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The impact of vedolizumab on COVID-19 outcomes among adult IBD patients in the SECURE-IBD registry

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Introduction

The impact of immune-modifying therapies on outcomes of Coronavirus disease of 2019 (COVID-19) is variable. The purpose of this study was to determine the impact of vedolizumab (VDZ), a gut-selective anti-integrin, on COVID-19 outcomes in inflammatory bowel disease (IBD) patients.

Methods

Using data from the Surveillance of Coronavirus Under Research Exclusion for IBD (SECURE-IBD), an international registry of IBD patients with confirmed COVID-19, we studied the impact of VDZ on COVID-19 hospitalization and severe COVID-19 (intensive care unit stay, mechanical ventilation and/or death).

Results

Of 3,647 adult patients on any IBD medication in the registry, 457 (12.5%) patients were on VDZ. On multivariable analyses using backward selection of covariates, VDZ use was not associated with hospitalization or severe COVID-19 when comparing to patients on all other medications [adjusted odds ratio (aOR) 0.87; 95% confidence interval (CI) 0.71, 1.1 and aOR 0.95; 95% CI 0.53; 1.73, respectively]. On comparing VDZ monotherapy to anti-TNF monotherapy, the odds for hospitalization, but not severe COVID-19, were higher (aOR CI 1.39; 95% CI 1.001, 1.90 and aOR 2.92; 95% CI 0.98, 8.71, respectively). In an exploratory analysis, VDZ monotherapy, compared to anti-TNF monotherapy, was associated with new-onset GI symptoms at the time of COVID-19, especially among patients whose IBD was in remission.

Conclusions

COVID-19 outcomes among IBD patients on VDZ are comparable to those on all other therapies. Hospitalization, but not severe COVID-19, is more likely with VDZ monotherapy than with anti-TNF monotherapy. Overall, VDZ appears to be safe in IBD patients with COVID-19.

Key words: inflammatory bowel disease; Crohn’s disease; ulcerative colitis; Coronavirus disease 2019; vedolizumab; outcomes.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to an unrelenting pandemic, affecting over 85 million persons globally with 2.32 million deaths until February 8, 2021 (1). Comorbid disease is a risk factor for worse outcomes (2), and medications that modulate the immune system can have varying effects on COVID-19, depending on their mechanism of action. SARS-CoV-2, in addition to infecting the respiratory epithelium, can also infect the gastrointestinal (GI) tract mucosa via angiotensin converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TRMPRSS) (3). In addition to upper and lower respiratory symptoms, COVID-19 can be associated with GI symptoms such as anorexia, vomiting and diarrhea (4).

Vedolizumab (VDZ), a monoclonal antibody against $\alpha_4\beta_7$ integrin, blocks the interaction between $\alpha 4\beta 7$ integrin on CD4+ T cells and its receptor mucosal addressin cell adhesion molecule (MAdCAM) on high endothelial venules (HEV) in the GI tract, with downstream blockage of lymphocyte trafficking into gut-associated lymphoid tissue (GALT), (5). VDZ is approved for the treatment of moderate-severe ulcerative colitis (UC) and Crohn's disease (CD) in adult patients (5, 6). Given its gut-specific mechanism of action, VDZ does not impact systemic immunity significantly and has a favorable safety profile (7). However, VDZ is associated with an increased risk of *Clostridium difficile* and other intestinal infections (8). Recent data report that VDZ may modulate ACE2 expression in the GI tract (9).

We aimed to determine the outcomes of COVID-19 infection among IBD patients on VDZ compared to other IBD therapies. We also determined the proportion of IBD patients on VDZ who had new-onset GI symptoms at the time of COVID-19.

Methods

Data source

The Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry is a global, web-based, collaborative database, which was established at the start of the COVID-19 pandemic in March 2020 to study characteristics and outcomes in IBD patients with confirmed COVID-19, as well as the impact of IBD therapies (10). Healthcare providers voluntarily report confirmed COVID-19 cases using a REDCap (Research Electronic Data Capture) survey at our website covidibd.org, hosted at the University of North Carolina. SECURE-IBD collects only de-identified data, and the Office of Human Research Ethics at the University of North Carolina, Chapel Hill determined that the storage and analysis of de-identified data for this project did

not constitute human subjects research. Details of the data collection and quality control are described in detail in a previous publication (10).

Statistical analysis

Using data reported though January 26, 2021, we compared baseline and demographic characteristics, and COVID-19 outcomes of adult IBD patients on VDZ therapy to those on all other IBD medications. As VDZ is approved for treatment of adult IBD patients only, we excluded patients ≤18 years of age from this analysis. Our primary outcome was adverse COVID-19, defined as hospitalization or death due to COVID-19. Our secondary outcome was severe COVID-19 defined as a composite of intensive care unit (ICU) admission, mechanical ventilation and/or death. We compared all outcomes among adult patients on VDZ vs all other IBD therapies in the registry (VDZ vs. non-VDZ). As the category of all other medications is heterogenous, we additionally compared VDZ monotherapy with anti-tumor necrosis factor (TNF) monotherapy, which is the largest homogenous category of reported medications in the registry. Lastly, as an exploratory analysis, we compared the frequency of GI symptoms due to COVID-19 between VDZ and non-VDZ groups as well as between VDZ monotherapy and anti-TNF monotherapy groups.

We analyzed categorical variables using Chi-square or Fisher-Exact tests, and continuous variables using Wilcoxon rank-sum or t-test when applicable. Using generalized estimating equations (GEE) to account for clustering by country, and applying the logit link function, we estimated the odds of each of the two binary outcomes, adverse and severe COVID-19. In addition to the primary predictor variable medication group, covariates in each of the models were determined by backward selection to obtain the most parsimonious models from clinically-relevant covariates determined *a priori*, or if associated with medication group at p value ≤0.10 level on bivariate analysis. Considered covariates included age, sex, race/ethnicity, IBD type, IBD activity [remission vs active disease, based on physician global assessment (PGA)] and comorbidities (0, 1, ≥2). Additionally, as IBD activity may modify the association between treatment and each study outcome, and treatment and GI symptoms, we repeated all analyses stratified by IBD activity categorized as remission versus active disease. P values ≤0.05 were considered statistically significant for all analyses. Data preparation and analyses were conducted using SAS version 9.3 (SAS Institute, Cary, North Carolina).

Results

Cohort baseline characteristics

Of 3,647 patients ≥18 years old in the SECURE-IBD registry on one or more IBD medication, 457 (12.5%) patients were reported to be on VDZ, of whom 334 (9.2%) were on VDZ monotherapy. 1043 (28.6%) patients were on an anti-TNF monotherapy. Of these, 536 (51.4%) patients were on an intravenous anti-TNF while the remaining 507 (48.6%) patients were on a subcutaneous anti-TNF. 354 (9.7%) patients were on combination therapy with an

anti-TNF and an immunomodulator. The baseline demographic and clinical characteristics of all patients in VDZ vs. non-VDZ groups are reported in Table 1. Compared to the non-VDZ group, patients on VDZ were slightly older (mean age 43.8 years vs 42.0 years, p=0.03), more likely to be white (86.0% vs 81.2%, p=0.01) and less likely to be Asian or Hispanic (1.8% vs. 5.0%, p=0.002 and 10.9% vs 14.9%, p<0.001, respectively). Of patients on VDZ, 209 (45.7%) were from the United States, whereas of those on other therapies, 1110 (34.8%) were from the United States (p<0.001). Compared to the non-VDZ group, more patients in the VDZ group had UC (53.8% vs 40.2%, p<0.001). Other baseline and clinical characteristics were similar between the two groups. Baseline characteristics of VDZ monotherapy compared to anti-TNF monotherapy are reported in the supplementary table.

COVID-19 outcomes in adult IBD patients on VDZ compared to other therapies

Six hundred and sixty-four hospitalization and 166 severe COVID events occurred in the cohort. Compared to non-VDZ use, VDZ use was not associated with hospitalization [adjusted odds ratio (aOR) 0.87; 95% confidence interval (CI) 0.71, 1.1, Table 2] after adjusting for age, Asian and Other race/ethnicity groups compared to non-Hispanic White group, IBD type, sex and number of comorbidities. Similarly, compared to non-VDZ use, VDZ use was not associated with severe COVID-19 (aOR 0.95; 95% CI 0.53, 1.73) on adjusting for age, IBD type, comorbidities and IBD activity. Upon stratifying by IBD activity (active disease vs remission), the results were not significantly altered. In the stratum of active IBD, compared to non-VDZ use, VDZ use was not associated with hospitalization (aOR 0.95; 95% CI 0.72, 1.25) or severe COVID-19 (aOR 0.91; 95% CI 0.46, 1.81). Similarly, in the stratum of IBD remission, compared to non-VDZ use, VDZ was not associated with hospitalization (aOR 0.84; 95% CI 0.61, 1.15) or severe COVID-19 (aOR 1.40; 95% CI 0.53, 3.67).

Upon comparing to anti-TNF monotherapy, VDZ monotherapy was associated with higher odds of hospitalization (aOR 1.38; 95% CI 1.001, 1.90, Table 2) after adjusting for age, number of comorbidities, Asian and Other races compared to non-Hispanic White group and IBD activity. The magnitude and direction of the association of VDZ monotherapy, compared to anti-TNF monotherapy, with severe COVID-19 outcomes were similar but not statistically significant after adjusting for age and number of comorbidities (aOR 2.92; 95% CI 0.98, 8.71). Upon stratifying by IBD activity, results remained similar in magnitude and direction. The association of VDZ monotherapy with hospitalization was not significant in the stratum of active IBD (aOR 1.32; 95% CI 0.75, 2.33), but it was significant in the stratum of IBD in remission (aOR 1.54; 95% CI 1.05, 2.25). The number of severe COVID-19 outcomes in the VDZ and anti-TNF monotherapies groups were too few for stratified analyses.

GI symptoms due to COVID-19

All GI symptoms (nausea, vomiting, abdominal pain, diarrhea and “other”) were comparable between VDZ and non-VDZ groups (p >0.05), Table 3). On stratifying by IBD activity, all GI symptoms were comparable in both strata except nausea, which was more common with VDZ in those with IBD in remission (8.8% vs 4.4%, p=0.004).

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On comparing VDZ monotherapy with anti-TNF monotherapy, all GI symptoms except other symptoms were more common with VDZ monotherapy ($p < 0.05$ for each comparison). When we stratified these comparisons by IBD activity, among patients with active IBD, all GI symptoms were similar in frequency with VDZ and anti-TNF monotherapies. Among IBD patients in remission, all GI symptoms, except vomiting and other, were more common with VDZ monotherapy ($p \leq 0.001$ for each comparison except vomiting and other).

Discussion

In this analysis of 3,647 adult patients from 63 countries in the SECURE-IBD registry, we report COVID-19 outcomes among 457 patients on VDZ therapy compared to other IBD therapies. Overall, we observed comparable COVID-19 outcomes among IBD patients on VDZ versus those on all other therapies. New-onset GI symptoms were reported in 29.6% of patients on VDZ monotherapy and 19.2% of patients on anti-TNF monotherapy. Hospitalization and the development of GI symptoms were more frequently observed with VDZ monotherapy than with anti-TNF monotherapy.

Hospitalization and severe COVID-19 outcomes were comparable among VDZ and non-VDZ users, unchanged upon stratification by IBD activity. These findings are consistent with other data on COVID-19 outcomes among IBD patients on VDZ, although there are few such patients in each of these analyses. Lukin, Kumar et al reported in a case-control study that COVID-19 outcomes of patients on all biologic therapies, including VDZ (n=10), were comparable, although VDZ was not studied individually (11). Similarly, Axelrad et al reported in a descriptive case series that there were no differences in outcomes among patients on VDZ (n=5) compared to other IBD therapies (12). Given the gut-selective mechanism of action of VDZ and lack of significant systemic adverse effects (7), its safety in patients with COVID-19 is reassuring. It is important to note that the comparator, non-VDZ group is heterogenous and includes patients on all other medications such as 5-aminosalisylic acid, corticosteroids, immunomodulators, biologics and combination therapies, each of which can have varying impact on COVID-19 outcomes (13).

In order to characterize the impact of VDZ in more homogenous medication groups, we additionally compared COVID-19 outcomes among patients on VDZ monotherapy to those on anti-TNF monotherapy. In adjusted analyses, hospitalization was 38% more likely to occur with VDZ monotherapy compared to anti-TNF monotherapy. There was no difference in severe COVID-19 between the two groups, but the direction of the effect was consistent with that of hospitalization. These findings may reflect a potentially protective effect of anti-TNF therapy, as demonstrated in previous data from our registry (13) and other emerging studies (14, 15). Data on mucosal gene expression suggest downregulation of ACE2 in UC patients who respond to TNFi, but not in patients treated with VDZ (16). Furthermore, VDZ

mediated attenuation of lymphocyte aggregates in the GI tract may explain these findings, at least in part (17).

As an exploratory analysis, we also noted that new-onset GI symptoms in IBD patients with COVID-19, while reported in a minority of patients, were similar in frequency in patients on VDZ, when compared to other therapies overall. With stratification by IBD activity, nausea, but not other symptoms, was more common among patients in remission and on VDZ. However, compared to patients on anti-TNF monotherapy, patients on VDZ monotherapy more frequently experienced most GI symptoms. Upon stratification by IBD activity, GI symptoms tended to be more common among patients on VDZ who were in remission. However, the number of patients reporting GI symptoms due to COVID-19 in each subgroup is few, making clinically meaningful interpretation difficult. The higher frequency of GI symptoms in VDZ-treated patients, as compared to anti-TNF treated patients, may partially explain the higher odds of hospitalization in VDZ- treated patients.

Our study has several strengths. We have data on COVID-19 outcomes on close to 3,500 adult IBD patients in a large collaborative registry of IBD patients from 63 different countries on diverse IBD medications, of which more than 450 patients were on VDZ. This is the largest report of COVID-19 outcomes among patients on VDZ therapy. Limitations of this voluntary registry include the risk of reporting bias, which may lead to documentation of the more severe cases that come to the attention of healthcare providers, while the milder cases may remain undiagnosed or underreported. Conversely, frequently tested asymptomatic patients may be diagnosed incidentally. However, given the large sample size and representation of patients in various subgroups, this is less likely. Other limitations include unmeasured confounding, risk of misclassification of the cause of GI symptoms (IBD vs COVID-19) and missing data, although the latter was <4% for all variables except ethnicity and body mass index.

In conclusion, COVID-19 outcomes among IBD patients on VDZ are comparable to those on other therapies. Hospitalization, but not severe COVID-19, is slightly more likely with VDZ monotherapy than with anti-TNF monotherapy, possibly due to higher frequency of GI symptoms with VDZ. These findings reiterate the overall safety of VDZ in IBD patients with COVID-19.

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Table 1: Demographic and clinical characteristics of IBD patients on vedolizumab compared with other IBD therapies in the SECURE-IBD registry

Characteristic[a,b]	All patients on ≥1 medication and ≥18 years of age		Vedolizumab		Other IBD therapy		
	N	%	N	%	N	%	P-value[c]
Total number of patients	3647		457	12.5%	3190	87.5%	
Age							
Mean (SD)	42.2	16.4	43.8	17.82	42.0	16.12	0.031
Median (IQ range)	40	29.0 ,53.0	40	29.0 ,55.0	40	29.0, 53.0	0.137
Female sex	1847	50.6%	239	52.3%	1608	50.4%	0.450
Race							
Reported at least selected one race	3620	99.3%	454	99.3%	3166	99.2%	1.000
White	2983	81.8%	393	86.0%	2590	81.2%	0.013
Black or African American	175	4.8%	22	4.8%	153	4.8%	0.987
American Indian/Native Alaskan	8	0.2%	0	0.0%	8	0.3%	0.607
Asian	167	4.6%	8	1.8%	159	5.0%	0.002
Native Hawaiian/Pacific Islander	1	0.0%	0	0.0%	1	0.0%	1.000
Other	205	5.6%	18	3.9%	187	5.9%	0.095
Unknown	184	5.0%	20	4.4%	164	5.1%	0.485
Hispanic/Latino							<0.001
Yes	524	14.4%	50	10.9%	474	14.9%	
No	2493	68.4%	349	76.4%	2144	67.2%	
Unknown	403	11.1%	31	6.8%	372	11.7%	
Missing	227	6.2%	27	5.9%	200	6.3%	
Reporting Country							
United States	1319	36.2%	209	45.7%	1110	34.8%	<0.001
Spain	279	7.7%	24	5.3%	255	8.0%	0.039
Russian Federation	261	7.2%	37	8.1%	224	7.0%	0.405
United Kingdom	156	4.3%	16	3.5%	140	4.4%	0.380
France	106	2.9%	10	2.2%	96	3.0%	0.328
Italy	150	4.1%	23	5.0%	127	4.0%	0.290
Brazil	101	2.8%	9	2.0%	92	2.9%	0.265
Iran, Islamic Republic of	51	1.4%	0	0.0%	51	1.6%	0.006
Belgium	136	3.7%	22	4.8%	114	3.6%	0.191
Argentina	59	1.6%	4	0.9%	55	1.7%	0.179
Germany	99	2.7%	20	4.4%	79	2.5%	0.019
Turkey	73	2.0%	7	1.5%	66	2.1%	0.443
Netherlands	158	4.3%	13	2.8%	145	4.5%	0.095
Canada	63	1.7%	7	1.5%	56	1.8%	0.731
Other	636	17.4%	56	12.3%	580	18.2%	0.002
Disease Type:							<0.001
Crohn's Disease	2049	56.2%	201	44.0%	1848	57.9%	
Ulcerative colitis	1527	41.9%	246	53.8%	1281	40.2%	
IBD unspecified	57	1.6%	8	1.8%	49	1.5%	
IBD disease activity[d]							0.149
Remission	1982	54.3%	228	49.9%	1754	55.0%	
Mild	792	21.7%	104	22.8%	688	21.6%	
Moderate/Severe	720	19.7%	103	22.5%	617	19.3%	
Smoking	145	4.0%	12	2.6%	133	4.2%	0.114
Comorbidity summary score							0.194
0	2517	69.0%	320	70.0%	2197	68.9%	
1	772	21.2%	83	18.2%	689	21.6%	
2	208	5.7%	33	7.2%	175	5.5%	
≥3	150	4.1%	21	4.6%	129	4.0%	
Cardiovascular disease	206	5.6%	25	5.5%	181	5.7%	0.860
Diabetes	178	4.9%	23	5.0%	155	4.9%	0.872

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Asthma	177	4.9%	29	6.3%	148	4.6%	0.112
COPD	50	1.4%	7	1.5%	43	1.3%	0.752
Other chronic lung disease	50	1.4%	5	1.1%	45	1.4%	0.586
Hypertension	378	10.4%	41	9.0%	337	10.6%	0.296
Cancer	56	1.5%	9	2.0%	47	1.5%	0.420
History of stroke	33	0.9%	3	0.7%	30	0.9%	0.791
Chronic renal disease	71	1.9%	13	2.8%	58	1.8%	0.137
Chronic liver disease	105	2.9%	17	3.7%	88	2.8%	0.250
Other comorbidity	412	11.3%	58	12.7%	354	11.1%	0.314
BMI							0.280
BMI<30	2440	66.9%	320	70.0%	2120	66.5%	
BMI ≥30	609	16.7%	72	15.8%	537	16.8%	
Missing	598	16.4%	65	14.2%	533	16.7%	

[a] Unless otherwise specified, percentages do not include missing values or "unknown." For all characteristics, unless noted above, less than 4% of data were missing and unknown, respectively, for each category.

[b] Percentages and n from each subcategory may not add up to the exact number of total reported cases due to missing values and/or non-mutually exclusive variables.

[c] P-values for tests comparing variables between vedolizumab and other medications groups

[d] By physician global assessment (PGA) at time of COVID-19 infection

Abbreviations: COVID-19 = Coronavirus Disease 2019; ICU = intensive care unit; COPD = chronic obstructive pulmonary disease; IBD = inflammatory bowel disease; PSC = primary sclerosing cholangitis; NAFLD = non-alcoholic fatty liver disease

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Table 2: Multivariable regression analyses with backward selection of covariates for COVID-19 outcomes by medication class from adult cases in the SECURE-IBD registry

Outcome	Adjusted OR (95% CI)	P value
Hospitalization		
VDZ vs. all other IBD therapies[#]	0.87 (0.72, 1.06)	0.17
VDZ monotherapy vs. anti-TNF monotherapy[##]	**1.38 (1.001, 1.90)**	**0.049**
Severe COVID-19		
VDZ vs. all other IBD therapies*	0.95 (0.53, 1.73)	0.88
VDZ monotherapy vs. anti-TNF monotherapy**	2.92 (0.98, 8.71)	0.055

[#] adjusted for age, sex, Asian and other race/ethnicity category (reference: non-Hispanic White), IBD type, active IBD (reference: remission; based on Physician Global Assessment [PGA]) and number of comorbid conditions (1, ≥2; reference: 0)

[##] adjusted for age and IBD activity, Asian and other race/ethnicity category and number of comorbid conditions

* adjusted for age, IBD type, IBD activity and number of comorbid conditions

** adjusted for age and number of comorbid conditions

Statistically significant associations are in bold.

Abbreviations: COVID-19 = Coronavirus Disease 2019; SECURE-IBD = Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease; VDZ = vedolizumab; TNF = tumor necrosis factor; vs. = versus; OR = odds ratio.

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Table 3: Gastrointestinal symptoms due to COVID-19 in adult patients on VDZ compared to those on other IBD therapies, and on VDZ monotherapy compared to anti-TNF monotherapy, in the SECURE-IBD registry, overall and stratified by IBD activity

Overall										
	VDZ use vs. non-use					VDZ monotherapy vs. anti-TNF monotherapy				
Gastrointestinal symptom	VDZ		All other IBD therapies			Vedolizumab monotherapy		Anti-TNF monotherapy		
	N	(%)	N	(%)	P value	N	(%)	N	(%)	P value
Abdominal pain	37	8.1%	250	7.8%	0.847	**30**	**9.0%**	**58**	**5.6%**	**0.026**
Diarrhea	89	19.5%	616	19.3%	0.934	**74**	**22.2%**	**167**	**16.0%**	**0.010**
Nausea	32	7.0%	167	5.2%	0.120	**29**	**8.7%**	**38**	**3.6%**	**<0.001**
Vomiting	14	3.1%	86	2.7%	0.653	**12**	**3.6%**	**18**	**1.7%**	**0.042**
Other	10	2.2%	88	2.8%	0.481	9	2.7%	19	1.8%	0.325
Any GI symptom	116	25.4%	770	24.1%	0.822	**99**	**29.6%**	**200**	**19.2%**	**<0.001**
Among patients with active IBD*										
	VDZ use vs. non-use					VDZ monotherapy vs. anti-TNF monotherapy				
Gastrointestinal symptom	VDZ		All other IBD therapies			Vedolizumab monotherapy		Anti-TNF monotherapy		
	N	(%)	N	(%)	P value	N	(%)	N	(%)	P value
Abdominal pain	18	8.7%	148	11.3%	0.258	13	10.0%	35	10.6%	0.840
Diarrhea	41	19.8%	289	22.1%	0.449	30	23.1%	80	24.3%	0.779
Nausea	12	5.8%	84	6.4%	0.726	10	7.7%	15	4.6%	0.183
Vomiting	6	2.9%	43	3.3%	0.765	5	3.8%	8	2.4%	0.532
Other	4	1.9%	41	3.1%	0.341	3	2.3%	11	3.3%	0.766
Any GI symptom	49	23.7%	353	27.0%	0.556	37	28.5%	95	28.9%	0.875
Among patients with IBD in remission*										
	VDZ use vs. non-use					VDZ monotherapy vs. anti-TNF monotherapy				
Gastrointestinal symptom	VDZ		All other IBD therapies			Vedolizumab monotherapy		Anti-TNF monotherapy		
	N	(%)	N	(%)	P value	N	(%)	N	(%)	P value
Abdominal pain	18	7.9%	93	5.3%	0.109	**17**	**9.0%**	**23**	**3.4%**	**0.001**

Diarrhea	46	20.2 %	292	16.6 %	0.183	**43**	**22.9%**	**82**	**12.3%**	**<0.001**
Nausea	**20**	**8.8%**	**77**	**4.4%**	**0.004**	**19**	**10.1%**	**23**	**3.4%**	**<0.001**
Vomiting	8	3.5%	38	2.2%	0.205	**7**	**3.7%**	**10**	**1.5%**	**0.072**
Other	5	2.2%	39	2.2%	0.977	5	2.7%	7	1.0%	0.150
Any GI symptom	**64**	**28.1 %**	**374**	**21.3 %**	**0.027**	**60**	**31.9%**	**99**	**14.8%**	**<0.001**

Statistically significant associations are in bold.

*based on Physician Global Assessment (PGA)

Abbreviations: COVID-19 = Coronavirus Disease 2019; SECURE-IBD = Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease; VDZ = vedolizumab; TNF = tumor necrosis factor.

References

1. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) 2020 [updated July 6, 2020. Available from: https://coronavirus.jhu.edu/map.html.
2. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet (London, England). 2020;395(10239):1763-70.
3. Burgueño JF, Reich A, Hazime H, Quintero MA, Fernandez I, Fritsch J, et al. Expression of SARS-CoV-2 Entry Molecules ACE2 and TMPRSS2 in the Gut of Patients With IBD. Inflammatory bowel diseases. 2020;26(6):797-808.
4. Chen A, Agarwal A, Ravindran N, To C, Zhang T, Thuluvath PJ. Are Gastrointestinal Symptoms Specific for Coronavirus 2019 Infection? A Prospective Case-Control Study From the United States. Gastroenterology. 2020;159(3):1161-3.e2.
5. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. The New England journal of medicine. 2013;369(8):699-710.
6. Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel JF, Sands BE, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. The New England journal of medicine. 2013;369(8):711-21.
7. Colombel JF, Sands BE, Rutgeerts P, Sandborn W, Danese S, D'Haens G, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut. 2017;66(5):839-51.
8. Kirchgesner J, Lemaitre M, Carrat F, Zureik M, Carbonnel F, Dray-Spira R. Risk of Serious and Opportunistic Infections Associated With Treatment of Inflammatory Bowel Diseases. Gastroenterology. 2018;155(2):337-46.e10.
9. Suárez-Fariñas M, Tokuyama M, Wei G, Huang R, Livanos A, Jha D, et al. Intestinal Inflammation Modulates the Expression of ACE2 and TMPRSS2 and Potentially Overlaps With the Pathogenesis of SARS-CoV-2-related Disease. Gastroenterology. 2021;160(1):287-301.e20.
10. Brenner EJ, Ungaro RC, Gearry RB, Kaplan GG, Kissous-Hunt M, Lewis JD, et al. Corticosteroids, But Not TNF Antagonists, Are Associated With Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results From an International Registry. Gastroenterology. 2020;159(2):481-91.e3.
11. Lukin DJ, Kumar A, Hajifathalian K, Sharaiha RZ, Scherl EJ, Longman RS. Baseline Disease Activity and Steroid Therapy Stratify Risk of COVID-19 in Patients With Inflammatory Bowel Disease. Gastroenterology. 2020;159(4):1541-4.e2.
12. Axelrad JE, Malter L, Hong S, Chang S, Bosworth B, Hudesman D. From the American Epicenter: Coronavirus Disease 2019 in Patients with Inflammatory Bowel Disease in the New York City Metropolitan Area. Inflammatory bowel diseases. 2020.
13. Ungaro RC, Brenner EJ, Gearry RB, Kaplan GG, Kissous-Hunt M, Lewis JD, et al. Effect of IBD medications on COVID-19 outcomes: results from an international registry. Gut. 2021;70(4):725-32.
14. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI, Gossec L, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Annals of the rheumatic diseases. 2020;79(7):859-66.

15. Strangfeld A, Schäfer M, Gianfrancesco MA, Lawson-Tovey S, Liew JW, Ljung L, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Annals of the rheumatic diseases. 2021.
16. Arijs I, De Hertogh G, Lemmens B, Van Lommel L, de Bruyn M, Vanhove W, et al. Effect of vedolizumab (anti-α4β7-integrin) therapy on histological healing and mucosal gene expression in patients with UC. Gut. 2018;67(1):43-52.
17. Uzzan M, Tokuyama M, Rosenstein AK, Tomescu C, SahBandar IN, Ko HM, et al. Anti-alpha4beta7 therapy targets lymphoid aggregates in the gastrointestinal tract of HIV-1-infected individuals. Sci Transl Med. 2018;10(461).