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 enpoint (death or hospitalization for COVID-19).

N=14 N=548	Variable	Death or hospitalization	Cure	p value
Time from symptoms onset, days, median (IQRs) 4.5 (3-5) 3 (2-4) 0.014 Male sex 7 (50%) 295 (53.8%) 0.776 Vaccination status 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 Number of comorbidities Selection of comorbidities 12 (85.7%) 418 (76.3%) 0.039 ≥ 2 comorbidities 14 (3.2%) 418 (76.3%) 0.038 0.005 Comorbidities 0 129 (23.5%) 0.039 ≥ 2 comorbidities 14 (3.2%) 418 (76.3%) 0.038 ≥ 3 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities 00esity, BMI ≥ 30 kg/m² 3 (21.4%) 139 (25.4%) 0.038 Chronic lung disease 6 (42.9%) 150 (27.4%) 0.005 Chronic lung disease 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		N=14	N=548	
(IQRs) Male sex 7 (50%) 295 (53.8%) 0.776	Age, ys, median (IQRs)	76.5 (74.5-82)	68 (54-78)	0.008
Male sex 7 (50%) 295 (53.8%) 0.776 Vaccination status Adequate COVID-19 vaccination 10 (71.4%) 445 (81.2%) 0.358 Adequate COVID-19 vaccine dose, days, median (IQRs) 119 (109-124) 132 (89-179) 0.641 Number of comorbidities 2 1 19 (109-124) 132 (89-179) 0.641 Number of comorbidities 0 129 (23.5%) 0.039 ≥ 2 comorbidities 14 (3.2%) 418 (76.3%) 0.038 ≥ 3 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities 4 139 (25.4%) 0.738 Obesity, BMI ≥ 30 kg/m² 3 (21.4%) 139 (25.4%) 0.005 Comorbidities 4 123 (22.4%) 0.738 Obssity, BMI ≥ 30 kg/m² 3 (21.4%) 139 (25.4%) 0.738 Chronic lung disease 6 (42.9%) 123 (22.4%) 0.073 Diabetes mellitus 5 (35.7%)	Time from symptoms onset, days, median	4.5 (3-5)	3 (2-4)	0.014
Vaccination status 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 Number of comorbidities 19 (109-124) 132 (89-179) 0.641 SI comorbidities 41 (3.2%) 418 (76.3%) 0.039 ≥ 2 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities Comorbidities Obesity, BMI ≥ 30 kg/m² 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 5 (35.7%) 20 (37%) 0.922 Cerebrovascular disease 5 (35.7%) 114 (20.8%) 0.177 Hematological disease	(IQRs)			
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 Number of comorbidities Sel comorbidities 12 (85.7%) 0.039 0.039 0.039 0.039 0.039 0.039 0.039 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.009 0.009 0.009 0.009 0.009 0.009 0.009 0.009 0.009 0.005 0.0	Male sex	7 (50%)	295 (53.8%)	0.776
Time from the last COVID-19 vaccine dose, days, median (IQRs) 119 (109-124) 132 (89-179) 0.641 Number of comorbidities Selection of comorbidities 14 (3.2%) 418 (76.3%) 0.039 ≥ 2 comorbidities 14 (3.2%) 418 (76.3%) 0.038 ≥ 3 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities Obesity, BMI ≥ 30 kg/m² 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%) 0.093 Arterial hypertension 10 (71.4%) 256 (46.7%) 0.087 Cardiovascular disease 5 (35.7%) 202 (37%) 0.922 Cerebrovascular disease 5 (35.7%) 20 (20.37%) 0.922 Cerebrovascular disease 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%)<	Vaccination status			
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Number of comorbidities 0 129 (23.5%) 0.039 ≤1 comorbidities 14 (3.2%) 418 (76.3%) 0.038 ≥ 2 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities Obesity, BMI ≥ 30 kg/m² 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%) 0.017 Solid cancer 5 (35.7%) 202 (37%) 0.922 Cerebrovascular disease 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.001 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic kidney disease 3 (21.4%) <td>Time from the last COVID-19 vaccine dose,</td> <td>119 (109-124)</td> <td>132 (89-179)</td> <td>0.641</td>	Time from the last COVID-19 vaccine dose,	119 (109-124)	132 (89-179)	0.641
≤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%) 0.005 Comorbidities Obesity, BMI ≥ 30 kg/m² 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%) 0.017 Solid cancer 5 (35.7%) 202 (37%) 0.922 Cerebrovascular disease 5 (35.7%) 20 (37%) 0.017 Hematological disease 5 (35.7%) 60 (10.9%) 0.017 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic liver disease 3 (21.4%) 22 (4%) 0.022 Solid organ transplantation 0	days, median (IQRs)			
≥ 2 comorbidities 14 (3.2%) 418 (76.3%) 0.038 ≥ 3 comorbidities 12 (85.7%) 260 (47.4%) 0.005 Comorbidities 0 260 (47.4%) 0.005 Comorbidities 0 139 (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%) 0.017 Solid cancer 5 (35.7%) 202 (37%) 0.922 Cerebrovascular disease 4 (28.6%) 51 (9.3%) 0.017 Solid cancer 5 (35.7%) 60 (10.9%) 0.001 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease<	Number of comorbidities			
	≤1 comorbidity	0	129 (23.5%)	0.039
Comorbidities Obesity, BMI ≥ 30 kg/m² 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%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 5 <td>≥ 2 comorbidities</td> <td>14 (3.2%)</td> <td>418 (76.3%)</td> <td>0.038</td>	≥ 2 comorbidities	14 (3.2%)	418 (76.3%)	0.038
Obesity, BMI ≥ 30 kg/m² $3 (21.4\%)$ $139 (25.4\%)$ 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 $4 (28.6\%)$ $51 (9.3\%)$ 0.017 Solid cancer $5 (35.7\%)$ $114 (20.8\%)$ 0.177 Hematological disease $5 (35.7\%)$ $60 (10.9\%)$ 0.004 Chronic kidney disease $2 (14.3\%)$ $35 (6.4\%)$ 0.239 Chronic liver disease $3 (21.4\%)$ $22 (4\%)$ 0.002 Autoimmune disease $5 (35.7\%)$ $79 (14.4\%)$ 0.027 Solid organ transplantation 0 0 0 0 0 0 0 0 0 0 0 0 0	≥ 3 comorbidities	12 (85.7%)	260 (47.4%)	0.005
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%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 Dyspnea <td>Comorbidities</td> <td></td> <td></td> <td></td>	Comorbidities			
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%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.082 Cough 6 (42.9%) 32 (5.8%) 0.191 Fatigu	Obesity, BMI $\geq 30 \text{ kg/m}^2$	3 (21.4%)	139 (25.4%)	0.738
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%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 5 5 6 6 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.082 0.082 0.082 0.082 0.082 0.082 0.082 0.082 0.082 0.082 0.082 0.082 <	Chronic lung disease	6 (42.9%)	150 (27.4%)	0.201
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%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 (42.9%) 358 (65.3%) 0.444 Symptoms of COVID-19 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013	Immunosuppression (primary or acquired)	6 (42.9%)	123 (22.4%)	0.073
Cardiovascular disease 5 (35.7%) 202 (37%) 0.922 Cerebrovascular disease 4 (28.6%) 51 (9.3%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 250 (45.6%) <td< td=""><td>Diabetes mellitus</td><td>5 (35.7%)</td><td>100 (18.2%)</td><td>0.098</td></td<>	Diabetes mellitus	5 (35.7%)	100 (18.2%)	0.098
Cerebrovascular disease 4 (28.6%) 51 (9.3%) 0.017 Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 5 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 250 (45.6%) <td>Arterial hypertension</td> <td>10 (71.4%)</td> <td>256 (46.7%)</td> <td>0.067</td>	Arterial hypertension	10 (71.4%)	256 (46.7%)	0.067
Solid cancer 5 (35.7%) 114 (20.8%) 0.177 Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 250 (45.6%)	Cardiovascular disease	5 (35.7%)	202 (37%)	0.922
Hematological disease 5 (35.7%) 60 (10.9%) 0.004 Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 250 (45.6%)	Cerebrovascular disease	4 (28.6%)	51 (9.3%)	0.017
Chronic kidney disease 2 (14.3%) 35 (6.4%) 0.239 Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 5 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Solid cancer	5 (35.7%)	114 (20.8%)	0.177
Chronic liver disease 3 (21.4%) 22 (4%) 0.002 Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Hematological disease	5 (35.7%)	60 (10.9%)	0.004
Autoimmune disease 5 (35.7%) 79 (14.4%) 0.027 Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Chronic kidney disease	2 (14.3%)	35 (6.4%)	0.239
Solid organ transplantation 0 19 (3.5%) 0.478 Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 Cough 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Chronic liver disease	3 (21.4%)	22 (4%)	0.002
Neurological disease 0 22 (4%) 0.444 Symptoms of COVID-19 5 0 0.082 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Autoimmune disease	5 (35.7%)	79 (14.4%)	0.027
Symptoms of COVID-19 Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Solid organ transplantation	0	19 (3.5%)	0.478
Fever 6 (42.9%) 358 (65.3%) 0.082 Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Neurological disease	0	22 (4%)	0.444
Cough 14 (100%) 418 (76.3%) 0.038 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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	Symptoms of COVID-19			
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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)				
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%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)			* * * * * * * * * * * * * * * * * * * *	
Myalgia 6 (42.9%) 186 (33.9%) 0.487 Gastrointestinal symptoms 5 (35.7%) 62 (11.3%) 0.005 Antiviral treatments 0.013 Molnupinavir 2 (14.3%) 112 (20.4%) Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)	* *	` ′		
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Nirmaltrevir/ritonavir 2 (14.3%) 250 (45.6%)		2 (14.3%)	112 (20.4%)	
	<u> </u>		, ,	
	Remdesivir	10 (71.4%)	186 (33.9%)	

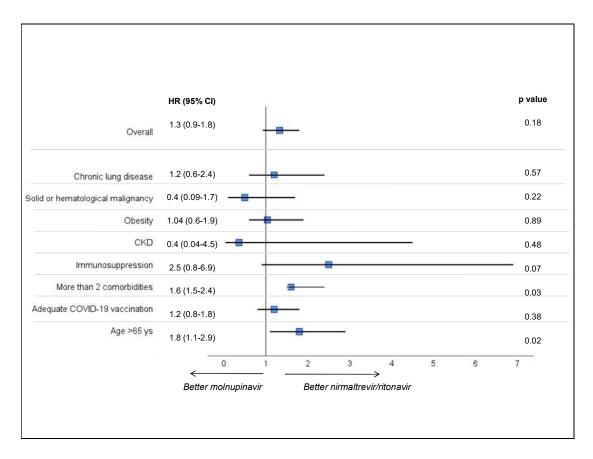
Italics indicates statistical significance (p<0.05)

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	Negative	p value
	nasopharyngeal swab	nasopharyngeal swab	P
	within 10 days	> 10 days	
	N=234	N=328	
Age, ys, median (IQRs)	64 (50-76)	70.5 (57-80)	< 0.001
Time from symptoms onset to anvitiral,	3 (2-4)	3 (2-4)	< 0.001
days, median (IQRs)	,		
Time from symptoms onset to anvitiral,	3 (1.2)	3.4 (1.4)	< 0.001
days, mean (SD)	,		
Male sex	126 (53.8%)	176 (53.7%)	0.965
Vaccination status			
Adequate COVID-19 vaccination	202 (86.3%)	253 (77.1%)	0.006
Time from the last COVID-19 vaccine dose,	136 (91-172)	129 (86-181)	0.973
days, median (IQRs)			
Number of comorbidities			
≤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
Comorbidities			
Obesity, BMI $\geq 30 \text{ kg/m}^2$	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
Symptoms of COVID-19			
Fever	153 (65.4%)	211 (64.3%)	0.796
Cough	171 (73.1%)	261 (79.6%)	0.072
Dyspnea Estima	12 (5.1%)	22 (6.7%)	0.439
Fatigue Myalgia	111 (47.4%) 84 (35.9%)	135 (41.2%) 108 (32.9%)	0.139 0.464
Gastrointestinal symptoms	21 (9%)	46 (14%)	0.464
Antiviral discontinuation for adverse event	6 (2.6%)	3 (0.9%)	0.174
Antivirals	\ - /		< 0.001
Molnupinavir	43 (18.4%)	71 (21.6%)	
Nirmaltervir/ritonavir	133 (56.8%)	119 (36.3%)	
Remdesivir	58 (24.8%)	138 (42.1%)	

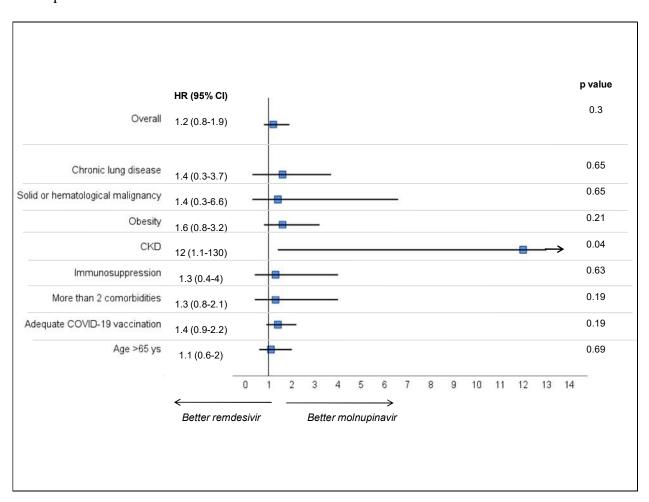
Italics indicates statistical significance (p<0.05)

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, ≥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, ≥2 comorbidities, hypertension, time from symptoms onset, hematological malignancy, immunosuppression, chronic lung disease. Antiviral treatments were modeled as time-dependent variable