

## Viral screening before initiation of biologics in patients with inflammatory bowel disease during the COVID-19 outbreak

We read with interest the Comment by Ren Mao and colleagues on the implications of coronavirus disease 2019 (COVID-19) in patients with pre-existing digestive diseases, and the strategies implemented in China to restrict the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with inflammatory bowel disease.<sup>1</sup>

We agree with the current evidence that does not support drug suspension and also with the European Crohn's and Colitis Organisation COVID-19 Task Force's suggestion that, whenever possible during the COVID-19 pandemic, initiation of treatment with immunosuppressive drugs and biologics should be postponed based on an individual risk assessment.<sup>2</sup> However, for patients with substantial clinical activity, delaying the initiation of treatment might not always be possible.

A meta-analysis<sup>3</sup> of clinical trial data including 4135 patients given anti-tumor necrosis factor (TNF) therapy found that the relative risk of developing an opportunistic infection was 2.05 (95% CI 1.10–3.85) with anti-TNF therapy compared with placebo; opportunistic infections included tuberculosis, herpes simplex infection, oral or oesophageal candidiasis, herpes zoster virus, cytomegalovirus, and Epstein-Barr virus. A pooled analysis of 2266 patients given adalimumab found that higher disease activity was

associated with significantly increased risks of both serious and opportunistic infections at 1 year.<sup>4</sup> Furthermore, vedolizumab, a humanised monoclonal antibody with gut selectivity, has been associated with airway and bowel infections, although to a lesser extent than with anti-TNF drugs.<sup>5</sup> The risk of opportunistic infection seems to be increased in patients with inflammatory bowel disease who are older than 50 years and receiving immunosuppression.<sup>6,7</sup>

As a result of this increased risk of opportunistic infections, inflammatory bowel disease guidelines suggest giving patients a viral screening before starting biologics.<sup>8</sup> In particular, the screening should include serology for hepatitis B virus, hepatitis C virus, HIV, and varicella zoster virus (in patients without a clear history of previous infection or vaccination), and tuberculosis screening through a combination of clinical risk stratification, chest x-ray, and IFN- $\gamma$  release assays. Additionally, an assessment of history of specific infections is suggested, including herpes simplex virus, varicella zoster virus, and tuberculosis, and of immunisation status.<sup>3</sup>

Patients with inflammatory bowel disease might be at an increased risk of SARS-CoV-2 infection, and the risk of a severe clinical course of COVID-19 might be increased in individuals with chronic disease on immunomodulatory treatment. Furthermore, the risk of inducing clinical activation in individuals with asymptomatic SARS-CoV-2 infection cannot be excluded. As such, we believe that current recommendations for screening before initiation of biologics should be updated (at least temporarily) to include testing for SARS-CoV-2. In view of the rapid

spread of the COVID-19 pandemic, we believe physicians should screen for COVID-19 even if patients are asymptomatic or do not have a history of high-risk travel or contact. However, importantly, the exact method of such screening should be decided on the basis of local policy and available health-care resources.

We declare no competing interests.

\**Fabiana Zingone, Edoardo Vincenzo Savarino*  
fabiana.zingone@unipd.it

Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, 35121 Padua, Italy

- 1 Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases. *Lancet Gastroenterol Hepatol* 2020; published online March 11. [https://doi.org/10.1016/S2468-1253\(20\)30076-5](https://doi.org/10.1016/S2468-1253(20)30076-5)
- 2 1st Interview COVID-19 ECCO Taskforce. ECCO Crisis Task Force, March 13, 2020. [https://www.ecco-ibd.eu/images/6\\_Publication/6\\_8\\_Surveys/1st\\_interview\\_COVID-19%20ECCOTaskforce\\_published.pdf](https://www.ecco-ibd.eu/images/6_Publication/6_8_Surveys/1st_interview_COVID-19%20ECCOTaskforce_published.pdf) (accessed March 20, 2020).
- 3 Ford AC, Peyrin-Biroulet L. Opportunistic infections with anti-tumor necrosis factor- $\alpha$  therapy in inflammatory bowel disease: meta-analysis of randomized controlled trials. *Am J Gastroenterol* 2013; **108**: 1268–76.
- 4 Osterman MT, Sandborn WJ, Colombel JF, et al. Crohn's disease activity and concomitant immunosuppressants affect the risk of serious and opportunistic infections in patients treated with adalimumab. *Am J Gastroenterol* 2016; **111**: 1806–15.
- 5 Singh S, Murad MH, Fumery M, et al. First- and second-line pharmacotherapies for patients with moderate to severely active ulcerative colitis: an updated network meta-analysis. *Clin Gastroenterol Hepatol* 2020; Published online Jan 13. DOI:10.1016/j.cgh.2020.01.008.
- 6 Naganuma M, Kunisaki R, Yoshimura N, Takeuchi Y, Watanabe M. A prospective analysis of the incidence of and risk factors for opportunistic infections in patients with inflammatory bowel disease. *J Gastroenterol* 2013; **48**: 595–600.
- 7 Toruner M, Loftus EV Jr, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. *Gastroenterology* 2008; **134**: 929–36.
- 8 Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019; **68** (suppl 3): s1–106.

*Lancet Gastroenterol Hepatol* 2020

Published Online  
March 25, 2020  
[https://doi.org/10.1016/S2468-1253\(20\)30085-6](https://doi.org/10.1016/S2468-1253(20)30085-6)