

Cover page

Dear Sir,

“A Retrospective Observational Study on COVID-19 Patients Receiving Treatment with Nirmatrelvir/Ritonavir (PAXLOVID)”

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Supplemental table 1: Patient-reported COVID-19 symptoms at baseline

	Total	Untreated PAXLOVID*	Treated with PAXLOVID	p-value
	N=3,011	N=1,006	N=2,005	
Stuffy or runny nose	1,971 (65%)	556 (55%)	1,415 (71%)	<0.001
Sore throat	1,791 (59%)	488 (49%)	1,303 (65%)	<0.001
Shortness of Breath	285 (9%)	81 (8%)	204 (10%)	0.061
Cough	2,420 (80%)	688 (68%)	1,732 (86%)	<0.001
Low energy/Tiredness/fatigue	1,020 (34%)	293 (29%)	727 (36%)	<0.001
Muscle ache/body aches	1,397 (46%)	382 (38%)	1,015 (51%)	<0.001
Headache	1,110 (37%)	307 (31%)	803 (40%)	<0.001
Chills or shivering	521 (17%)	149 (15%)	372 (19%)	0.010
Feeling hot/feverish	898 (30%)	237 (24%)	661 (33%)	<0.001
Nausea or vomiting	363 (12%)	94 (9%)	269 (13%)	0.001
Diarrhea	197 (7%)	66 (7%)	131 (7%)	0.98
Loss of sense of smell	319 (11%)	85 (8%)	234 (12%)	0.007
Loss of sense of taste	298 (10%)	75 (7%)	223 (11%)	0.001

P-values from Pearson chi-squared test

Supplementary table 2: Breakdown of comorbidities conditions of participants at baseline

	Total	Not treated with PAXLOVID*	Treated with PAXLOVID	p-value
	N=3,011	N=1,006	N=2,005	
	n(%)	n(%)	n(%)	
Immunocompromised Condition	202 (7%)	102 (10%)	100 (5%)	<0.001
Acute myocarditis	0 (0%)	0 (0%)	0 (0%)	
Enteritis and colitis	9 (0%)	4 (0%)	5 (0%)	0.48
Inflammatory polyarthropathy	14 (0%)	2 (0%)	12 (0%)	0.13
Neutropenia	0 (0%)	0 (0%)	0 (0%)	
Chronic kidney disease	47 (2%)	33 (3%)	14 (1%)	<0.001
Crystal arthropathies	47 (2%)	25 (2%)	22 (1%)	0.004
Rheumatologic or other inflammatory condition	20 (1%)	11 (1%)	9 (0%)	0.040
Sickle cell disease	42 (1%)	18 (2%)	24 (1%)	0.19

P-values from Pearson chi-squared test

Supplementary table 3: Generalized ordinal logistic regression with no assumption of proportional odds for number of hospitalizations, days of antibiotic use and ICU length of stay

	Unadjusted Analysis ¹		Adjusted for WHO risk categories ¹	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Number of Hospitalizations²				
0 vs ≥ 1	0.53 (0.41-0.68)	<0.001	0.60 (0.46-0.78)	<0.001
≤ 1 vs ≥ 2	0.30 (0.17-0.42)	<0.001	0.40 (0.23-0.70)	0.001
≤ 2 vs ≥ 3	0.35 (0.13-0.92)	0.033	0.47 (0.17-1.22)	0.119
Number of Hospitalizations among Patients with Readmissions				
0 vs ≥ 1	0.35 (0.20-0.63)	<0.001	0.47 (0.26-0.85)	0.013
≤ 1 vs ≥ 2	0.35 (0.20-0.63)	<0.001	0.47 (0.26-0.85)	0.013
≤ 2 vs ≥ 3	0.33 (0.12-0.94)	0.037	0.43 (0.15-1.22)	0.144
Non ICU Length of Stay (Days)				
0 vs ≥ 1	0.52 (0.40-0.68)	<0.001	0.59 (0.45-0.77)	<0.001
≤ 7 vs ≥ 8	0.77 (0.38-1.55)	0.464	0.97 (0.48-1.97)	0.940
≤ 14 vs ≥ 15	1.17 (0.30-4.54)	0.820	1.47 (0.39-5.53)	0.570
Days of Antibiotics Use for any cause				
0 vs ≥ 1	0.76 (0.65-0.90)	<0.001	0.79 (0.67-0.94)	0.006
≤ 7 vs ≥ 8	0.88 (0.70-1.10)	0.275	0.92 (0.73-1.16)	0.501
≤ 14 vs ≥ 15	0.96 (0.69-1.33)	0.806	0.99 (0.71-1.38)	0.972
Days of Antibiotics Use taken for COVID-19				
0 vs ≥ 1	0.54 (0.41-0.72)	<0.001	0.58 (0.43-0.76)	<0.001
≤ 7 vs ≥ 8	0.63 (0.25-1.59)	0.323	0.66 (0.26-1.69)	0.392
≤ 14 vs ≥ 15	<0.001 (NE, NE)	0.981	<0.001 (NE, NE)	0.991

NE=Not estimable; non-ICU = non-intensive care unit hospitalized patient

¹ generalised ordinal logistic regression models with no proportional odds assumption results

² generalised ordinal logistic regression models are essentially a series of binary logistic regressions. Taking hospitalizations as an example, 0 hospitalizations vs 1, 2 and 3+ hospitalizations combined (which is already presented in Table 4), then 0 and 1 hospitalizations combined vs 2 and 3+ hospitalizations combined and then 0, 1 and 2 hospitalizations combined vs 3+ hospitalizations.

Supplementary Table 4: Sensitivity analysis of Health-care utilisation in the 24 months following COVID-19 (n=2012)

	Adjusted for World Health Organization risk categories ¹	
	OR (95% CI) or RRR (95% CI)	p-value
Emergency room visits	1.13 (0.90-1.44)	0.294
Hospitalization	0.68 (0.51-0.91)	0.011
Number of Hospitalizations		
0	<i>Reference</i>	
1	0.82 (0.59-1.13) ²	0.222
2	0.23 (0.09-0.60) ²	0.003
3+	0.44 (0.14-1.40) ²	0.165
Hospitalization among Patients with Readmissions	0.32 (0.14-0.73)	0.006
Number of Hospitalizations among Patients with Readmissions		
0	<i>Reference</i>	
1	NE	
2	0.30 (0.11-0.80) ²	0.017
3+	0.38 (0.10-1.43) ²	0.153
ICU Admission	1.01 (0.61-16.45)	0.997
Non-ICU Length of Stay (Days)		
0	<i>Reference</i>	
1-7	0.63 (0.46-0.87) ²	0.005
8-14	0.86 (0.34-2.21) ²	0.755
15+	1.62(0.36-7.40) ²	0.531
Supplemental Oxygen Usage	1.42 (0.65-3.10)	0.371
Use of Antibiotics for any cause	0.94 (0.78-1.14)	0.518
Days of Antibiotics Use for any cause		
0	<i>Reference</i>	
1-7	0.87 (0.69-1.10) ²	0.255
8-14	1.04 (0.74-1.46) ²	0.811
15+	1.04 (0.72-1.53) ²	0.816
Use of Antibiotics taken for COVID-19	0.70 (0.51-0.95)	0.025
Days of Antibiotics Use taken for COVID-19		
0	<i>Reference</i>	
1-7	0.69 (0.50-0.97)	0.031
8-14	1.00(0.35-2.88)	0.996
15+	NE	

ICU: intensive care unit; non-ICU = non-intensive care unit hospitalized patient; IMV: invasive mechanical ventilation; NE: Not estimable; RRR: Relative Risk Ratios; OR: Odds Ratio; CI: Confidence Intervals

¹ Propensity score matching was conducted using age, gender, BMI (based on categories, underweight, normal, overweight and obese) nationality, and ethnicity; this yielded a matched cohort of 2,012 observations. All analyses were repeated in the propensity score–matched cohort to assess the robustness of the findings. Logistic regression was used to model binary outcomes and results are presented as odds ratios and 95% confidence intervals. Multinomial logistic regression was used to model nominal outcome variable, and results are presented as relative risk ratios and 95% confidence intervals.

² Multinomial logistic regression model, RRR (95%CI)

Supplemental table 5: Vaccinations for cases and controls

	Total	Refused PAXLOVID	PAXLOVID treated	p-value
	N=8,534	N=2,773	N=5,761	
Vaccination				<0.001
BBIBP-CorV (Sinopharm)	4,381 (51%)	1,493 (54%)	2,888 (50%)	
BNT162b2 (Pfizer)	3,414 (40%)	1,082 (39%)	2,332 (40%)	
ChAdOx1-SARS-COV-2/AZD1222 (CoviShield; AstraZeneca)	236 (3%)	38 (1%)	198 (3%)	
Gam-COVID-Vac (Sputnik V)	499 (6%)	158 (6%)	341 (6%)	
Missing Data	3 (0%)	1 (0%)	2 (0%)	
Moderna	1 (0%)	1 (0%)	0 (0%)	
Dose, mean(SD)	2 (1)	2 (1)	2 (1)	0.26
Dose, median(IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.35

SD = standard deviation; IQR=interquartile range

*Data are presented as mean (SD) or median (IQR) for continuous measures, and n (%) for categorical measures. P-values from Fishers exact test for those presented as n(%), t-test for mean(SD), or Wilcoxon rank-sum test for median(IQR).