

# Letter: SARS-CoV-2 induced gastrointestinal inflammation— authors' reply

EDITORS,

We thank Reuken et al for their comments and interest in our study reporting the incidence and clinical characteristics of COVID-19 among IBD patients.<sup>1,2</sup> A relevant finding of our study was the high rate of diarrhoea as a presenting symptom among IBD patients with COVID-19.

Reuken et al based their comment on new data from a study that included hospitalised COVID-19 patients in a single centre. The authors aimed to correlate the presence of SARS-CoV-2-RNA in faecal samples with clinical symptoms, faecal calprotectin and markers of systemic inflammation.<sup>1</sup> The proportion of patients with diarrhoea at admission was considerably lower than in our IBD patients with COVID-19, but their study included non-IBD patients. SARS-CoV-2 has a high affinity for angiotensin-converting enzyme 2 (ACE2), which is responsible for the viral invasion of human cells and is abundantly expressed in gastrointestinal cells.<sup>3</sup> Differences in the expression of intestinal membrane-bound ACE2 or of plasma ACE2 observed in IBD patients<sup>4</sup> could be associated with the high rate of diarrhoea in IBD patients with COVID-19 in our study.<sup>2</sup>

Reuken et al reported higher faecal calprotectin levels in patients with detection of SARS-CoV-2-RNA in faecal samples, indicating active viral replication in enterocytes causing significant gastrointestinal inflammation. A prior study reported high faecal calprotectin levels in COVID-19 non-IBD patients whose diarrhoea had resolved, and even higher levels in those with ongoing diarrhoea when compared with COVID-19 patients without diarrhoea.<sup>5</sup> In both studies, faecal calprotectin concentrations were associated with higher serum interleukin-6 concentration, indicating more severe systemic inflammation.<sup>1,5</sup> This finding raises the possibility that patients with SARS-CoV-2 infection causing relevant intestinal inflammation may potentially have more severe COVID-19. Conversely, a recently published study reported that among COVID-19 patients, the presence of gastrointestinal symptoms such as diarrhoea was associated with a trend towards lower intensive care unit admission rate and lower mortality during short-term follow-up.<sup>6</sup> Furthermore, patients with IBD, who often have diarrhoea as a presenting symptom of SARS-CoV-2 infection, do not appear to have an increased risk of progression to severe forms

of COVID-19.<sup>7,8</sup> It has been proposed that maintenance therapy with biologics in IBD patients, and anti-TNF agents in particular, may also play a protective role for severe COVID-19.<sup>9</sup> These combined findings may suggest that gastrointestinal symptoms such as diarrhoea indicating significant gastrointestinal inflammation can be associated with a more indolent form of COVID-19, although this hypothesis needs to be further evaluation in larger studies.

## ACKNOWLEDGEMENTS

The authors thank Dr G. Morley for reviewing the English manuscript.

*Declaration of personal interests:* The authors' declarations of personal and financial interests are unchanged from those in the original article.<sup>2</sup>

## LINKED CONTENT

This article is linked to Taxonera et al and Reuken et al papers. To view these articles, visit <https://doi.org/10.1111/apt.15804> and <https://doi.org/10.1111/apt.16087>

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