Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

due to the larger statistical power of the UKB. Moreover, these findings are in line with the recent report from Åberg et al,[8] showing an increased risk for advanced liver disease that was dependent on the amount of alcohol consumption and apparent even for consumption of 10 to 19 g/d compared with lifetime abstainers.

Consistently with Luukkonen et al,[1] smoking was rare (2.5% of Pi*MZ subjects) and did not significantly modify the effect of Pi*MZ on liver-related death (aHR 1.82; 95% CI 0.28–9.08 in smokers; aHR 1.81; 95% CI 0.98–2.21 in nonsmokers; both adjusted for age, sex, and BMI).

In conclusion, both the data from Luukkonen et al[1] and the findings presented herein further support the previous observations suggesting that obesity, diabetes mellitus, metabolic syndrome, and alcohol consumption constitute key modifiers in Pi*MZ-related liver disease.[7,9] These findings are relevant to the clinical routine, because all factors are potentially modifiable and should spur an early diagnosis and appropriate counseling of all Pi*MZ individuals presenting with signs of liver disease.

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Most current article

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Could Patients With Inflammatory Bowel Disease Treated With Immunomodulators or Biologics Be at Lower Risk for Severe Forms of COVID-19?

Dear Editors:

The Coronavirus Disease 2019 (COVID-19) pandemic is undoubtedly the global health crisis of our time. In this regard, we read with interest the paper by Iago Rodríguez-Lago and colleagues[1] on the outcome of patients with inflammatory bowel disease (IBD) during the severe acute respiratory syndrome coronavirus 2 pandemic in the Basque Country, Spain. Interestingly, patients with IBD and COVID-19 had a good overall prognosis, despite that approximately one-third of them were under immunomodulator therapy, and 18% were on biologics.

The interplay between COVID-19 and the medications used for IBD is currently undefined; however, it is well known that several drugs used in patients with IBD may promote the occurrence of infections, including the opportunistic and viral ones. Nonetheless, the specific impact of immunosuppression on the severity of COVID-19 remains unclear. Data reported on 1099 patients from China did not observe immunomodulator use as a risk factor for severe disease.[2] Furthermore, the level of immunosuppression, and thus the theoretical risk of developing severe forms of COVID-19, varies depending by the specific drug. In this regard, Infectious Diseases Society of America guidelines distinguish patients with low-level vs high-level immunosuppression,[3] and only patients receiving daily corticosteroid therapy with a dosage >20 mg of prednisone or equivalent for >14 days, and those receiving tumor necrosis factor-alpha (TNF-α) inhibitors should be considered as individuals with high-level immunosuppression. We believe that this simple classification is reliable also in patients with IBD. Other drugs are not specifically mentioned by Infectious Diseases Society of America guidelines, as they were developed after the formulation of these indications. Therefore, the gut-specificity of vedolizumab should make the possibility that the drug may increase the risk of COVID-19 complications quite unlikely, whereas the anti-interleukin (IL)-12/23p40 block induced by ustekinumab has been associated with an excellent safety profile.[4] Regarding tofacitinib (and JAK inhibitors in general), some concerns may arise due to its potent multicytokine suppressive interference, even if its safety profile in IBD still needs to be clearly defined.[5] Recently, the British Society of

Gastroenterology published a document of advice for management of IBD during the COVID-19 pandemic.[6] The authors distinguished patient risk into highest, moderate, and lowest for COVID-19–related poor outcome. In summary, patients under treatment with any drug used for IBD, with the exception of mesalamine, budesonide, beclomethasone, or rectal therapies, were considered to have at least a moderate risk, whereas they were in the highest risk group if they also had a comorbidity and/or were ≥70 years old. Even if the authors stressed the concept that patients should continue their current medications until different medical advice, we believe that the use of terms such as "moderate" or "highest" risk may induce an unjustified alarmism among doctors and patients, which could lead to erroneously considering the opportunity to reduce or suspend the treatments for IBD, with the potential risk for flares of the disease.

Another relevant point to consider is that, in patients with severe COVID-19, a "cytokine storm" syndrome has been documented: a condition characterized by hyperactivation of T cells and massive production of several ILs. As a consequence, on a purely speculative level, it may be hypothesized that patients with IBD on immunomodulatory treatments, particularly those who directly interfere with cytokine action and production, may be protected even against the severe forms of COVID-19. Indeed, TNF-α is involved in the "cytokine storm" syndrome across key points of the cytokines cascade,[7] so that TNF-α inhibitors could be beneficial in this context, at least theoretically. In this line, adalimumab has been proposed as a biologic to test in the management of COVID-19.[8] In addition, preliminary evidence supported the use of tocilizumab, an IL-6 receptor antagonist, in the treatment of severe acute respiratory syndrome coronavirus 2–driven pneumonia, and similar effects could be induced by other anti-IL drugs, such as ustekinumab. Similar considerations may be argued also for JAK inhibitors, as their multicytokine block could be beneficial in preventing the "cytokine storm" syndrome. Not by chance, ruxolitinib, a JAK1/2 selective inhibitor used for the treatment of primary myelofibrosis, polycythemia vera, and graft-versus-host disease, has very recently started to be tested for COVID-19.[8]

In conclusion, the real risk of developing severe forms of COVID-19 in patients with IBD treated with immunomodulators or biologics is currently not defined, and should be clarified by large studies, which will be surely performed in the coming months and years. Although there is never too much prudence when evidence is lacking, excessive alarms should be avoided.

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Conflicts of interest
The authors disclose no conflicts.

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Cytokine Storm in IBD: Balancing the Risks of IBD Medical Therapy

Dear Editors:

We thank our colleagues for their interest in our report on the treatment strategies and outcomes of patients with inflammatory bowel disease (IBD) during the first months of the coronavirus disease 2019 (COVID-19) pandemic.[1] This series described the outcomes of 40 patients (23 ulcerative colitis, 13 Crohn's disease, and 4 IBD unclassified) diagnosed between February 27 and April 8, 2020. Approximately 20%–30% of patients were under biologic or immunosuppressive therapy, respectively, but we did not observe a relationship between any of these therapies and major adverse outcomes, including the development of systemic inflammatory response syndrome or acute respiratory distress syndrome, need for hospital or intensive care unit admission, or death. Age was the only predictive factor associated with a worse prognosis; patients >65 years of age showed a higher probability of being admitted (90% vs 40%; $P = .009$), or developing acute respiratory distress syndrome (30% vs 0%; $P = .013$), which is in line with findings across different cohorts irrespective of the presence of a previous diagnosis of IBD.

Our personal, social, and working conditions have changed dramatically since then, and >77 million people have been infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) according to the Center for Systems Science and Engineering at Johns Hopkins University (https://coronavirus.jhu.edu/map.html; accessed December 21, 2020). Many researchers worldwide have evaluated the impact of this infection on IBD patient care. A