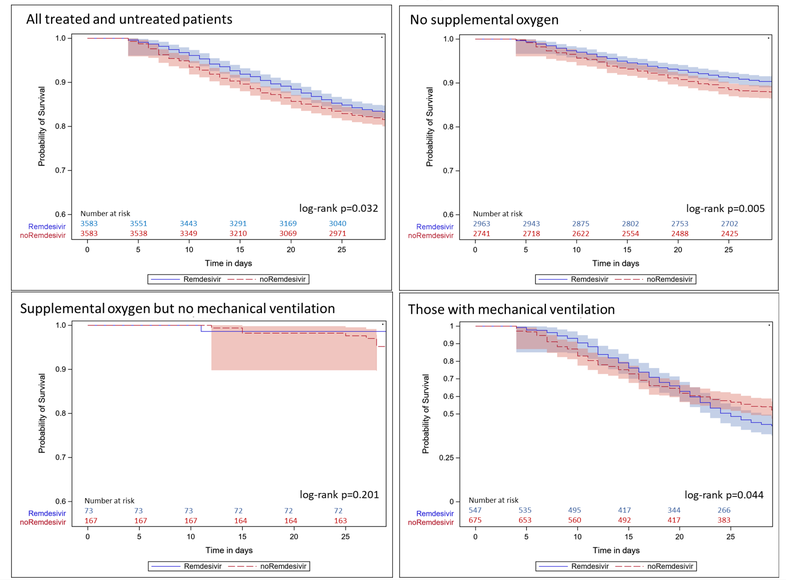


Baseline characteristics

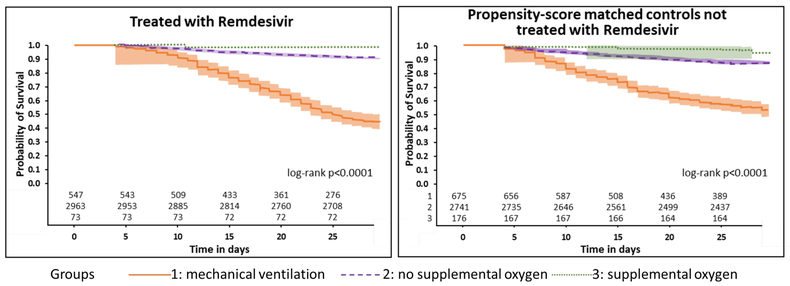
	Before matching			Propensity-score matched cohort		
	Remdesivir	No Remdesivir		Remdesivir	No Remdesivir	
	N=13,147	*N=16,888*	P-value	*N=3,583*	*N=3,583*	SMD
Median age (IQR) years	71 (62,77)	70 (59,76)	<.0001	71 (63,77)	72 (64,79)	-0.14
Male sex, %	94.68%	93.21%	<.0001	95.06%	95.45%	-0.02
Race, %			<.0001			0.00
White	68.17%	63.00%		67.57%	67.68%	
Black	21.89%	28.73%		22.77%	22.75%	
Other/unknown	9.94%	8.27%		9.66%	9.57%	
Mean Body mass index (SD), kg/m^2						
Comorbidities at or before baseline, %						
Hypertension	78.47%	77.07%	0.0038	79.57%	80.24%	-0.02
Diabetes	49.75%	46.91%	<.0001	50.40%	52.72%	-0.05
Cardiovascular disease	52.99%	55.48%	<.0001	53.84%	57.02%	-0.06
Hemorrhagic Stroke	0.43%	0.69%	0.004	0.70%	0.61%	0.01
Ischemic Stroke	8.25%	10.33%	<.0001	9.24%	12.62%	-0.11
Chronic kidney disease	24.29%	29.87%	<.0001	24.87%	30.45%	-0.13
Chronic lung disease (COPD)	30.43%	26.09%	<.0001	28.91%	33.80%	-0.11
Cancer diagnosis	28.37%	28.13%	0.6479	28.55%	27.74%	0.02
Concomitant medication use at baseline						
Systemic steroids, %	48.92%	43.88%	<.0001	48.34%	48.98%	-0.01
Tocilizumab use, %	0.09%	0.08%	0.6699	0.06%	0.14%	-0.03
Vaccination status at baseline			0.001			0.12
Unvaccinated or pr series incomplete	57.69%	58.72%		57.05%	61.65%	
Primary series completed	18.07%	18.84%		17.89%	18.28%	
Primary series PLUS booster	24.23%	22.44%		25.06%	20.07%	
Mechanical ventilation at baseline, %	15.62%	6.08%	<.0001	15.27%	18.84%	-0.10
Admission to ICU, %	50.17%	32.38%	<.0001	51.69%	56.99%	-0.11

RESULTS (contd.)

Probability of survival among Remdesivir treated and propensity-score matched untreated persons, overall and stratified by oxygen requirement at admission.



Probability of event-free survival by oxygen requirement status among remdesivir recipients and untreated controls.



CONCLUSIONS

- Our study confirms the earlier findings of a modest overall benefit in short-term mortality among hospitalized COVID-19 patients who received remdesivir.
- This benefit is driven primarily by those not receiving any supplemental oxygen.
- Number of those receiving supplemental oxygen were too small to make any meaningful conclusions.

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