Reply to the Letter to the Editor: The Incidence and Outcomes of COVID-19 in Patients With IBD: A Rapid Review and Meta-Analysis

Key Words: inflammatory bowel disease, COVID-19, SARS-CoV-2

To the Editors,

We appreciate the interest of Aziz et al in our work examining the expression of the SARS-CoV-2 entry molecules angiotensin I converting enzyme 2 (ACE2) and transmembrane serine protease 2 in mouse models of colitis, samples of patients with IBD, and databases.[1] Our findings showed that inflammation does not increase the expression of ACE2 and transmembrane serine protease 2 in the ileum and colon and that certain medications can reduce their expression in patients with IBD. We speculated that patients with IBD are not at increased risk of infection from SARS-CoV-2. However, a 2019 study reported higher ACE2 at a protein level in colonic biopsies and an increased ratio of circulating ACE2 to ACE in patients with IBD when compared with healthy control patients,[2] implying that patients with IBD could be at increased risk of developing COVID-19. Therefore, we read with great enthusiasm the Letter to the Editor by Aziz and colleagues addressing the incidence and outcomes of patients with IBD with COVID-19. Their meta-analysis combining data from studies in countries severely affected by the pandemic suggests a low incidence of COVID-19 in patients with IBD compared with the general population. These data add to the ongoing effort of the SECURE-IBD registry[3] in bringing epidemiologic reassurance to patients with IBD.

Discontinuation of medication, especially immunosuppressants, has also emerged as a recurrent question in the management of IBD during COVID-19. Our data suggested that medication does not increase ACE2 expression and that indeed, anti-tumor necrosis factor (anti-TNF) biologics and steroids may reduce intestinal ACE2. We wonder whether Aziz and colleagues found any differences regarding the risk of infection from COVID-19 among patients with IBD receiving no medication compared with those receiving therapy. Because diverse studies have associated the use of medication with reduced risk of hospitalization,[4, 5] general guidelines recommend not interrupting treatment. However, a 2020 study has associated the use of vedolizumab with a higher risk of hospitalization of patients with IBD affected by COVID-19.[5]

Overall, as we keep learning to confront SARS-CoV-2 infection, epidemiologic studies focused on patients with IBD are needed to estimate their risk of developing COVID-19 compared with that of the general population. For now, the outcomes reported in COVID-19 positive patients with IBD offer reassurance for patients on biologics, especially anti-TNFs as monotherapy, but they raise caution for immunomodulators and high-dose steroids.[3, 5] Our study offers mechanistic insight into why anti-TNFs may be protective.

Juan F. Burgueño, DVM/PhD,*,[o] and Maria T. Abreu, MD*

From the *Division of Gastroenterology, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida

Supported by: This work was supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (grant number R01DK09907), Takeda Pharmaceuticals, U.S.A. (grant number IISR-2014–1000892), the Pfizer-ASPIRE Award (grant number WI227247), The Micky & Madeleine Arison Family Foundation Crohn's & Colitis Discovery Laboratory, and the Martin Kalser Chair (Maria Abreu).

Conflicts of interest: Maria Abreu has served as a scientific advisory board member for Boehringer Ingelheim Pharmaceuticals, Gilead, AbbVie, Seres Therapeutics, Shire, and Landos Biopharma; serves as a trainer or lecturer for Imedex, Focus Medical Communications, and Cornerstones Health, Inc; has served as a consultant for Ferring Pharmaceuticals, Allergan, Amgen, Celltrion Healthcare CO, Millennium Pharmaceuticals, Theravance Biopharma Inc., and UCB Biopharma SRL; and has funded projects by Pfizer, Prometheus Laboratories, and Takeda Pharmaceuticals. This does not alter the authors' adherence to the journal's policies on sharing data and materials.

Address correspondence to: Maria T. Abreu, MD, 1011 NW 15th Street (D-149), Gautier Building, Suite 510, Miami, FL 33136 (MAbreu1@med.miami.edu).

REFERENCES

1. Burgueño JF, Reich A, Hazime H, et al. Expression of SARS-CoV-2 entry molecules ACE2 and TMPRSS2 in the gut of patients with IBD. *Inflamm Bowel Dis.* 2020;26:797–808.
2. Garg M, Royce SG, Tikellis C, et al. Imbalance of the renin-angiotensin system may contribute to inflammation and fibrosis in IBD: a novel therapeutic target? *Gut.* 2020;69:841–851.
3. Kappelman MD, Brenner EJ, Ungaro RCet al. Coronavirus and IBD reporting database. Accessed June 17, 2020. https://covidibd.org
4. Mao EJ, Hazlewood GS, Kaplan GG, et al. Systematic review with meta-analysis: comparative efficacy of immunosuppressants and biologics for reducing hospitalisation and surgery in Crohn's disease and ulcerative colitis. *Aliment Pharmacol Ther.* 2017;45:3–13.
5. Lukin DJ, Kumar A, Hajifathalian K, et al. Baseline disease activity and steroid therapy stratify risk of COVID-19 in patients with inflammatory bowel disease. *Gastroenterology.* Published online May 29, 2020. doi: 10.1053/j.gastro.2020.05.066

doi: 10.1093/ibd/izaa172
Published online 3 July 2020