Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Efficacy of Paxlovid and Lagevrio for COVID-19 Infection in Patients With Inflammatory Bowel Disease: A Propensity-Matched Study

The world has been faced with the coronavirus disease 2019 (COVID-19) pandemic. Several antiviral medications have been granted emergency use authorization for treatment of patients with COVID-19 including Paxlovid (nirmatrelvir and ritonavir) (Pfizer. Location, New York City, NY) and Lagevrio (molnupiravir) (Merck, Kenilworth, NJ).[1] There are no data on the use of these medications in patients with inflammatory bowel disease (IBD) who develop a COVID-19 infection. This report compares the outcomes of patients with IBD who received antiviral medications for COVID-19 with those who did not and with non-IBD patients who received antiviral medications.

A retrospective cohort study was performed using TriNetX (Cambridge, MA) which provides real-time access to deidentified electronic health records of more than 78 million patients. A real-time search and analysis of the TriNetX platform was conducted through August 18, 2022. Patients with IBD were identified using the International Classification of Diseases, 9th and 10th revisions, Clinical Modification codes plus RxNorm codes for any IBD-related medication (Supplementary Tables 1 and 2). We identified patients who received Paxlovid or Lagevrio (Table 1). The IBD control cohort included patients with IBD and COVID-19 who did not receive Paxlovid or Lagevrio. The non-IBD control cohort included patients without IBD or other immune-mediated inflammatory diseases who received Paxlovid or Lagevrio. The primary outcome was to assess the risk of any-cause hospitalization within 48 hours and 30 days after initiation of COVID-19 antiviral therapies or diagnosis of COVID-19. Secondary outcomes included the risk for intensive care unit (ICU) care, intubation/respiratory support, and mortality. All statistical analyses were conducted using the TriNetX software. Propensity-score matching and statistical analyses are described in Supplementary Table 1.

Of 29,598 patients with IBD and COVID-19, 532 (1.7%) received Paxlovid (mean age, 55.2 ± 16.2 y; female, 62%). A total of 78% received Paxlovid after developing COVID-19 for the first time, of whom 97% received Paxlovid within 24 hours of diagnosis. Of these patients, 94 (17.6%) had received at least 2 doses of the COVID-19 vaccine. Seventy-nine (84%) patients received the BNT162b2 (Pfizer, New York City, NY) vaccine and 15 (16%) received the messenger RNA-1273 (Moderna, Merck, Kenilworth, NJ) vaccine. Only 27 (5%) patients had received a COVID-19 vaccine within 6 months before Paxlovid prescription. Supplementary Table 1 shows the comparison between demographics, comorbid diseases, IBD types, and medications between the Paxlovid and control cohorts. The overall rate of hospitalization was as high as 1.8% in patients with IBD who received Paxlovid compared with 5% in the IBD control cohort. After propensity-score matching, the Paxlovid cohort had a decreased risk of hospitalization (adjusted odds ratio [aOR], 0.35; 95% CI, 0.17–0.74) compared with the IBD control cohort. No patients died, required ICU care, or intubation/respiratory support in the Paxlovid arm while as many as 1.8% of patients in the IBD control arm died (Table 1). After propensity-score matching, there was no difference in risk of hospitalization (aOR, 1; 95% CI, 0.41–2.43) between the Paxlovid and non-IBD control cohort that also received Paxlovid. No patients died, required ICU care, or intubation/respiratory support in these 2 cohorts.

A total of 150 patients with IBD (mean age, 59.6 ± 16.5 y; female, 67%) received Lagevrio. Sixty-four percent received Lagevrio after developing COVID-19 for the first time, and 85% of these patients received Lagevrio within 24 hours of diagnosis. Of these patients, 13 (8.6%) received at least 2 doses of COVID-19 vaccine. Supplementary Table 2 shows the comparison between demographics, comorbid diseases, IBD types, and medications between the Lagevrio and control cohorts. The overall rate of hospitalization was 6.7% in patients with IBD who received Lagevrio compared with 8.7% in the IBD control cohort (Table 1). After propensity-score matching, there was no difference in risk of hospitalization (aOR, 0.75; 95% CI, 0.31–1.77) between the Lagevrio and IBD control cohort. After propensity-score matching, there was no difference in risk of hospitalization (aOR, 1; 95% CI, 0.40–2.31) between the molnupiravir and non-IBD control cohort. No patients in the molnupiravir cohort died, required ICU care, or intubation/respiratory support.

Abbreviations used in this paper: aOR, adjusted odds ratio; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; ICU, intensive care unit.

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Table 1. Outcomes of COVID-19 in IBD Patients in the Paxlovid and Lagevrio Cohorts Compared With the IBD Control Cohort After Propensity-Score Matching

Outcome	Cohort	N (%)	aOR	95% CI
Hospitalization	Paxlovid	10 (1.8)[a]	0.35	0.17–0.74
	No antiviral	27 (5.0)		
ICU care	Paxlovid	0 (0)	N/A	N/A
	No antiviral	10 (1.8)[a]		
Intubation/respiratory support	Paxlovid	0 (0)	N/A	N/A
	No antiviral	10 (1.8)[a]		
Mortality	Paxlovid	0 (0)	N/A	N/A
	No antiviral	10 (1.8)[a]		
Hospitalization	Lagevrio	10 (6.7)[a]	0.75	0.31–1.77
	No antiviral	13 (8.7)		
ICU care	Lagevrio	0 (0)	N/A	N/A
	No antiviral	10 (6.7)[a]		
Intubation/respiratory support	Lagevrio	0 (0)	N/A	N/A
	No antiviral	10 (6.7)[a]		
Mortality	Lagevrio	0 (0)	N/A	N/A
	No antiviral	10 (6.7)[a]		

NOTE. The Paxlovid cohort included patients with IBD who had RxNorm codes for ritonavir (85762) and nirmatrelvir (2587892). The Lagevrio cohort included patients with IBD who had a RxNorm code for molnupiravir (2587901).
aOR, adjusted odds ratio; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; ICU, intensive care unit; N/A, not applicable.
[a]To maintain patient confidentiality, when numbers of events are >1 but <10, TriNetX rounds up events to 10.

In one study of 2246 unvaccinated patients who were at high risk for progression to severe disease, those receiving Paxlovid within 5 days of symptom onset had an 89% reduction in progression to severe COVID infection.[2] In a recent database study, Paxlovid and COVID-19 vaccination were found to decrease the severity of COVID-19 and associated mortality.[3] This study found that Paxlovid was more effective in immunosuppressed older patients, and those with neurologic or cardiovascular comorbidities.[3] In the Lagevrio study, there was a 30% reduction in risk of any-cause hospitalization (6.8% vs 9.7%) and a lower death rate (0.1% vs 1.3%) in unvaccinated adults with COVID-19 when early treatment with molnupiravir was used.[4]

There are drug-to-drug interactions to consider with these antivirals.[5] Paxlovid inhibits cytochrome P450 3A, so caution should be used when co-administering medications that rely on cytochrome P450 3A for clearance. When Paxlovid is co-administered with tofacitinib, it is recommended to dose-adjust tofacitinib because such a combination would result in a higher tofacitinib exposure.[6,7] Combining Paxlovid with immunosuppressants such as cyclosporine and tacrolimus should be avoided unless close therapeutic concentration monitoring is available. Similarly, Paxlovid may increase the concentration of systemic corticosteroids, increasing the risk of adrenal suppression and Cushing's syndrome.

Major limitations of our study were related to small sample sizes, especially in the Lagevrio cohort, and an inability to assess the impact of type and timing of COVID-19 vaccine, IBD phenotypes, and immunosuppressive therapies on antiviral efficacy. Our study found that Paxlovid decreased the risk of hospitalization in patients with IBD and COVID-19 compared with patients with IBD who did not receive antiviral medications. There was no difference between patients with IBD and those without IBD who received Paxlovid for their COVID-19 infection, indicating no decreased efficacy of Paxlovid in IBD patients when compared with propensity-matched non-IBD controls. In the small cohort of patients who received Lagevrio, we did not show any reduction in hospitalization. We encourage clinicians to consider use of Paxlovid in high-risk patients with IBD who develop COVID-19 infection as described by the National Institutes of Health.[8]

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2022.09.011.

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Conflicts of interest
These authors disclose the following: Francis A. Farraye is a consultant for BMS, Braintree Labs, GSK, IBD Educational Group, Innovation Pharmaceuticals, Janssen, Pfizer, and Sebela; and is a member of the Data and Safety Monitoring Board for Adiso Therapeutics and Lilly. The remaining authors disclose no conflicts.

Supplementary Table 1. Comparison of Demographic Parameters, IBD Types, Comorbid Diseases, and IBD Medications Between Patients in the Paxlovid and Control Cohorts Before and After Propensity-Score Matching

	Before propensity-score matching			After propensity-score matching		
Demographics	Paxlovid cohort (n = 532)	Control cohort (n = 29,589)	*P* value	Paxlovid cohort (n = 531)	Control cohort (n = 531)	*P* value
Age, *y*, mean ± SD	55.2 ± 16.2	50.3 ± 19.5	<.0001	55.2 ± 16.2	56.2 ± 17.1	.34
BMI, means ± SD	30.5 ± 6.5	29.1 ± 7.2	.01	30.5 ± 6.5	29.6 ± 6.8	.95
Female gender	331 (62%)	17811 (60%)	.32	330 (62%)	339 (63%)	.56
Hispanic or Latino	11 (2%)	1391 (4.7%)	.004	11 (2%)	14 (2.6%)	.54
Race						
White	477 (89%)	23825 (80%)	<.0001	476 (89%)	467 (87%)	.38
African American	28 (5.2%)	3437 (11%)	<.0001	28 (5.2%)	33 (6.2%)	.50
COVID vaccine						
BNT162b2 (Pfizer)	80 (15%)	1074 (3.6%)	<.0001	79 (14%)	71 (13%)	.48
Messenger RNA-1273 (Moderna)	16 (3%)	226 (0.7%)	<.0001	16 (3%)	20 (3.7%)	.49
Ad26.COV2.S (Johnson & Johnson)	10 (1.8%)	18 (0.06%)	<.0001	10 (1.8%)	10 (1.8%)	1
IBD type and subtype						
UC[a]	319 (59%)	13873 (46%)	<.0001	318 (59%)	331 (62%)	.41
Ulcerative proctitis	52 (9.7%)	2134 (7.2%)	.02	51 (9.6%)	50 (9.4%)	.91
Ulcerative rectosigmoiditis	47 (8.8%)	1491 (5%)	<.0001	46 (8.6%)	45 (8.4%)	.91
Left-sided colitis	24 (4.5%)	1381 (4.6%)	.86	24 (4.5%)	21 (3.9%)	.64
UC pancolitis	110 (20%)	4458 (15%)	.0003	109 (21%)	107 (20%)	.87
CD[a]	297 (55%)	14318 (48%)	.0007	296 (55%)	287 (54%)	.57
CD of small intestine	132 (24%)	5648 (19%)	.0009	132 (24%)	126 (23%)	.66
Intestinal obstruction/stricture	25 (4.6%)	855 (2.8%)	.01	25 (4.7%)	21 (3.9%)	.54
Fistula	19 (3.5%)	441 (1.4%)	.0001	19 (3.5%)	25 (4.7%)	.35
Abscess	10 (1.8%)	186 (0.6%)	.0004	10 (1.8%)	10 (1.8%)	1
CD of large intestine	164 (30%)	5752 (19%)	<.0001	163 (30%)	158 (29%)	.73
Intestinal obstruction/stricture	13 (2.4%)	367 (1.2%)	.01	13 (2.4%)	10 (1.8%)	.52
Fistula	22 (4.1%)	665 (2.2%)	.003	22 (4.1%)	21 (3.9%)	.87
Abscess	11 (2%)	312 (1%)	.02	11 (2%)	14 (2.6%)	.54
CD of small and large intestine	130 (24%)	4404 (14%)	<.0001	130 (24%)	118 (22%)	.38
Fistula	25 (4.6%)	726 (2.4%)	.001	25 (4.7%)	19 (359%)	.35
Abscess	11 (2%)	279 (0.9%)	.008	11 (2%)	12 (2.2%)	.83
Small intestine resection	10 (1.8%)	342 (1.1%)	.12	10 (1.8%)	10 (1.8%)	1
Total colectomy	10 (1.8%)	86 (0.2%)	<.0001	10 (1.8%)	10 (1.8%)	1
Comorbid diseases						
Diabetes mellitus	113 (21%)	7833 (26%)	.006	113 (21%)	116 (21%)	.82
Nicotine dependence	92 (17%)	6151 (20%)	.04	91 (17%)	81 (15%)	.40
Ischemic heart disease	91 (17%)	6560 (22%)	.005	91 (17%)	90 (16%)	.93
Chronic lower respiratory disease	230 (43%)	12122 (40%)	.28	230 (43%)	221 (41%)	.57
Chronic kidney disease	81 (15%)	6841 (23%)	<.0001	81 (15%)	81 (15%)	1
Heart failure	42 (7.8%)	3990 (13%)	.0002	42 (7.9%)	47 (8.8%)	.57
Medications						
Prednisone[b]	97 (18%)	5411 (18%)	.97	97 (18%)	88 (16%)	.46
Budesonide[b]	35 (6.5%)	2268 (7.6%)	.35	35 (6.5%)	31 (5.8%)	.61
Methylprednisolone[b]	79 (14%)	3591 (12%)	.05	78 (14%)	69 (12%)	.42
Infliximab	78 (14%)	3396 (11%)	.02	78 (14%)	68 (12%)	.37

Supplementary Table 1. Continued

Demographics	Before propensity-score matching			After propensity-score matching		
	Paxlovid cohort (n = 532)	Control cohort (n = 29,589)	*P* value	Paxlovid cohort (n = 531)	Control cohort (n = 531)	*P* value
Adalimumab	92 (17%)	3736 (11%)	.001	91 (17%)	80 (15%)	.35
Golimumab	10 (1.8%)	175 (0.5%)	.0002	10 (1.8%)	10 (1.8%)	1
Certolizumab	10 (1.8%)	405 (1.3%)	.31	10 (1.8%)	10 (1.8%)	1
Vedolizumab	42 (7.8%)	1522 (5%)	.004	41 (7.7%)	36 (6.7%)	.55
Ustekinumab	50 (9.3%)	1375 (4.6%)	<.0001	50 (9.4%)	46 (8.6%)	.66
Tofacitinib	10 (1.8%)	329 (1.1%)	.09	10 (1.8%)	10 (1.8%)	1
Azathioprine	62 (11%)	3132 (10%)	.42	62 (11%)	42 (7.9%)	.03
Methotrexate	41 (7.7%)	2120 (7.1%)	.62	41 (7.7%)	44 (8.2%)	.73
Mercaptopurine	32 (6%)	1437 (4.8%)	.21	31 (5.8%)	32 (6%)	.89

NOTE. One-to-one (1:1) propensity-score matching was performed for age, gender, race, ethnicity, obesity, diabetes mellitus, tobacco abuse, chronic lower respiratory disease, ischemic heart disease, heart failure, chronic kidney disease, steroids, IBD medications, and COVID-19 vaccine. After propensity-score matching, the risk of each outcome was expressed as an adjusted odds ratio with 95% CI. Baseline demographic characteristics, laboratory parameters, and medication use within 3 months of initiation of COVID-19 antiviral therapies were described using means, SDs, and proportions. Two-sided *P* values less than .05 were considered statistically significant. To maintain patient confidentiality, when numbers of events are greater than 1 but fewer than 10, TriNetX rounds up events to 10.

BMI, body mass index; CD, Crohn's disease; COVID-19, coronavirus disease 2019; IBD, inflammatory bowel disease; N/A, not applicable; UC, ulcerative colitis.

[a]Total UC and CD is not 100% owing to possible overlap of International Classification of Diseases, 10th revision, Clinical Modification codes in patients

[b]Medications prescribed within 6 months before prescription of Paxlovid.

Supplementary Table 2. Comparison of Demographic Parameters, IBD Types, Comorbid Diseases, and IBD Medications Between Patients in the Lagevrio and Control Cohorts Before and After Propensity-Score Matching

	Before propensity-score matching			After propensity-score matching		
Demographics	Lagevrio cohort (n = 150)	Control cohort (n = 29,589)	*P* value	Lagevrio cohort (n = 149)	Control cohort (n = 149)	*P* value
Age, *y*	59.7 ± 16.5	50.3 ± 19.5	<.0001	59.6 ± 16.5	59 ± 16.8	.75
BMI	29.9 ± 6.09	29.1 ± 7.26	<.0001	29.9 ± 6.11	30.2 ± 6.69	.78
Female gender	100 (66%)	17811 (60%)	.10	99 (66%)	101 (67%)	.80
Hispanic or Latino	10 (6.6%)	1391 (4.7%)	.25	10 (6.7%)	10 (6.7%)	1
Race						
White	139 (92%)	23825 (80%)	.0002	138 (92%)	134 (89%)	.41
African American	10 (6.7%)	3437 (11%)	.05	10 (6.7%)	11 (7.3%)	.82
COVID vaccine						
BNT162b2 (Pfizer)	10 (6.7%)	1074 (3.6%)	.04	10 (6.7%)	13 (8.7%)	.51
Messenger RNA-1273 (Moderna)	10 (6.7%)	226 (0.7%)	<.0001	10 (6.7%)	10 (6.7%)	1
Ad26.COV2.S (Johnson & Johnson)	10 (6.7%)	18 (0.06%)	<.0001	0	0	N/A
IBD type and subtype						
UC[a]	84 (56%)	13873 (46%)	.02	83 (55%)	71 (47%)	.16
Ulcerative proctitis	15 (10%)	2134 (7.2%)	.18	15 (10%)	15 (10%)	1
Ulcerative rectosigmoiditis	10 (6.7%)	1491 (5%)	.36	10 (6.7%)	10 (6.7%)	1
Left-sided colitis	10 (6.7%)	1381 (4.6%)	.24	10 (6.7%)	10 (6.7%)	1
UC pancolitis	32 (21%)	4458 (15%)	.03	32 (21%)	22 (14%)	.13
CD[a]	82 (54%)	14318 (48%)	.12	52 (34%)	43 (28%)	.26
CD of small intestine	30 (20%)	5648 (19%)	.77	30 (20%)	34 (22%)	.57
Intestinal obstruction/stricture	10 (6.7%)	855 (2.8%)	.006	10 (6.7%)	10 (6.7%)	1
Fistula	10 (6.7%)	441 (1.4%)	<.0001	10 (6.7%)	10 (6.7%)	1
Abscess	0	186 (0.6%)	.33	0	0	N/A
CD of large intestine	30 (20%)	5742 (19%)	.85	30 (20%)	22 (14%)	.87
Intestinal obstruction/stricture	10 (6.7%)	367 (1.2%)	<.001	10 (6.7%)	0	.001
Fistula	10 (6.7%)	665 (2.2%)	.0003	10 (6.7%)	0	.0013
Abscess	0	312 (1%)	.20	0	0	N/A
CD of small and large intestine	21 (14%)	4404 (14%)	.76	21 (14%)	31 (20%)	.1
Fistula	0	726 (2.4%)	.05	0	0	N/A
Abscess	0	279 (0.9%)	.23	0	0	N/A
Small intestine resection	0	10 (0.03%)	.82	0	0	N/A
Total colectomy	10 (6.6%)	86 (0.2%)	<.0001	10 (6.7%)	10 (6.7%)	1
Comorbid diseases						
Diabetes mellitus	52 (34%)	7833 (26%)	.02	52 (34%)	43 (28%)	.26
Nicotine dependence	22 (14%)	6151 (20%)	.06	22 (14%)	20 (13%)	.73
Ischemic heart disease	43 (28%)	6560 (22%)	.05	43 (28%)	39 (26%)	.60
Chronic lower respiratory disease	87 (58%)	12122 (40%)	<.0001	86 (57%)	86 (57%)	1
Chronic kidney disease	51 (34%)	6841 (23%)	.001	51 (34%)	47 (31%)	.62
Heart failure	23 (15%)	3990 (13%)	.50	23 (15%)	22 (14%)	.87
Medications						
Prednisone[b]	22 (14%)	5411 (18%)	.25	22 (14%)	21 (14%)	.86
Budesonide[b]	10 (6.6%)	2268 (7.6)	.64	10 (6.6%)	10 (6.6%)	1
Methylprednisolone[b]	12 (8%)	3591 (12%)	.12	12 (8%)	10 (6.6%)	.65
Infliximab	15 (10%)	3396 (11%)	.57	15 (10%)	15 (10%)	1
Adalimumab	21 (14%)	3736 (12%)	.61	21 (14%)	23 (15%)	.74
Golimumab	10 (6.6%)	175 (0.5%)	<.0001	10 (6.6%)	10 (6.6%)	1
Certolizumab	10 (6.6%)	405 (1.3%)	<.0001	10 (6.6%)	10 (6.6%)	1
Vedolizumab	10 (6.6%)	1522 (5.1%)	.39	10 (6.6%)	10 (6.6%)	1

Supplementary Table 2. Continued

Demographics	Before propensity-score matching			After propensity-score matching		
	Lagevrio cohort (n = 150)	Control cohort (n = 29,589)	*P* value	Lagevrio cohort (n = 149)	Control cohort (n = 149)	*P* value
Ustekinumab	10 (6.6%)	1375 (4.6%)	.24	10 (6.6%)	10 (6.6%)	1
Tofacitinib	10 (6.6%)	329 (1.1%)	<.0001	10 (6.6%)	10 (6.6%)	1
Azathioprine	20 (13%)	3132 (10%)	.27	20 (13%)	22 (14%)	1
Methotrexate	12 (8%)	2120 (7%)	.69	12 (8%)	17 (11%)	.32
Mercaptopurine	10 (6.6%)	1437 (4.8%)	.30	10 (6.6%)	10 (6.6%)	1

NOTE. To maintain patient confidentiality, when numbers of events are greater than 1 but fewer than 10, TriNetX rounds up events to 10.
BMI, body mass index; CD, Crohn's disease; COVID, coronavirus disease; IBD, inflammatory bowel disease; N/A, not applicable; UC, ulcerative colitis.
[a]Total UC and CD is not 100% owing to possible overlap of International Classification of Diseases, 10th revision, Clinical Modification codes in patients
[b]Medications prescribed within 6 months before prescription of Lagevrio.