



SARS-CoV-2 vaccination in IBD: more pros than cons

Ferdinando D'Amico^{1,2}, Christian Rabaud³, Laurent Peyrin-Biroulet⁴ and Silvio Danese^{1,2}✉

Data on the efficacy and safety of SARS-CoV-2 vaccines are now available, but evidence for these vaccines in those who are immunocompromised (including patients with inflammatory bowel diseases) are lacking. As vaccination begins, questions on advantages and disadvantages can be partially addressed using the experience from other vaccines or immune-mediated inflammatory disorders.

Efforts to develop a vaccine to prevent the ongoing pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have led to multiple vaccines available and approved for use. Current evidence shows that patients with inflammatory bowel disease (IBD) do not have an increased risk of developing SARS-CoV-2 infection and coronavirus disease 2019 (COVID-19)¹. However, ~30% of patients with IBD are >65 years of age and approximately one-third of patients with IBD have comorbidities (including high-risk factors for COVID-19 such as cardiovascular diseases and diabetes)¹. In addition, patients with IBD are frequently treated with immunosuppressants, biologic agents, or small molecules that expose them to increased risk of severe or opportunistic infections. It is therefore of crucial importance to define when any vaccine is recommended and the appropriate timing of vaccination in patients with IBD, especially for those on immunosuppressive treatment. The association between IBD and vaccines has been debated for decades, but an umbrella review of meta-analyses published in 2019 showed that vaccinations are not associated with an increased risk of IBD².

Several SARS-CoV-2 vaccines are being tested³, and the first phase III clinical trials reporting efficacy and safety of vaccines are now published (Supplementary Table 1)⁴. Importantly, however, patients with IBD or those treated with immunosuppressive drugs or corticosteroids were excluded from these studies. There are several pros and cons regarding SARS-CoV-2 vaccination for patients with IBD (BOX 1), and it is unknown whether SARS-CoV-2 vaccine efficacy and safety in populations with IBD are comparable with those found in the general population, whether treatment with immunosuppressive drugs affects response to vaccination or disease activity, and what is the optimal timing for any vaccination⁵. Long-term outcomes of any SARS-CoV-2 vaccine are also lacking, and this question of safety is crucial as vaccines will be administered to millions of people with IBD worldwide.

To date, studies on SARS-CoV-2 vaccination in IBD populations are lacking but, in this health-emergency setting, some data on safety and efficacy could be extrapolated from previous evidence with other vaccines. A prospective study by Fiorino et al.⁶ investigated the efficacy of pneumococcal vaccination in 96 patients with IBD undergoing immunosuppressive therapy. Treatment with anti-TNF agents or combination therapy (anti-TNF agents plus thiopurines) was associated with an impaired immune response compared with patients treated with mesalazine (57.6% and 62.5% versus 88.6%; $P < 0.05$ for both comparisons), whereas azathioprine alone did not influence the antibody titres, suggesting that vaccination should be performed before starting anti-TNF therapy⁶. Similarly, a controlled paediatric study evaluated efficacy and safety of the influenza vaccine in 51 patients with IBD (mean age 13.9 years) and 29 healthy individuals as controls (mean age 12.7 years), measuring haemagglutinin inhibition titres before and after immunization. Those patients with IBD treated with anti-TNF drugs had a reduced response to vaccination compared with patients treated with thiopurines, steroids, or anti-inflammatory compounds (mesalazine, antibiotics, and nutritional therapy)⁷.

Additional data can be extrapolated from other immune-mediated diseases. A randomized placebo-controlled phase II trial enrolling 383 patients with rheumatoid arthritis showed that individuals starting tofacitinib 2–3 weeks after live zoster vaccination had an antibody titre concentration comparable to that of the placebo group, in the absence of an increased risk of serious adverse events⁸. In rheumatoid arthritis, the response to pneumococcal and influenza vaccines was reduced in patients with ongoing tofacitinib therapy, which supports that vaccinations should be performed before starting treatment⁸. With regard to the association between vaccines and disease activity, the [International Psoriasis Council](#) states that there is no evidence that vaccines affect psoriasis onset or severity, supporting

¹Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy.

²IBD Center, Humanitas Clinical and Research Center-IRCCS, Rozzano, Milan, Italy.

³Department of Infectious Disease, University Hospital of Nancy, University of Lorraine, Vandoeuvre-lès-Nancy, France.

⁴Department of Gastroenterology and Inserm NGERE U1256, University Hospital of Nancy, University of Lorraine, Vandoeuvre-lès-Nancy, France.

✉e-mail: sdanese@hotmail.com

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Box 1 | Considerations for SARS-CoV-2 vaccination in patients with IBD

Pros

- Protection against SARS-CoV-2 infection
- Promising safety profile
- Social responsibility (to protect those who might be vulnerable)
- Potential protection against other viruses
- Herd immunity

Cons

- Unknown long-term safety
- Unknown vaccination outcomes in IBD
- Unknown effect on IBD disease activity
- Unknown vaccination outcomes during immunosuppression

Research gaps associated with SARS-CoV-2 vaccination in IBD

- Is SARS-CoV-2 vaccine equally effective in patients with IBD and in the general population?
- Does SARS-CoV-2 vaccine affect IBD disease activity?
- Do IBD medications affect the response to SARS-CoV-2 vaccination?
- Should the antibody titre after SARS-CoV-2 vaccination be monitored? If so, what is the optimal timing for monitoring?
- Should asymptomatic and/or paucisymptomatic SARS-CoV-2-infected patients with IBD and those with COVID-19 be vaccinated? If so, at what timing after infection?

IBD, inflammatory bowel disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

vaccination in individuals with psoriasis. Similarly, the [American College of Rheumatology](#), despite the lack of data on the efficacy of the SARS-CoV-2 vaccine in patients with rheumatological diseases, recommends vaccine administration to all patients with rheumatological diseases as the benefits of vaccination outweigh the risks of any vaccine-related adverse events.

Regarding the safety profile, other vaccines have already proved to be safe and not to affect disease activity in patients with IBD⁹. Importantly, in a study enrolling >500 patients with IBD, only 3.9% of participants experienced a self-limiting clinical disease flare after influenza vaccine, supporting the hypothesis that there is no increased risk of IBD re-exacerbation after vaccination⁹. Data on efficacy and safety of SARS-CoV-2 vaccines are promising in the general population, with no major adverse effects (Supplementary Table 1). We believe that SARS-CoV-2 vaccination should be recommended for all patients with IBD regardless of therapy or comorbidities, although its use in paediatric patients and during pregnancy is currently debated. Notably, any reservation to vaccinate in the IBD population and in vulnerable individuals (such as children and pregnant women) is not associated with a known contraindication (such as live virus vaccine), but as a cautionary perspective relative to uncertainty of vaccine efficacy and safety in a subgroup of individuals who were excluded from the randomized clinical trials. The [British Society of Gastroenterology](#) has recently published key recommendations strongly supporting SARS-CoV-2 vaccination in patients with IBD, underlining that the main concern in patients treated with biologic agents or small molecules is the theoretical risk of suboptimal vaccine responses rather than vaccine adverse effects. However, the risk of morbidity and mortality associated with complications

of COVID-19 far outweighs the risk of data uncertainty in an underestimated population. In line with previous vaccine experiences, it is reasonable to assume that any vaccination should be performed prior to initiating immunosuppressive therapy⁵. In patients with IBD treated with immunosuppressive treatment, vaccine administration should be recommended based on a favourable risk:benefit ratio and supported by an apparently reassuring safety profile and a clinically significant risk of hospitalization, complications and death associated with SARS-CoV-2 infection¹. Vaccine advantages are constituted not only by the individual and herd protection against SARS-CoV-2, but also by the potential immunity against other coronaviruses¹⁰. The management of patients with IBD who have already experienced SARS-CoV-2 infection remains to be defined and efficacy and safety of vaccination in this specific setting must be investigated. Studies are also needed to define whether the antibody titre should be monitored after vaccination and, if so, how often and for how long such monitoring should be performed.

A year has passed since SARS-CoV-2 was initially identified, but major steps have been made in research to address this dangerous threat — SARS-CoV-2 vaccine development represents a fundamental tool to control the viral spread. For this purpose, the SARS-CoV-2 vaccination programme should include the millions of people with immune-mediated diseases to protect this vulnerable population and achieve the ultimate goal of the highest possible vaccination coverage. For adequate management of patients with IBD, it is essential that gastroenterologists are appropriately updated on efficacy and safety of the SARS-CoV-2 vaccine to provide clear information and guidance to patients with IBD, improving their attitude towards vaccination and reducing the skepticism and hesitation of some individuals. Moreover, social responsibility towards vaccination should be taken into account in the decision to receive a SARS-CoV-2 vaccine. During the early stages of vaccine distribution there will be a possible disproportion between number of available vaccine doses and patients to be treated, requiring patient selection. In this scenario, patients >65 years and those with comorbidities (such as obesity, diabetes, and cardiovascular disease) should have priority as they are at greater risk of negative outcomes (for example, hospitalization or need for oxygen therapy), as should workers at high risk of contagion (such as health-care or frontline workers and teachers). Data collection on patients with IBD receiving SARS-CoV-2 vaccines is mandatory to ensure the best preventive strategy.

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Competing interests

L.P.-B. has served as a speaker, consultant and advisory board member for Merck, Abbvie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Hospira/Pfizer, Celltrion, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, H.A.C. Pharma, Index Pharmaceuticals, Amgen, Sandoz, Forward Pharma, Celgene, Biogen, Lycera, Samsung Bioepis and Theravance. S.D. has served as a speaker, consultant, and advisory board member for

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Supplementary information

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RELATED LINKS

American College of Rheumatology: <https://www.rheumatology.org/>

British Society of Gastroenterology: <https://www.bsg.org.uk/covid-19-advice/british-society-of-gastroenterology-inflammatory-bowel-disease-section-and-ibd-clinical-research-group-position-statement-on-sars-cov2-vaccination>

International Psoriasis Council: <https://www.psoriasis-council.org/blog/IPC-Statement-on-SARS-CoV-2-Vaccines-and-Psoriasis.htm>