

Characteristics and Outcomes of IBD Patients with COVID-19 on Tofacitinib Therapy in the SECURE-IBD Registry

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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 unprecedented loss of life and health on a global scale.¹ COVID-19 outcomes are more severe among those with comorbid conditions,¹ which raises concerns for patients with inflammatory bowel disease (IBD), especially given the increased infection risk with immunosuppression used for IBD therapy.

Tofacitinib is a Janus kinase inhibitor (JAKi) approved for the treatment of ulcerative colitis (UC)² and other immune-mediated diseases. Tofacitinib is associated with higher risk of herpes zoster (HZ) infection.² Although HZ is a DNA virus, little is known regarding risks and outcomes of RNA viral infections such as SARS-CoV-2 with JAKi. Type 1 interferons, central to anti-SARS-CoV-2 activity and induced by the JAK-STAT pathway, were found to be impaired in severe COVID-19 in some studies and conversely upregulated in others, possibly reflecting heterogeneity in COVID-19 severity.³ Emerging data

in non-IBD patients suggest that JAKi may blunt the cytokine storm that characterizes severe COVID-19 and potentially improve outcomes.⁴ In fact, a number of JAKi such as tofacitinib, baricitinib and ruxolitinib are being studied in clinical trials for COVID-19 treatment.

Moreover, hospitalized COVID-19 patients are at a greater risk of thromboembolic events. This is important because findings from an interim analysis of a rheumatoid arthritis study for tofacitinib in older patients with ≥ 1 cardiovascular risk factor, alongside data from other JAKi clinical programs, suggest a higher risk of venous thromboembolic events.⁵

Emerging data on COVID-19 outcomes in patients with immune-mediated diseases treated with JAKi do not indicate worse outcomes compared with other immunosuppressive therapies; prior studies have been limited by very small sample sizes of fewer than 10 patients.⁶⁻⁹ To address this critical knowledge gap, we analyzed characteristics and outcomes of tofacitinib-treated IBD patients with COVID-19 compared with those on other medications in a global registry.

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TABLE 1. Demographic and Clinical Characteristics of IBD Patients on Tofacitinib Compared With Other IBD Therapies in the SECURE-IBD Registry

Characteristic ^{a,b}	All Patients on ≥1 Medication			Tofacitinib			Other IBD Therapy			P ^c
	N (Mean)	% (SD)	N (Mean)	% (SD)	N (Mean)	% (SD)	N (Mean)	% (SD)		
Total number of patients	2326		37		2289					
Mean age	41.5	18.1	42.4	17.18	41.5	18.08				0.747
Median age (IQR)	39	27.0, 54.0	41	30.5, 55.0	39	27.0, 54.0				0.670
Female sex	1150	49.4%	15	40.5%	1135	49.6%				0.275
Race										
White	1840	79.1%	29	78.4%	1811	79.1%				0.913
Black or African American	158	6.8%	1	2.7%	157	6.9%				0.512
American Indian/Native Alaskan	4	0.2%	0	0.0%	4	0.2%				>0.999
Asian	132	5.7%	2	5.4%	130	5.7%				>0.999
Native Hawaiian/Pacific Islander	0	0.0%	0	0.0%	0	0.0%				—
Other	175	7.5%	3	8.1%	172	7.5%				0.755
Unknown	96	4.1%	3	8.1%	93	4.1%				0.194
Hispanic/Latinx										0.480
Yes	407	17.5%	4	10.8%	403	17.6%				
No	1484	63.8%	27	73.0%	1457	63.7%				
Unknown	278	12.0%	4	10.8%	274	12.0%				
Missing	157	6.7%	2	5.4%	155	6.8%				
Reporting Country										
United States	926	39.8%	19	51.4%	907	39.6%				0.148
Spain	247	10.6%	6	16.2%	241	10.5%				0.276
Russian Federation	140	6.0%	3	8.1%	137	6.0%				0.485
United Kingdom	95	4.1%	0	0.0%	95	4.2%				0.401
France	102	4.4%	1	2.7%	101	4.4%				>0.999
Italy	81	3.5%	0	0.0%	81	3.5%				0.638
Brazil	85	3.7%	1	2.7%	84	3.7%				>0.999
Iran, Islamic Republic of	53	2.3%	1	2.7%	52	2.3%				0.577
Belgium	48	2.1%	1	2.7%	47	2.1%				0.541
Argentina	49	2.1%	0	0.0%	49	2.1%				>0.999
Germany	46	2.0%	1	2.7%	45	2.0%				0.525
Turkey	41	1.8%	0	0.0%	41	1.8%				>0.999
Netherlands	32	1.4%	1	2.7%	31	1.4%				0.403
Canada	33	1.4%	1	2.7%	32	1.4%				0.413
Other	348	15.0%	2	5.4%	346	15.1%				0.100
Disease Type*										<0.001
Crohn's Disease	1299	55.8%	6	16.2%	1293	56.5%				
Ulcerative Colitis	976	42.0%	30	81.1%	946	41.3%				
IBD-unspecified	45	1.9%	1	2.7%	44	1.9%				

TABLE 1. Continued

Characteristic ^{a,b}	All Patients on ≥1 Medication		Tofacitinib		Other IBD Therapy		P ^c
	N (Mean)	% (SD)	N (Mean)	% (SD)	N (Mean)	% (SD)	
IBD disease activity ^{d,*}							0.031
Remission	1290	55.5%	12	32.4%	1278	55.8%	
Mild	454	19.5%	12	32.4%	442	19.3%	
Moderate/Severe	496	21.3%	12	32.4%	484	21.1%	
Concomitant systemic corticosteroids	192	8.3%	5	13.5%	187	8.2%	0.106
Comorbidity summary score							>0.999
0	1541	66.3%	23	62.2%	1518	66.3%	
1	513	22.1%	9	24.3%	504	22.0%	
2	150	6.4%	3	8.1%	147	6.4%	
≥3	122	5.2%	2	5.4%	120	5.2%	
Comorbid conditions							
Cardiovascular disease	153	6.6%	3	8.1%	150	6.6%	0.732
Diabetes	130	5.6%	2	5.4%	128	5.6%	>0.999
Asthma	115	4.9%	2	5.4%	113	4.9%	0.705
COPD	40	1.7%	0	0.0%	40	1.7%	>0.999
Other chronic lung disease	33	1.4%	1	2.7%	32	1.4%	0.413
Hypertension	272	11.7%	6	16.2%	266	11.6%	0.433
Cancer	39	1.7%	1	2.7%	38	1.7%	0.468
History of stroke	30	1.3%	1	2.7%	29	1.3%	0.384
Chronic renal disease	54	2.3%	1	2.7%	53	2.3%	0.584
Chronic liver disease	80	3.4%	1	2.7%	79	3.5%	>0.999
Other comorbidity	293	12.6%	3	8.1%	290	12.7%	0.616
Current smoker	88	3.8%	0	0.0%	88	3.8%	0.400
BMI							0.122
BMI<30	1524	65.5%	23	62.2%	1501	65.6%	
BMI>=30	370	15.9%	10	27.0%	360	15.7%	
Missing	432	18.6%	4	10.8%	428	18.7%	

^aUnless 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.

^bPercentages 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.

^cP-values for tests comparing variables between tofacitinib and other medications groups

^dBy physician global assessment (PGA) at time of COVID-19 infection

*Statistically significant association.

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.

METHODS

The Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) is a global, web-based, collaborative registry established in March 2020 to understand COVID-19 outcomes in IBD patients, including the impact of immunosuppression.⁶ The collection and categorization of data have been reported previously.⁶

Using data reported through September 2020, we compared characteristics and COVID-19 outcomes of IBD patients on tofacitinib and those on other medications. We determined the proportion of patients with severe COVID-19, defined as a composite of intensive care unit (ICU) admission, mechanical ventilation, and/or death. In June 2020, we added the SECURE-IBD data collection form to include questions pertaining to thrombotic complications. We compared the proportion of patients with thrombotic complications who were on tofacitinib with those on other IBD therapies. We performed bivariate analyses using χ^2 or Fisher exact test for categorical variables and Wilcoxon rank-sum or *t* test for continuous variables. *P* values ≤ 0.05 were considered statistically significant for all analyses. SAS version 9.3 (SAS Institute, Cary, North Carolina) was used for data preparation and analyses.

As SECURE-IBD collects only de-identified data, the UNC-Chapel Hill Office for Human Research Ethics has determined that the storage and analysis of de-identified data for this project does not constitute human subjects research.

RESULTS

Of 2326 patients who were on ≥ 1 IBD medication in the SECURE-IBD registry, 37 (1.6%) were treated with tofacitinib; 17 (45.9%) and 20 (54.1%) patients were on ≥ 20 and < 20 mg total daily dose of tofacitinib, respectively. Baseline demographic and clinical characteristics of patients on tofacitinib compared with those on other medications are reported in the Table 1. Thirty (81.1%) patients in the tofacitinib group had UC compared with 946 (41.3%) patients on other IBD medications

(*P* < 0.001). Significantly fewer patients were in remission in the tofacitinib group compared with those on other medications (32.4% vs 55.8%, *P* = 0.03). All other baseline demographic and clinical characteristics were comparable between the 2 groups.

With respect to COVID-19 outcomes, there were no significant differences between tofacitinib-treated patients and other patients in the occurrence of hospitalization (21.6% vs 23.3%), admission to the ICU (5.4% vs 4.5%), and severe COVID-19 (6.2% in both groups, Table 2). In the subgroup of patients on tofacitinib for whom information on thrombotic events were available (*n* = 19), none experienced a thrombotic event. Among those on other IBD medications, thrombotic events occurred in 9 of 1270 (0.7%).

DISCUSSION

We describe characteristics and outcomes of COVID-19 in 37 patients with IBD treated with tofacitinib compared with other medications in the SECURE-IBD registry. Overall, we found no difference in COVID-19 outcomes between the 2 groups.

Our findings are consistent with previous descriptive reports of patients on JAKi for UC and other immune-mediated disease; although in each of these studies, COVID-19 outcomes are reported jointly among the few patients on JAKi along with other immunosuppression.⁶⁻⁹ In a case report of a 33-year-old woman with UC on tofacitinib, respiratory symptoms resolved in 5 days, and the patient recovered completely in 2 weeks with no change to tofacitinib treatment.¹⁰

In addition, although patients with COVID-19 may experience thrombotic complications, and tofacitinib at the higher dose has been associated with venous thromboembolism,⁵ none of the tofacitinib-treated patients in SECURE-IBD experienced thrombotic complications. Overall, these early data should be viewed as cautiously reassuring to patients and providers while we await larger studies and more granular analyses to parse out the impact of JAKi on COVID-19 outcomes.

TABLE 2. COVID-19 Outcomes Among IBD Patients on Tofacitinib Compared With Other IBD Therapies in the SECURE-IBD Registry

Outcome	All Patients on ≥ 1 Medication		Tofacitinib, n (%)		Other IBD therapy, n (%)		<i>P</i>
	n	(%)	n	(%)	n	(%)	
Outpatient care	1753	75.4%	29	78.4%	1724	75.3%	0.668
Hospitalization	542	23.3%	8	21.6%	534	23.3%	0.807
ICU admission	106	4.6%	2	5.4%	104	4.5%	0.685
Mechanical ventilation	77	3.3%	1	2.7%	76	3.3%	>0.999
Death	61	2.6%	1	2.7%	60	2.6%	>0.999
Severe COVID-19 outcomes ^a	144	6.2%	2	5.4%	142	6.2%	>0.999

^aIncludes composite of ICU admission, mechanical ventilation, and death.

Strengths of this study include the use of a large, international registry of adult and pediatric IBD patients with diverse characteristics and outcomes. Limitations include the small number of patients on tofacitinib and even fewer outcomes precluding adjusted analyses; however, most demographic and clinical characteristics were comparable between tofacitinib-treated and other IBD patients. The only notable differences were the higher proportion of tofacitinib-treated patients with UC and active IBD. This is likely due to the real-world use of tofacitinib in moderate-severely active UC refractory to tumor necrosis factor antagonists.² There are also risks of reporting bias and missing data in this voluntary registry.

In summary, in our descriptive analysis, characteristics and COVID-19 outcomes among IBD patients on tofacitinib were comparable to those on other IBD medications. Future larger studies of patients on tofacitinib are needed to understand clinical implications.

Data Availability: The data underlying this article are available in the article and in its online supplementary material.

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