Supplementary file

Table S1. Demographic and clinical characteristics of included patients.

Variable[a]	No anti-viral treatment (n = 2387)	NMV-r or MOV (n = 880)	p-value
Age (years), Median [IQR]	82 [73 – 89]	83 [73 – 89]	0.046
Male	1762 (73.8%)	579 (65.8%)	<0.001
Ethnic group			
Chinese	2363 (99.0%)	873 (99.2%)	0.802
Caucasian	4 (0.2%)	0 (0%)	
Southeast Asian	6 (0.3%)	2 (0.2%)	
South Asian	9 (0.4%)	3 (0.3%)	
Japanese	1 (0%)	1 (0.1%)	
Others	4 (0.2%)	1 (0.1%)	
Respiratory diseases			<0.001
Asthma	474 (19.9%)	211 (24.0%)	
Bronchiectasis	358 (15.0%)	157 (18.1%)	
COPD	1555 (65.1%)	510 (58.0%)	
CCI, Median [IQR]	1 [1-2]	0 [0-1]	0.003
Medication			
Statin	1040 (43.6%)	436 (49.5%)	0.002
Anti-epileptic	28 (1.2%)	13 (1.5%)	0.488
DOACs	191 (8.0%)	67 (7.6%)	0.715
Calcium channel blocker	1294 (54.2%)	497 (56.5)	0.248
Baseline blood test, Median [IQR]			
Leucocyte count[b]	6.08 [4.90 – 7.38]	6.01 [4.91 – 7.40]	0.437
Neutrophil count[b]	3.86 [2.93 – 4.92]	3.90 [3.07 – 4.93]	0.448
Lymphocyte count[b]	0.82 [0.50 – 1.32]	0.94 [0.58 – 1.47]	0.046
Eosinophil count[b]	0.04 [0.00 – 0.14]	0.05 [0.00 – 0.14]	0.210
Estimated GFR, mL/min/1.73m^2	58.2 [40.5 – 77.0]	59.6 [38.8 – 77.0]	0.360
ALT (unit/L)	12.0 [8.0 – 16.6]	12.9 [8.8 – 18.0]	0.107
COVID-related outcomes			
Hospitalization	228 (9.6%)	59 (6.7%)	0.011
Respiratory failure	209 (8.8%)	36 (4.1%)	0.068
Severe respiratory failure	91 (3.8%)	19 (2.2%)	0.020
Mortality	120 (5.0%)	19 (2.2%)	<0.001
Length of stay (days), Median [IQR]	9 [4-16]	9 [3-21]	0.135

ALT, Alanine aminotransferase; CCI, Charlson co-morbidity index; COPD, Chronic obstructive pulmonary disease; DOACs, direct-acting oral anticoagulants; GFR, glomerular filtration rate; IQR, interquartile range; MOV, Molnupiravir; m, Meter; min, minute; mL, millilitre; NMV-r, nirmatrelvir-ritonavir; continuous variables are compared by unpaired t-test for continuous variables, categorical variables are compared by χ^2 test

Table S2. Risk ratio (RR) for disease outcomes in univariate and multivariate log-binomial regression

COVID-related outcomes	No. of patients (% in group)			RR (95% CI)[#] (Compared with no treatment)		Adjusted RR (95% CI)[a#] (Compared with no treatment)	
	No anti-viral treatment (n = 2387)	NMV-r (n = 302)	MOV (n = 578)	NMV-r	MOV	NMV-r	MOV
Hospitalization	228 (9.6%)	15 (5.0%)	44 (7.6%)	0.52 (0.31 – 0.87) p=0.01*	0.80 (0.59 – 1.09) p=0.15	0.56 (0.31 – 1.02) p=0.06	0.78 (0.55 –1.11) p=0.16
Respiratory failure	209 (8.8%)	10 (3.3%)	40 (6.9%)	0.38 (0.20 – 0.71) p <0.01*	0.79 (0.57 – 1.10) p=0.16	0.33 (0.15 – 0.74) p <0.01*	0.74 (0.51 – 1.06) p=0.10
Severe respiratory failure	91 (3.8%)	3 (1.0%)	16 (2.8%)	0.26 (0.08 – 0.82) p=0.02*	0.73 (0.43 – 1.23) p=0.23	0.23 (0.06 –0.93) p=0.04*	0.52 (0.27 – 0.99) p=0.048*
Mortality	120 (5.0%)	4 (1.3%)	15 (2.6%)	0.26 (0.01 – 0.71) p=0.008*	0.52 (0.30 – 0.88) p=0.01*	0.37 (0.14 –1.01) p=0.051	0.42 (0.23 – 0.77) p<0.01*

*p <0.05 indicated by box shading.

CI, Confidence interval; MOV, Molnupiravir; NMV-r, nirmatrelvir-ritonavir; RR, Risk ratio

[a]Adjusted for age, gender, underlying respiratory disease, baseline estimated glomerular filtration rate, and Charlson co-morbidity index.

Boxes highlighted in blue represent statistical significant findings

Table S3. Odds ratio (OR) for disease outcomes in univariate and multivariate logistic regression in sensitivity analysis

COVID-related outcomes	No. of patients (% in group)			OR (95% CI) (Compared with no treatment)		Adjusted OR (95% CI)[a] (Compared with no treatment)	
	No anti-viral treatment (n = 2387)	NMV-r (n = 302)	MOV (n = 578)	NMV-r	MOV	NMV-r	MOV
Hospitalization	228 (9.6%)	15 (5.0%)	44 (7.6%)	0.50 (0.29 – 0.85) p=0.01*	0.78 (0.56 – 1.09) p=0.15	0.54 (0.28 – 1.01) p=0.05	0.76 (0.52 – 1.12) p=0.16
Respiratory failure	209 (8.8%)	10 (3.3%)	40 (6.9%)	0.45 (0.22 – 0.93) p=0.03*	0.84 (0.56 – 1.28) p=0.42	0.31 (0.14 – 0.71) p <0.01*	0.72 (0.48 – 1.07) p=0.10
Severe respiratory failure	91 (3.8%)	3 (1.0%)	16 (2.8%)	0.25 (0.08 – 0.81) p=0.02*	0.72 (0.42 – 1.23) p=0.23	0.22 (0.05 – 0.91) p=0.04*	0.51 (0.26 – 0.99) p=0.05*
Mortality	120 (5.0%)	4 (1.3%)	15 (2.6%)	0.25 (0.09 – 0.69) p <0.01*	0.50 (0.29 – 0.87) p=0.01*	0.36 (0.13– 0.99) p=0.05*	0.40 (0.21 – 0.76) p<0.01*

*p <0.05 indicated by box shadingCI, Confidence interval; MOV, Molnupiravir; NMV-r, nirmatrelvir-ritonavir; OR, Odds ratio

[a]Adjusted for age, gender, underlying respiratory disease, baseline estimated glomerular filtration rate, and Charlson co-morbidity index.

Boxes highlighted in blue represent statistical significant findings

Table S4. Anti-viral effectiveness in subgroup as measured by adjusted odds ratios with logistic regression in sensitivity analysis

COVID-related outcomes	No. of patients (% in group)			Anti-viral effectiveness (95% CI) (Compared with no treatment)	
	No anti-viral treatment (n = 2387)	NMV-r (n = 302)	MOV (n = 578)	NMV-r	MOV
Hospitalization	228 (9.6%)	15 (5.0%)	44 (7.6%)	46.5% (-0.8 – 71.6%) p=0.053	23.7% (-11.6 – 47.9%) p=0.163
Respiratory failure	209 (8.8%)	10 (3.3%)	40 (6.9%)	69.1% (28.9 – 86.5%) p=0.006*	28.5% (-6.7 – 52.1%) p=0.101
Severe respiratory failure	91 (3.8%)	3 (1.0%)	16 (2.8%)	77.9% (8.8 – 94.6%) p=0.037*	49.2% (0.8 – 74.0%) p=0.047*
Mortality	120 (5.0%)	4 (1.3%)	15 (2.6%)	64.2% (1.1 – 87.0%) p=0.048*	59.9% (24.5 – 78.7%) p=0.005*

*p <0.05 indicated by box shading.

CI, Confidence interval; MOV, Molnupiravir; NMV-r, nirmatrelvir-ritonavir

Anti-viral effectiveness was calculated the formula, (1-adjusted odds ratio) x 100. The odd ratios were adjusted for age, gender underlying respiratory disease and Charlson co-morbidity index.

Boxes highlighted in blue represent statistical significant findings