

# **Efficacy and safety of nirmatrelvir/ritonavir, molnupiravir and remdesivir in a real-world cohort of outpatients with COVID-19 at high risk of progression: the PISA Outpatient Clinic experience**

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**TABLE S1.** Comparison of patients who met and those who did not the composite endpoint (death or hospitalization for COVID-19).

<b>Variable</b>	<b>Death or hospitalization N=14</b>	<b>Cure N=548</b>	<b>p value</b>
<b>Age, ys, median (IQRs)</b>	76.5 (74.5-82)	68 (54-78)	<i>0.008</i>
<b>Time from symptoms onset, days, median (IQRs)</b>	4.5 (3-5)	3 (2-4)	<i>0.014</i>
<b>Male sex</b>	7 (50%)	295 (53.8%)	0.776
<b>Vaccination status</b>			
Adequate COVID-19 vaccination	10 (71.4%)	445 (81.2%)	0.358
Time from the last COVID-19 vaccine dose, days, median (IQRs)	119 (109-124)	132 (89-179)	0.641
<b>Number of comorbidities</b>			
≤1 comorbidity	0	129 (23.5%)	0.039
≥ 2 comorbidities	14 (3.2%)	418 (76.3%)	0.038
≥ 3 comorbidities	12 (85.7%)	260 (47.4%)	<i>0.005</i>
<b>Comorbidities</b>			
Obesity, BMI ≥ 30 kg/m <sup>2</sup>	3 (21.4%)	139 (25.4%)	0.738
Chronic lung disease	6 (42.9%)	150 (27.4%)	0.201
Immunosuppression (primary or acquired)	6 (42.9%)	123 (22.4%)	0.073
Diabetes mellitus	5 (35.7%)	100 (18.2%)	0.098
Arterial hypertension	10 (71.4%)	256 (46.7%)	0.067
Cardiovascular disease	5 (35.7%)	202 (37%)	0.922
Cerebrovascular disease	4 (28.6%)	51 (9.3%)	<i>0.017</i>
Solid cancer	5 (35.7%)	114 (20.8%)	0.177
Hematological disease	5 (35.7%)	60 (10.9%)	<i>0.004</i>
Chronic kidney disease	2 (14.3%)	35 (6.4%)	0.239
Chronic liver disease	3 (21.4%)	22 (4%)	<i>0.002</i>
Autoimmune disease	5 (35.7%)	79 (14.4%)	<i>0.027</i>
Solid organ transplantation	0	19 (3.5%)	0.478
Neurological disease	0	22 (4%)	0.444
<b>Symptoms of COVID-19</b>			
Fever	6 (42.9%)	358 (65.3%)	0.082
Cough	14 (100%)	418 (76.3%)	<i>0.038</i>
Dyspnea	2 (14.3%)	32 (5.8%)	0.191
Fatigue	6 (42.9%)	240 (43.8%)	0.944
Myalgia	6 (42.9%)	186 (33.9%)	0.487
Gastrointestinal symptoms	5 (35.7%)	62 (11.3%)	<i>0.005</i>
<b>Antiviral treatments</b>			<i>0.013</i>
Molnupinavir	2 (14.3%)	112 (20.4%)	
Nirmaltrevir/ritonavir	2 (14.3%)	250 (45.6%)	
Remdesivir	10 (71.4%)	186 (33.9%)	

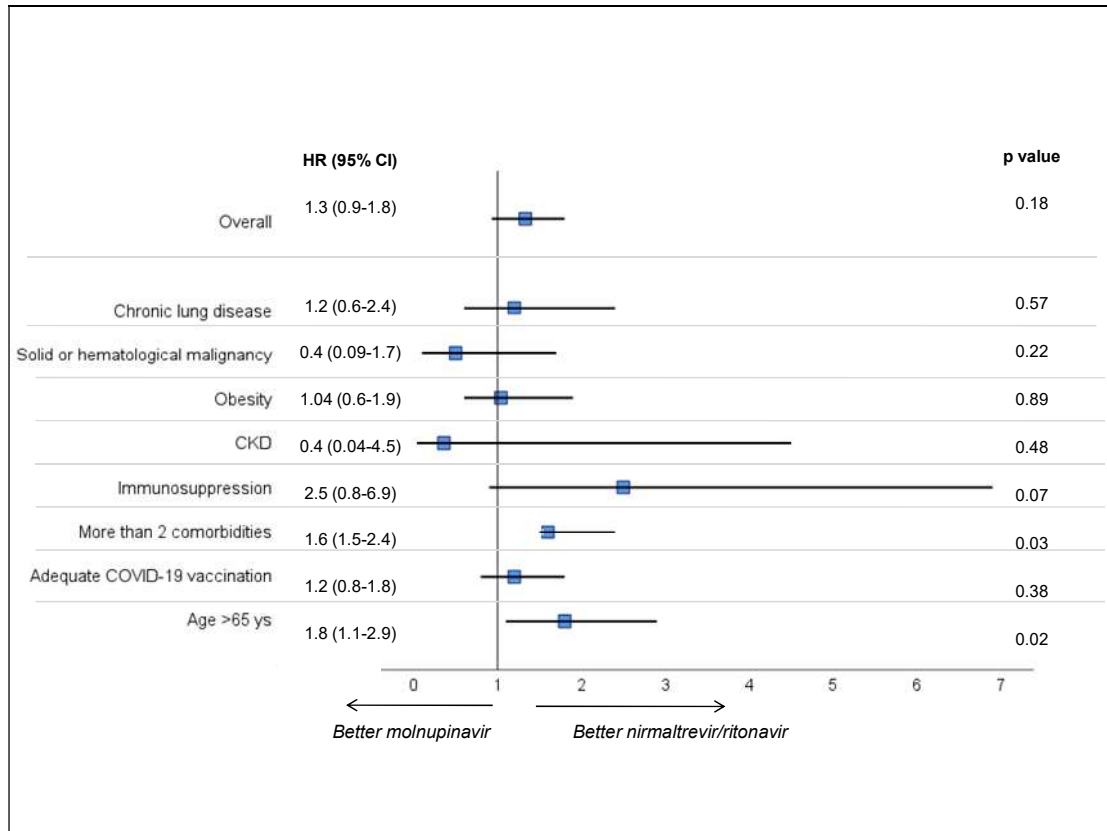
Italics indicates statistical significance (p<0.05)

**TABLE S2.** Comparison between patients with negative nasopharyngeal swab within 10 days versus those with negative nasopharyngeal swab > 10 days from the start of symptoms.

Variable	Negative nasopharyngeal swab within 10 days N=234	Negative nasopharyngeal swab > 10 days N=328	p value
<b>Age, ys, median (IQRs)</b>	64 (50-76)	70.5 (57-80)	<0.001
<b>Time from symptoms onset to antiviral, days, median (IQRs)</b>	3 (2-4)	3 (2-4)	<0.001
<b>Time from symptoms onset to antiviral, days, mean (SD)</b>	3 (1.2)	3.4 (1.4)	<0.001
<b>Male sex</b>	126 (53.8%)	176 (53.7%)	0.965
<b>Vaccination status</b>			
Adequate COVID-19 vaccination	202 (86.3%)	253 (77.1%)	0.006
Time from the last COVID-19 vaccine dose, days, median (IQRs)	136 (91-172)	129 (86-181)	0.973
<b>Number of comorbidities</b>			
≤1 comorbidity	66 (28.2%)	63 (19.2%)	0.012
≥ 2 comorbidities	167 (71.4%)	265 (80.8%)	0.009
≥ 3 comorbidities	103 (44%)	169 (51.5%)	0.079
<b>Comorbidities</b>			
Obesity, BMI ≥ 30 kg/m <sup>2</sup>	69 (29.5%)	73 (22.3%)	0.052
Chronic lung disease	60 (25.6%)	96 (29.3%)	0.344
Immunosuppression (primary or acquired)	50 (21.4%)	79 (24.1%)	0.450
Diabetes mellitus	46 (19.7%)	59 (18%)	0.617
Arterial hypertension	99 (42.3%)	167 (50.9%)	0.044
Cardiovascular disease	76 (32.5%)	131 (40.2%)	0.062
Cerebrovascular disease	18 (7.7%)	37 (11.3%)	0.158
Solid cancer	47 (20.1%)	72 (22%)	0.594
Hematological disease	23 (9.8%)	42 (12.8%)	0.277
Chronic kidney disease	11 (4.7%)	26 (7.9%)	0.128
Chronic liver disease	8 (3.4%)	17 (5.2%)	0.317
Autoimmune disease	37 (15.8%)	47 (14.3%)	0.627
Solid organ transplantation	5 (2.1%)	14 (4.3%)	0.168
Neurological disease	12 (5.2%)	10 (3.1%)	0.209
<b>Symptoms of COVID-19</b>			
Fever	153 (65.4%)	211 (64.3%)	0.796
Cough	171 (73.1%)	261 (79.6%)	0.072
Dyspnea	12 (5.1%)	22 (6.7%)	0.439
Fatigue	111 (47.4%)	135 (41.2%)	0.139
Myalgia	84 (35.9%)	108 (32.9%)	0.464
Gastrointestinal symptoms	21 (9%)	46 (14%)	0.069
<b>Antiviral discontinuation for adverse event</b>	6 (2.6%)	3 (0.9%)	0.174
<b>Antivirals</b>			<0.001
Molnupinavir	43 (18.4%)	71 (21.6%)	
Nirmaltrevir/ritonavir	133 (56.8%)	119 (36.3%)	
Remdesivir	58 (24.8%)	138 (42.1%)	

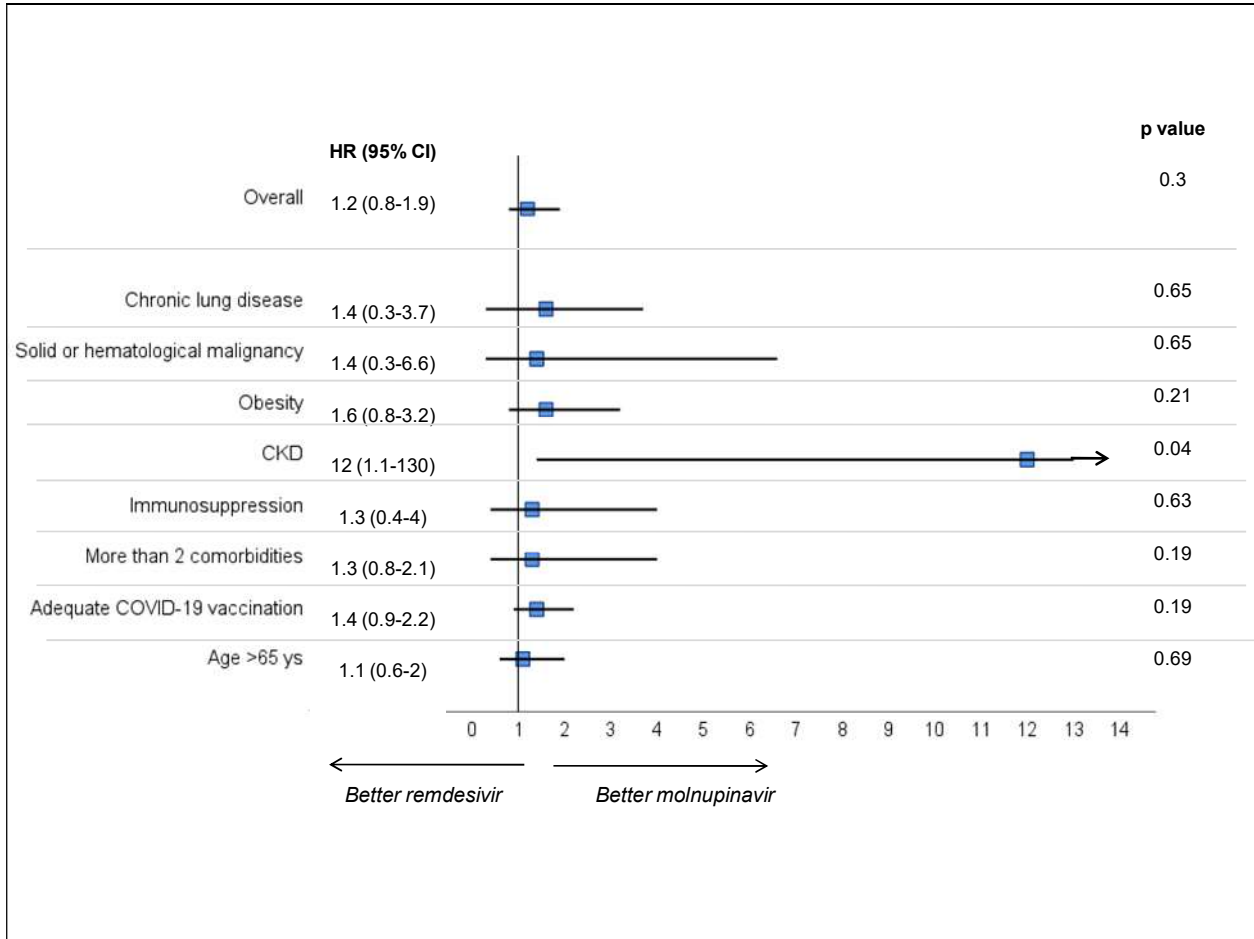
Italics indicates statistical significance (p<0.05)

**FIGURE S1.** Multivariable hazard ratios for factors associated with increased probability to have a negative nasopharyngeal swab within 10 days from the first positive one in patients treated with nirmatrelvir/ritonavir vs those treated with molnupinavir.



The multivariable model was adjusted for: age <80 ys, adequate COVID-19 vaccination,  $\geq 2$  comorbidities, hypertension, time from symptoms onset, hematological malignancy, immunosuppression, chronic lung disease. Antiviral treatments were modeled as time-dependent variable

**FIGURE S2.** Multivariable hazard ratios for factors associated with increased probability to have a negative nasopharyngeal swab within 10 days from the first positive one in patients treated with molnupinavir vs those treated with remdesivir.



The multivariable model was adjusted for: age <80 ys, adequate COVID-19 vaccination,  $\geq 2$  comorbidities, hypertension, time from symptoms onset, hematological malignancy, immunosuppression, chronic lung disease. Antiviral treatments were modeled as time-dependent variable