A Practical Update on COVID-19 and Inflammatory Bowel Disease: COVID-19 Disease Risk and Vaccine Safety and Efficacy

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Abstract: The COVID-19 pandemic introduced significant uncertainty regarding the care of patients with inflammatory bowel disease (IBD). Substantial research efforts have made progress in answering many of the questions that arose, but the constantly shifting paradigm of COVID-19–related research and recommendations has made it challenging for IBD clinicians to remain up-to-date. The goal of this article is to provide a concise and practical summary of the literature evaluating COVID-19 disease risk in addition to COVID-19 vaccine safety, immunogenicity, real-world effectiveness, and uptake among patients with IBD.

Keywords
Inflammatory bowel disease, COVID-19, vaccine, humoral immunogenicity, cell-mediated immunity, uptake

The COVID-19 pandemic has been a significant public health crisis. SARS-CoV-2 has caused enormous morbidity and mortality, has altered norms of modern society, and has also challenged the landscape of medical practice. Many questions arose regarding the pandemic's impact on the care of patients with inflammatory bowel disease (IBD), a population frequently treated with immunosuppressive medications. Focus groups revealed that patients with IBD were specifically worried about their risk of COVID-19 infection and severe disease and about COVID-19 vaccine safety and efficacy.[1] Many high-quality studies have since been carried out to address these issues. This article reviews recent research on COVID-19 incidence, severity, and impact on disease activity in patients with IBD, as well as studies evaluating COVID-19 vaccine safety, immunogenicity, efficacy, and uptake in this population.

COVID-19 Incidence and Severity

Owing to the immune dysregulation inherent to IBD and frequent treatment with immunosuppressive agents, there was theoretical concern among patients and providers alike toward the beginning of the pandemic that patients with IBD could be at increased risk of contracting COVID-19 and having a more severe disease course. Patient-reported

anxiety scores have been shown to correlate with population-level case burden.[2] Moreover, patients made significant adaptations to their lifestyles owing to these fears, including postponing scheduled medical appointments and interventions.

Khan and colleagues performed a retrospective cohort study using data from January 1, 2020 to June 30, 2022 from the US Veterans Affairs health care system.[3] The authors compared more than 30,000 patients with IBD with more than 60,000 patients without IBD, who were matched for age, sex, race, location, and comorbidities, and found that both groups had a similar incidence of COVID-19 infection. In a prospective study by Long and colleagues, a cohort comprised of roughly 4000 patients with IBD was followed from April 23, 2020 to August 30, 2021.[4] The authors found that advanced therapy did not increase the risk of developing COVID-19. IBD activity was not associated with infection risk either. Additionally, African American patients with IBD were found to have elevated risk for COVID-19, mirroring trends observed in the general population. Overall, these data indicate that most patients with IBD likely do not have increased risk for SARS-CoV-2 infection relative to the general population.

Although the IBD patient population largely does not appear to be at increased risk of developing COVID-19, the question remains whether patients with IBD are at increased risk of a more severe disease course once infected. Ungaro and colleagues have analyzed data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for IBD (SECURE-IBD) database, an international repository designed to monitor outcomes in patients with IBD infected with COVID-19.[5] The authors reported that patients treated with systemic corticosteroids were at increased odds of adverse COVID-19 outcomes, including severe COVID-19, hospitalizations, and death. Medications, including mesalamine, sulfasalazine, anti–tumor necrosis factors (anti-TNFs), interleukin (IL)-12/23 antagonists, vedolizumab (Entyvio, Takeda), and tofacitinib (Xeljanz, Pfizer), were not associated with adverse COVID-19–related outcomes. Moreover, treatment with biologics appeared to potentially exert a protective effect, with patients treated with anti-TNFs, IL-12/23 antagonists, and vedolizumab having decreased odds of hospitalization or death. Overall, these data indicate that IBD patients treated with systemic corticosteroids are at increased risk for severe COVID-19, whereas those patients treated with other medications are not. In fact, treatment with biologics may portend relative protection against severe COVID-19. This effect may be owing to inhibition of the robust, deleterious immune response that has been implicated in severe COVID-19 pathophysiology.[6]

Although IBD activity has not been associated with COVID-19 incidence, there is evidence to suggest that clinically active and severe IBD may be a risk factor for severe COVID-19. Using the SECURE-IBD cohort and controlling for demographics, medications, and COVID-19 diagnosis period, Ricciuto and colleagues reported that IBD activity corresponded with the frequency of adverse COVID-19–related outcomes.[7] In an Italian retrospective cohort study consisting of 121 patients with IBD, severe IBD was also found to be independently associated with severe COVID-19 using logistic regression models.[8] Of note, neither study controlled for nutritional status, which may confound result interpretation, as malnutrition may confer a state of relative immunosuppression. As to why IBD activity would be related to COVID-19 disease severity, Ricciuto and colleagues proposed that the reason is likely multifactorial and could be related to angiotensin-converting enzyme 2 expression (ie, the SARS-CoV-2 spike protein receptor), shared molecular pathways in pathogenesis, and risk of thromboembolism, in addition to deconditioning and poor overall functional status.[7]

COVID-19 Impact on Disease Activity of Inflammatory Bowel Disease

There has not been published data to suggest that COVID-19 infection alters IBD activity. Data from the SECURE-IBD database have shown that new gastrointestinal symptoms, such as diarrhea, are common in patients with IBD and are associated with an increased risk of hospitalization but not death owing to COVID-19. Increased gastrointestinal symptom burden in the setting of COVID-19 infection was not thought to be explained by increased IBD activity given the high frequency of patients with quiescent disease who reported new symptoms.[9] Nonetheless, further research is needed in this area.

COVID-19 Vaccine Safety

There has been apprehension among patients with IBD regarding COVID-19 vaccine safety owing to fears of precipitating an IBD flare. Studies evaluating COVID-19 vaccine safety in this population have overall provided data that vaccination is extremely safe. Hadi and colleagues performed a retrospective study analyzing roughly 5000 patients with IBD who had been vaccinated against COVID-19 using data from TriNetX, a multicenter research network.[10] Adverse reactions among patients with IBD were overall rare and occurred at rates similar to those of a control population comprised of patients without IBD. There was no difference in adverse event rates between patients treated with advanced therapies and

Table 1. Selected Studies on Humoral Immunogenicity of COVID-19 Vaccines in Patients With IBD

Study	Cohort	Sample size	Vaccine(s)	Timepoint(s) evaluated	Key findings
Two-dose humoral immunogenicity					
Wong et al[21]	ICARUS	n=48	BNT162b2, mRNA-1273	18 days after 2nd dose (median)	A seroconversion rate of 100% was observed following receipt of 2 mRNA vaccine doses. Patients treated with vedolizumab or anti-TNFs had relatively lower antibody concentrations compared with HCs.
Kappelman et al[40]	PREVENT-COVID	n=317	BNT162b2, mRNA-1273	8 weeks after 2nd dose	A seroconversion rate of 95% was observed in patients after 2 mRNA vaccine doses. The humoral immune response was relatively attenuated among patients treated with systemic corticosteroids.
Pozdnyakova et al[41]	CORALE-IBD	n=353	BNT162b2, mRNA-1273, Ad26.CoV2.S	2 weeks and 8 weeks after primary series completion	Seroconversion rates of 100%, 99%, and 90% were observed for recipients of BNT162b2, mRNA-1273, and Ad26.CoV2.S, respectively. Lower antibody concentrations were observed among patients being treated with immune-modifying therapy.
Caldera et al[42]	HERCULES	n=122	BNT162b2, mRNA-1273	28-35 days after 2nd dose	A seroconversion rate of 97% was observed following completion of the primary series. Patients who received mRNA-1273 had relatively higher antibody concentrations than patients who received BNT162b2. Antibody concentrations were lower in patients treated with immune-modifying therapy. Antibody concentrations were higher in HCs than patients with IBD.
Melmed et al[43]	CORALE-IBD	n=582	BNT162b2, mRNA-1273	2 weeks, 8 weeks, and 16 weeks after 2nd dose	A seroconversion rate of 99% was observed following completion of the primary series. Although antibody concentrations decreased over time among all medication categories, patients treated with anti-TNF combination therapy or systemic corticosteroids experienced the greatest interval decrease in serum antibody concentrations.
Edelman-Klapper et al[44]	RECOVER	n=185	BNT162b2	4 weeks after 2nd dose	A seroconversion rate of 100% was observed following completion of the primary series. Antibody concentrations were lower and neutralization activity was lower among anti-TNF–treated patients compared with both non–anti-TNF–treated patients with IBD and HCs.
Alexander et al[23]	VIP	n=287	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19	53-92 days after 2nd dose	Patients treated with anti-TNF monotherapy, anti-TNF combination therapy, or tofacitinib had lower antibody concentrations compared with HCs. Antibody concentrations were higher among mRNA vaccine recipients.
Three-dose humoral immunogenicity					
Long et al[27]	PREVENT-COVID	n=659	BNT162b2, mRNA-1273, Ad26.CoV2.S	3-8 weeks after additional dose	Receipt of an additional dose resulted in increased median antibody concentrations, and 96% of patients who initially had undetectable antibodies after the primary series developed quantifiable antibody concentrations after an additional dose. Patients who received mRNA-1273 had higher antibody concentrations, whereas antibody concentrations were lower among patients treated with anti-TNFs.

(Table continues on following page)

Table 1. *(Continued)* Selected Studies on Humoral Immunogenicity of COVID-19 Vaccines in Patients With IBD

Study	Cohort	Sample size	Vaccine(s)	Timepoint(s) evaluated	Key findings
Three-dose humoral immunogenicity					
Woelfel et al[29]	STAR SIGN	n=139	BNT162b2, mRNA-1273	2-16 weeks after 3rd dose	Patients with IBD treated with anti-TNFs had relatively lower antibody concentrations after a 3rd dose when compared with non–anti-TNF–treated patients and HCs. Rate of antibody concentration decline was comparable among anti-TNF– and non–anti-TNF–treated patients.
Alexander et al[30]	VIP	n=280	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19	28-49 days after 3rd dose	Mean antibody concentrations increased following a 3rd dose in patients with IBD. Patients treated with anti-TNF monotherapy, anti-TNF combination therapy with thiopurines, and tofacitinib had lower antibody concentrations compared with HCs.
Quan et al[31]	STOP COVID	n=232	BNT162b2, mRNA-1273	≥1 week after 3rd dose	A seroconversion rate of nearly 100% was observed following a 3rd dose. Patients treated with systemic corticosteroids had relatively lower antibody concentrations. Antibody concentrations decayed by 12% per week.
Caldera et al[34]	HERCULES	n=180	BNT162b2, mRNA-1273	28-65 days and 6 months after 3rd dose	A seropositivity rate of 99% was observed 1-2 months after 3 mRNA vaccine doses. Nearly all patients (99%) had persistence of serum antibodies roughly 6 months after a 3rd dose. Anti-TNF therapy and systemic corticosteroids were associated with lower antibody concentrations, whereas prior COVID-19 infection was associated with higher antibody concentrations.
Kennedy et al[36]	CLARITY-IBD	n=1360	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19	14-70 days after 3rd dose	Mean antibody concentrations increased following a 3rd dose. Antibody concentrations were lower and antibody half-life estimates were lower among patients on anti-TNFs compared with patients on vedolizumab.

Sample size refers to the number of patients with IBD. Timepoint(s) evaluated refers to timing of blood draw relative to date of vaccination.

HC, healthy control; IBD, inflammatory bowel disease; mRNA, messenger RNA; TNF, tumor necrosis factor.

those patients who were not. Additionally, rates of corticosteroid prescription at 1-month follow-up were similar between vaccinated and unvaccinated patients with IBD, indicating that vaccination does not cause an IBD flare. Other research has demonstrated that IBD activity, as measured by laboratory markers (eg, erythrocyte sedimentation rate/C-reactive protein, fecal calprotectin), does not significantly change after vaccination.[11]

The PREVENT-COVID cohort demonstrated a low rate of adverse events secondary to vaccination at a frequency similar to that observed in the general population.[12] Data from the CORALE-IBD cohort have indicated that side effect frequency and severity were both lower after a third dose compared with a second dose with exception of a very mild increase in frequency of gastrointestinal symptoms.[13] Of note, side effects were less frequent among patients with IBD in comparison with the general population. Collectively, these data indicate that COVID-19 vaccines are safe in patients with IBD and should aid in alleviating fears and decreasing vaccine hesitancy.

COVID-19 Vaccine Humoral Immunogenicity

Prior research has demonstrated that patients with IBD may have a relatively blunted humoral immune response to other vaccines such as influenza and pneumococcus.[14] Moreover, reduced humoral immunity to COVID-19 infection has been associated with anti-TNF treatment.[15,16] Immunosuppressed patients, such as those with IBD, were not included in the initial phase 3 clinical trials demonstrating excellent COVID-19 vaccine efficacy.[17-20] As such, there was concern that patients with IBD may

Table 2. Selected Studies on Cell-Mediated Immunity of COVID-19 Vaccines in Patients With IBD

Study	Cohort	Sample size	Vaccines	Timepoint(s) evaluated	Key findings
Two-dose cell-mediated immunity					
Lin et al[22]	CLARITY-IBD	n=123	BNT162b2, ChAdOx1 nCoV-19	4-6 weeks after 2nd dose	Roughly 20% of patients failed to mount a T-cell response after the primary series. There was no difference between anti-TNF and vedolizumab treatment groups.
Li et al[50]	CORALE-IBD	n=303	BNT162b2, mRNA-1273, Ad26.CoV2.S	2 weeks and 8 weeks after 2nd dose	The T-cell response was preserved among patients treated with antimetabolites, vedolizumab, ustekinumab, and systemic corticosteroids compared with untreated patients. The T-cell response was comparatively greater among anti-TNF–treated patients. Antibody concentrations corresponded poorly with T-cell response.
Caldera et al[49]	HERCULES	n=158	BNT162b2, mRNA-1273	28-35 days after 2nd dose	Patients with IBD had a cell-mediated immune response similar to that of HCs. The T-cell response was greater among patients on anti-TNF therapy and did not correlate with humoral immunity.
Cerna et al[28]	ISCARE	n=60	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19	26 weeks after 2nd dose	The T-cell response was lesser among patients with IBD compared with HCs. Patients with low or borderline T-cell responses were more commonly treated with anti-TNFs.
Three-dose cell-mediated immunity					
Woelfel et al[29]	STAR SIGN	n=139	BNT162b2, mRNA-1273	2-16 weeks after 3rd dose	There were more anti-TNF–treated patients than HCs with low T-cell responses. The T-cell response did not correlate with antibody concentrations.
Alexander et al[23]	VIP	n=280	BNT162b2, mRNA-1273, ChAdOx1 nCoV-19	28-49 days after 3rd dose	There was not a difference in the T-cell response among patients with IBD treated with thiopurine, ustekinumab, vedolizumab, anti-TNF monotherapy, or anti-TNF combination therapy with thiopurine when compared with HCs. Patients treated with tofacitinib had a lower T-cell response compared with HCs.
Zhang et al[37]	Royal Melbourne Hospital	n=100	BNT162b2, ChAdOx1 nCoV-19	1-3 months after 3rd dose	Patients with IBD had similar T-cell responses to HCs after a 2nd and 3rd dose. Treatment with anti-TNFs was associated with a comparatively greater T-cell response compared with non–anti-TNF–treated patients with IBD and HCs.

Sample size refers to the number of patients with IBD. Timepoint(s) evaluated refers to timing of blood draw relative to date of vaccination.

HC, healthy control; IBD, inflammatory bowel disease; TNF, tumor necrosis factor.

not derive the same protection from vaccination as the general population.

Numerous studies have since evaluated the immunogenicity of COVID-19 vaccines in the IBD population (Table 1).[11,21-46] A 95% to 100% seroconversion rate has been observed among patients with IBD following completion of the original 2-dose primary vaccine series.[11,21,40-43] The postvaccination seroconversion rate in

the IBD population appears to be similar to that of the general population based on studies that included healthy controls.[11,21,42,44] Data have shown that the humoral immune response may be relatively blunted among patients treated with anti-TNFs and systemic corticosteroids, citing lower serum antibody concentrations and relatively accelerated waning of humoral immunity when compared with other treatment groups and healthy controls.[11,21-23,25,26,32,40-44] Patients treated with anti-TNFs have also exhibited relatively reduced antibody neutralization function compared with those patients not treated with anti-TNFs.[25,44]

With respect to additional COVID-19 vaccine doses, receipt of a third dose has been shown to produce a robust humoral immune response and increase neutralization activity.[24,27,30,33-35,37,39,46] Durability of humoral immunity appears to be high in patients with IBD, with one study citing maintenance of 100% seropositivity rates 6 months after receipt of a third dose in their cohort.[34] Similar to the trends observed with 2 COVID-19 vaccine doses, the humoral immune response to 3 doses appears to be relatively blunted in patients treated with anti-TNFs and systemic corticosteroids, and humoral immunity appears to wane at a greater rate among these patients as well in comparison with healthy controls and patients not on such therapies.[24,27,30,34,37,39,46] Neutralization activity following receipt of a third monovalent dose is relatively lower among anti-TNF–treated patients and against the Omicron variant.[24,33,35] Humoral immunity appears to be augmented among patients with IBD who have additional antigen exposure by means of prior COVID-19 infection.[34,36] Following receipt of a fourth dose, the interval increase in serum antibody concentrations is similar to that observed between second and third doses and may be relatively diminished in patients treated with anti-TNF therapy and systemic corticosteroids.[31,36,47] Disease activity does not appear to be correlated to serum antibody concentrations following vaccination.[29] It should also be noted that anti–SARS-CoV-2 antibodies have not been definitively established as an absolute correlate of immunity against COVID-19.

COVID-19 Vaccine Cell-Mediated Immunity

Despite being an integral component of the adaptive immune system, cell-mediated immunity (CMI) has not been researched as extensively as humoral immunity, in part owing to the expensive, time-consuming, and labor-intensive nature of associated assays. With respect to SARS-CoV-2, although humoral immunity has been found to be significantly reduced against subvariants, the T-cell response appears to be largely preserved.[48] Studies evaluating SARS-CoV-2–specific CMI induced by COVID-19 vaccination among patients with IBD have been relatively mixed and somewhat few (Table 2). The HERCULES cohort reported that T-cell responses were similar between healthy controls and patients with IBD following a 2-dose primary messenger RNA (mRNA) vaccine series, and these findings were replicated by the Royal Melbourne Hospital group following a third vaccine dose.[37,49]

The effect of immunosuppressive therapy on CMI has been mixed in recent studies. Data from the CLARITY-IBD cohort consisting of 282 patients showed no difference in T-cell responses between patients treated with anti-TNFs and vedolizumab following vaccination with BNT162b2 (Pfizer-BioNTech) or ChAdOx1 nCoV-19 (AstraZeneca) formulations.[22] Meanwhile, both ISCARE and STAR SIGN cohorts demonstrated a relatively diminished T-cell response in patients treated with anti-TNFs, and the VIP cohort reported a comparatively decreased T-cell response among patients treated with tofacitinib.[28-30] Interestingly, although anti-TNF therapy has been associated with blunted humoral immunity as previously described, there are data to support an increased T-cell response in patients receiving anti-TNF therapy.[37,49,50] These findings are reinforced by data showing that humoral immunity and CMI are not correlated.[29,49] The heterogeneity among these data could be owing to various factors, including but not limited to differences in demographic or clinic factors within and between each cohort, vaccine manufacturer and dose timing, timing of blood collection, or distinctions related to the assay used (eg, assay type, manufacturer, collection timing relative to vaccination).

COVID-19 Vaccine Real-World Effectiveness

Although studies evaluating humoral and cell-mediated immunogenicity represent practical surrogates for vaccine efficacy, assessment of clinical outcomes in relation to vaccination status provides the highest level of evidence and external validity. Moreover, some studies were able to compare adaptive immunity with clinical outcomes. With respect to the original 2-dose primary vaccine series, vaccine efficacy has been reported to be high among patients who have IBD, including those receiving advanced therapy, and comparable with control populations.[10,51,52] In the CLARITY-IBD cohort, where humoral immunogenicity was found to be relatively diminished among patients treated with anti-TNFs, the rate of breakthrough infections was also relatively higher among such patients.[22] The authors reported a 5.8% and 3.9% difference in breakthrough infection rates among anti-TNF–treated and vedolizumab-treated patients. Similarly, data from SECURE-IBD signaled that patients

receiving anti-TNFs, particularly combination therapy, may be at greater risk of hospitalization.[53] In contrast, data from the epi-IIRN cohort, containing more than 12,000 patients who have IBD, indicated that vaccine efficacy is not affected by anti-TNF therapy.[54] Finally, serum antibody concentrations were previously found to correlate with vaccine efficacy earlier in the COVID-19 pandemic, such as in times of Delta variant predominance.[22,38] However, antibody levels following receipt of 2 monovalent mRNA vaccine doses in the STAR SIGN cohort were not found to be associated with breakthrough infection rates during times of Omicron predominance, demonstrating the phenomenon of vaccine escape by contemporary variants.[29]

With respect to the protection afforded by a third dose, Khan and Mahmud as well as Desai and colleagues reported that third doses in patients with IBD conferred decreased infection incidence and decreased rates of severe COVID-19 outcomes such as hospitalization.[55,56] Moreover, receipt of a booster dose was associated with decreased odds of hospitalization from COVID-19 infection compared with completion of only a primary vaccine series.[56] Again, CLARITY-IBD reported that patients treated with anti-TNFs displayed relatively decreased humoral immunity and were at relatively greater risk of breakthrough infection.[33,36] Although anti–spike receptor-binding domain antibodies were not correlated with protection from the BA.4/5 Omicron subvariant among patients with breakthrough infection, higher neutralizing antibody titers specifically directed against BA.4/5 were associated with a longer time to breakthrough infection. As such, it is conceivable that the blunted humoral immune response observed among patients treated with systemic immunosuppression such as anti-TNFs may have clinical implications. However, the broader findings of the aforementioned studies that vaccinated patients with IBD have decreased rates of infection and infection-related complications relative to unvaccinated patients, and that patients with IBD benefit from comparable vaccine efficacy to that of the general population, strongly indicate that this patient population largely gains significant clinical protection from vaccination.

COVID-19 Vaccine Uptake

Although vaccination protects patients with IBD from the negative effects of COVID-19 infection, patients need to receive the vaccine to realize the benefits of vaccination. Numerous studies have evaluated uptake of 2 doses in this patient population. Factors such as concerns regarding long-term safety and speed of vaccine development have contributed to vaccine hesitancy and have negatively impacted vaccination rates.[57-59] One single-center study reported a relatively high uptake rate of 84% for the original 2-dose primary series.[60] Variables associated with vaccine hesitancy and absence of vaccine uptake have included younger age, male sex, underrepresented minority race/ethnicity, rural status, neighborhood disadvantage, tobacco use, and lack of influenza vaccination.[58,60-63] Studies have also shown a higher vaccination rate among patients treated with biologics.[58,64]

Regarding uptake of additional doses, Kuenzig and colleagues evaluated third dose uptake among more than 100,000 patients with IBD in Ontario, Canada.[65] As of January 2022, the authors reported a 3-dose uptake rate of 58% among patients with IBD, which was significantly higher than the 44% observed in the general population. Wellens and colleagues analyzed patients within the United Kingdom and reported that third dose uptake was relatively lower among younger patients, patients of non-White ethnicity, and those of lower socioeconomic status.[66] Finally, Selim and colleagues reported that fourth dose uptake rates severely declined to 44% from 90% for third dose uptake in their cohort of roughly 500 patients receiving intravenous biologic therapy.[67] Vaccination rates were disproportionately lower among younger people. The authors proposed that suboptimal vaccination rates may have been owing to normalization and decreased concerns related to COVID-19 and decreased emphasis on vaccination by health care professionals and public health organizations. Finally, it should be noted that reported vaccine uptake rates may have been impacted by timing of updated vaccine recommendations in relation to timing of data collection.

These variables and disparities in vaccine uptake observed in the IBD population largely mirror those seen in the general population.[68,69] Moving forward, it is important to improve vaccine uptake in an equitable manner. These predictors of incomplete vaccination represent a means to guide targeted outreach programs as an intervention to increase vaccine uptake. Moreover, patients trust their health care providers as a reliable source for information regarding COVID-19 vaccination.[68] As such, gastroenterologists should seize the opportunity to recommend vaccination to their patients. A productive strategy to address COVID-19 vaccination includes legitimizing concerns, assuming patients are open to vaccination, employing positive framing techniques, reviewing risks of COVID-19 and benefits of vaccination, and strongly recommending immunization.[70] Finally, it is important to establish expectations. Although symptomatic infection following vaccination is possible, it should not be viewed as a failure, as the primary goals of vaccination are to reduce major complications of severe COVID-19, including hospitalization and death.

Table 3. Take-Home Points for COVID-19 Vaccination in Patients With IBD

• Patients with IBD, including those on advanced therapies, are not at increased risk of SARS-CoV-2 infection.
• Systemic corticosteroids portend an increased risk of severe COVID-19, whereas other medications, including advanced therapies (ie, anti-TNFs, non–anti-TNF biologics, and JAK inhibitors), do not.
• There has not been published data to suggest that COVID-19 infection alters IBD activity.
• Vaccination is safe in patients with IBD and does not affect disease activity; the side effect profile is similar to that of the general population.
• Vaccination decreases rates of COVID-19 infection and infection-related complications with similar efficacy to those observed in patients without IBD.
• Adult patients with IBD who have previously completed the original primary vaccine series should receive a dose of the updated 2023-2024 COVID-19 vaccine.

IBD, inflammatory bowel disease; JAK, Janus kinase; TNF, tumor necrosis factor.

Current COVID-19 Vaccine Recommendations

In the United States, the updated 2023 to 2024 COVID-19 vaccine is currently available from 3 manufacturers: Pfizer-BioNTech, Moderna (mRNA-1273), and Novavax (NVX-CoV2601). Although all 3 formulations are monovalent, the Pfizer-BioNTech and Moderna formulations are mRNA vaccines, whereas the Novavax formulation is a protein subunit vaccine. All updated vaccines are tailored to the circulating XBB1.5 Omicron subvariant. These vaccine formulations have been found to be safe as well as effective in neutralization assays.[71] Vaccine guidance by the Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices has tailored recommendations for patients with and without moderate-to-severe immunosuppression. For patients with IBD, moderate-to-severe immunosuppression is defined by treatment with systemic corticosteroids (ie, ≥20 mg prednisone), anti-TNF agents, and antimetabolites (ie, methotrexate, thiopurines).

According to the most recent vaccine guidance, immunocompetent adults who previously completed the original primary vaccine series should receive 1 updated COVID-19 vaccine dose. Immunocompetent adult patients who were previously unvaccinated should receive 1 updated mRNA vaccine dose or 2 updated protein subunit doses.[72] Adult patients with moderate-to-severe immunosuppression who previously completed the original primary vaccine series should receive 1 updated COVID-19 vaccine dose. Such patients who were previously unvaccinated may receive either 3 updated mRNA vaccine doses or 2 updated protein subunit doses. Guidance for patients with more nuanced vaccine histories may be found on the CDC website.[72]

Conclusion and Future Directions

The unknown of the COVID-19 pandemic posed a multitude of questions regarding the care of patients with IBD, and coordinated research efforts have made significant strides to shed light on the subject. Overall, it appears that patients with IBD are not at increased risk for acquiring COVID-19, and only those receiving systemic corticosteroids appear to have elevated risk of severe disease. COVID-19 vaccination is safe and effective in reducing adverse outcomes related to infection and is not associated with increased disease activity in patients with IBD (Table 3). Future work is needed to address disparities in COVID-19 vaccine uptake and increase vaccination rates with updated vaccine formulations.

Disclosures

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