NIRMATRELVIR USE AND HOSPITALIZATIONS OR DEATH IN INDIVIDUALS WITH COVID-19

Adeel A. Butt, MBBS, MS;[1,2,3] Peng Yan, MS;[1] Obaid S. Shaikh, MD;[1,4] Victor B. Talisa, PhD;[5] Saad B. Omer, MD, MPH, PhD;[6] Florian B. Mayr, MD, MS[1,5]

[1] VA Pittsburgh Healthcare System, Pittsburgh, PA, USA; [2] Departments of Medicine and Population Health Sciences, Weill Cornell Medicine, New York NY and Doha, Qatar; [3] Hamad Medical Corporation, Doha, Qatar' [4] Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh PA, USA; [5] CRISMA Center, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh PA, USA; [6] Institute for Global Health, Yale University, New Haven, CT, USA

Contact information:
Adeel Ajwad Butt, MBBS, MS, FACP, FIDSA
Mailstop 151, University Drive C
Pittsburgh, PA 15240
Email: aab2005@med.cornell.edu

BACKGROUND

- In December 2021, two novel oral antiviral agents, Nirmatrelvir/ritonavir (NMV/r) and Molnupiravir (MPV), were granted Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) for treatment of early symptomatic patients with mild to moderate COVID-19 at high risk of progression to severe disease.
- In EPIC-HR trial, NMV/r treatment initiated within 3 days of symptom onset was associated with 89% relative risk reduction for hospitalization or death by day 28.
- In another observational study, NMV/r during the Omicron variant predominant period was associated with a 73% reduction in hospitalization and a 79% reduction in death.
- The benefit observed in this study was limited to patients >65 years old.
- There are relatively scant real-world data regarding the use of NMV/r in high-risk populations.

OBJECTIVES

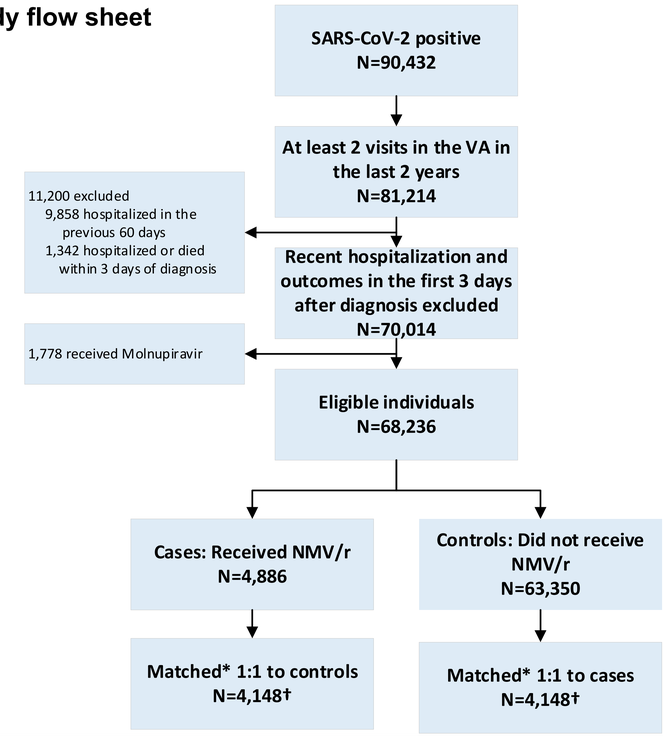
- To determine the rates of hospitalization or death within 30 days of the index COVID-19 diagnosis date among those treated with NMV/r and untreated controls.

METHODS

- We used a matched cohort design to emulate a target trial.
- Eligible individuals were those in the VA COVID-19 Shared Data Resource who had a first confirmed SARS-CoV-2 infection between January 1 and August 31, 2022, and were free of an outcome event (hospitalization or death) within 3 days of testing positive.
- Those who were hospitalized in the 60-days period prior to the index COVID-19 test date were ineligible.
- Among the eligible individuals, we matched those who were prescribed NMV/r with those who did not receive NMV/r within 3 days of COVID-19 diagnosis date.
- Controls were matched 1:1 on age (5-year blocks), race, sex, body mass index, Charlson Comorbidity Index, VA facility where NMV/r was prescribed, and vaccination status.
- Absolute risk difference (ARD) between the two groups along with 95% confidence intervals were estimated using logistic regression models fit using generalized estimating equations to account for correlated outcomes within each matched pair.
- The overall absolute difference between the groups, as well as for various sub-strata of the population by age, sex, body mass index, presence of various comorbidities, and vaccination status were tabulated and graphed.

RESULTS

Study flow sheet



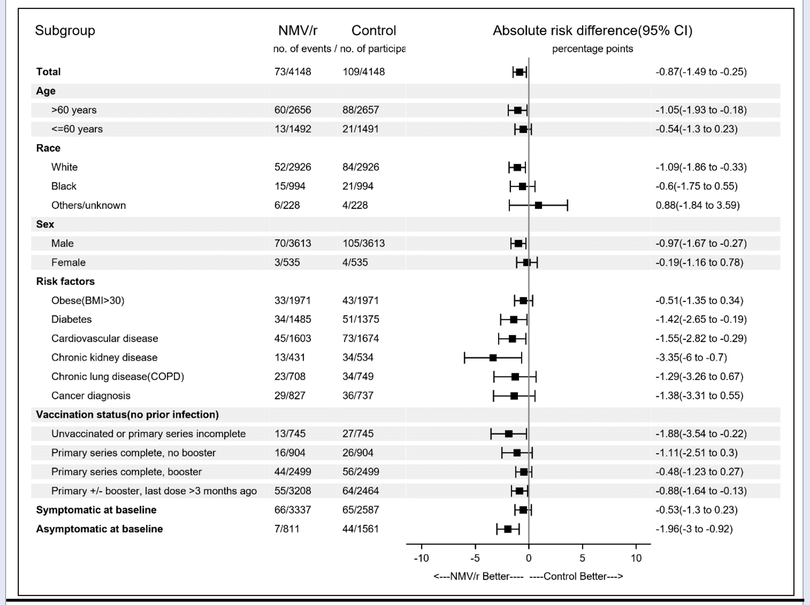
Baseline characteristics

	Before matching			Matched cohort		
	NMV/r group	Controls		NMV/r group	Controls	
	N=4886	N=63350	P-value	N=4148	N=4148	SMD*
Median age (IQR) years	65.1 (54.4,74)	57.1 (43.8,69)	<.0001	65 (54.6,73.6)	65 (54.7,73.7)	-0.004
Male sex, %	84.75%	73.02%	<.0001	87.10%	87.10%	0
Race, %			<.0001			0
White	65.96%	54.49%		70.54%	70.54%	
Black	24.76%	19.90%		23.96%	23.96%	
Other/unknown	9.27%	25.61%		5.50%	5.50%	
Mean Body mass index, kg/m^2, SD	30.9 (6.2)	30.7 (6.6)	0.03	31.1 (6.1)	31.1 (6.2)	0.0017
Median Charlson Comorbidity Index	1 (0,3)	1 (0,2)	<.0001	1 (0,3)	1 (0,3)	0
Comorbidities, %						
Diabetes	37.25%	25.22%	<.0001	35.80%	33.15%	-0.0558
Cardiovascular disease	39.73%	28.77%	<.0001	38.65%	40.36%	0.035
Chronic kidney disease	11.77%	10.69%	0.02	10.39%	12.87%	0.0775
Chronic lung disease	17.50%	13.43%	<.0001	17.07%	18.06%	0.026
Cancer diagnosis	21.02%	13.50%	<.0001	19.94%	17.77%	-0.0555
Vaccination status at baseline			<.0001			0
Unvaccinated or pr. series incomplete	18.26%	42.73%		17.96%	17.96%	
Primary series complete	22.10%	24.72%		21.79%	21.79%	
Primary series + booster	59.64%	32.55%		60.25%	60.25%	
Median days diagnosis to prescription	0 (0,1)	N/A		0 (0,1)	N/A	
Symptomatic at baseline, %	80.43%	55.34%	<.0001	80.45%	62.37%	-0.4084
Asymptomatic at baseline, %	19.57%	44.66%	<.0001	19.55%	37.63%	0.4084

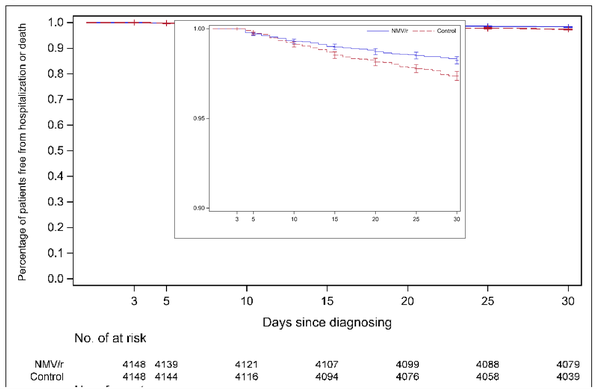
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RESULTS (contd.)

Absolute risk difference in incidence of hospitalization or death within 30 days among patients who received NMV/r and matched controls who did not receive NMV/r.



Kaplan-Meier curves depicting percentage of patients without hospitalization or death among those treated with NMV/r and untreated controls. Logrank P=0.007



CONCLUSIONS

- NMV/r use is associated with a modest reduction in hospitalization or death among previously uninfected, non-hospitalized population with COVID-19 who are at a high risk of progression to severe disease.
- The benefit is evident in older, unvaccinated, asymptomatic persons, but not in in younger, vaccinated, and symptomatic persons.

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