Risk of adverse events and reported clinical relapse after COVID-19 vaccination in patients with IBD

We have read with interest the recent papers of Kennedy *et al*[1 2] regarding the attenuated anti-SARS-CoV-2 antibody response in patients with IBD and the crucial role of the COVID-19 vaccine in this cohort. The COVID-19 vaccine has been recommended especially for the vulnerable population, including immune-mediated inflammatory diseases.[3–5] Therefore, we explored the rate of adverse events (AEs) and the onset of GI symptoms after vaccination with different COVID-19 vaccines in a large cohort of patients with IBD.

In this prospective study, we collected data (demographic and clinical variables, COVID-19 vaccine type, local, systemic or allergic AEs, and GI symptoms) from 488 (mean age±SD 55.3±14.4 years, 44.9% male) patients with IBD (UC 50.4%, Crohn's disease 47.8% and undetermined IBD 1.8%) on regular follow-up at our IBD unit who had been administered COVID-19 vaccination from June to July 2021.

Table 1 Patients' demographics and characteristics

Characteristics	Total (N=488)
Age (years), mean (SD)	55.3 (14.4)
Gender (male), n (%)	218 (44.9)
Type of disease, n (%)	
UC	246 (50.4)
CD	233 (47.8)
IBD-U	9 (1.8)
Disease duration (years), mean (SD)	18.4 (10.3)
Therapy, n (%)	
No treatment	132 (27.1)
Mesalamine	227 (46.5)
Corticosteroids	13 (2.7)
Azathioprine	32 (6.6)
Anti-tumour necrosis factor-α	75 (15.4)
Infliximab	21 (4.3)
Adalimumab	49 (10.0)
Golimumab	5 (1.0)
Vedolizumab	28 (5.7)
Ustekinumab	21 (4.3)
Tofacitinib	2 (0.4)
Previous COVID-19, n (%)	42 (8.6)
COVID-19 vaccine, n (%)	
Only one dose	55 (11.3)
Two doses	433 (88.7)
COVID-19 vaccine type, n (%)	
BNT162b2 (Pfizer)	320 (65.6)
mRNA-1273 (Moderna)	150 (30.7)
Vaxzevria (AstraZeneca)	18 (3.7)
Remission of disease, n (%)	397 (81.4)
State of mind before vaccine, n (%)	
Unconcerned	118 (24.2)
Afraid	23 (4.7)
Anxious	89 (18.2)
Wishful	246 (50.4)
Glad	12 (2.5)

CD, Crohn's disease; IBD-U, undetermined IBD; UC, Ulcerative Colitis.

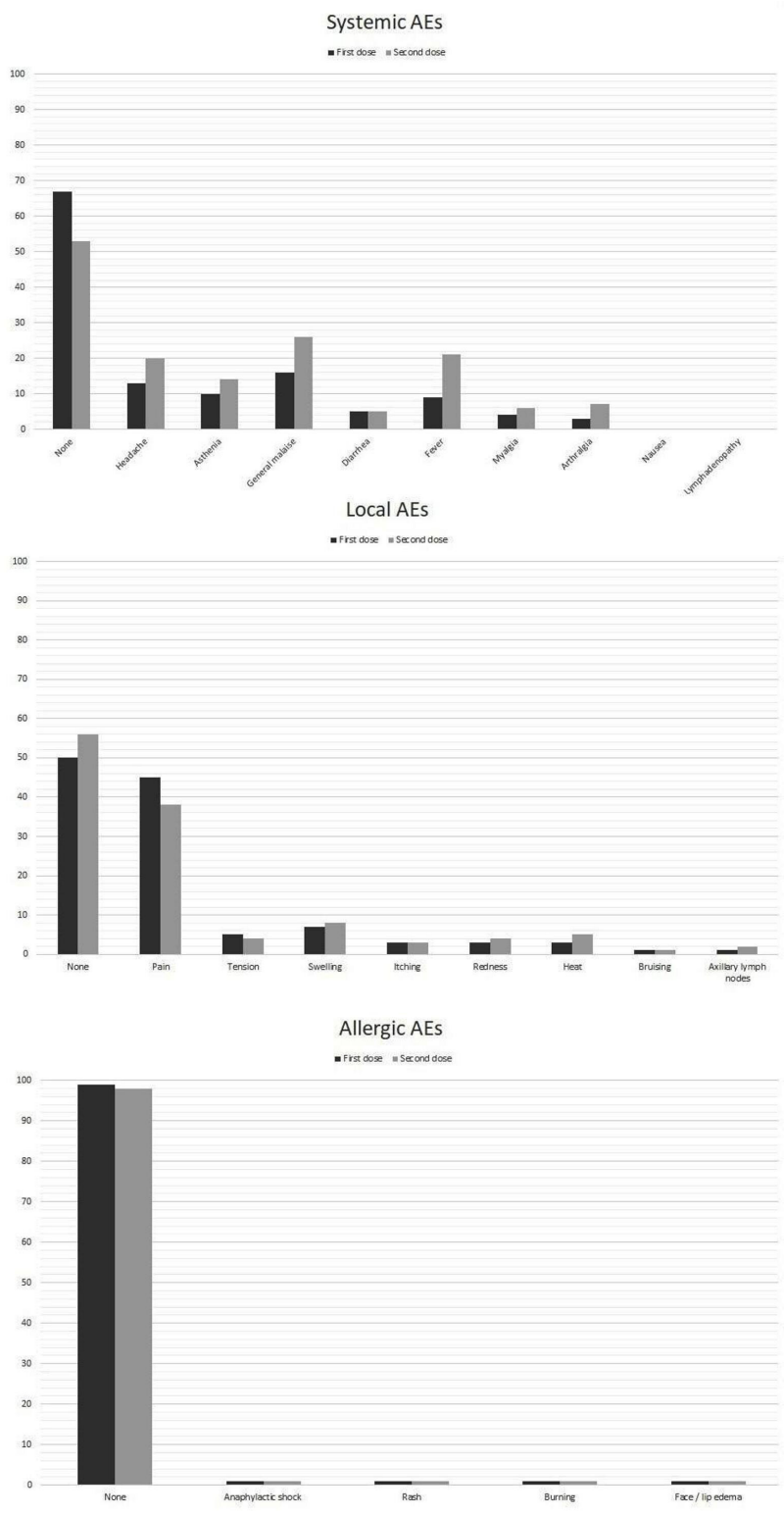

Figure 1 Systemic, local and allergic adverse events (AEs) in our IBD cohort. Data are expressed in %.

The demographic characteristics are shown in table 1. AEs were reported by 228 patients (46.7%) (figure 1). The most common systemic AE after the first dose was malaise (16.4%), followed by headache (12.9%) and asthenia (10.5%). After the second dose, there were more systemic AEs, such as malaise (26.4%), fever (20.7%) and headache (19.7%). Regarding local AEs, 220 (45.1%) and 186 (38.1%) patients experienced pain at the site of injection after the first and second dose, respectively. Finally, no severe allergic AEs were reported. The overall rate of AEs was similar to that reported in the general population.[6]

GI symptoms suggestive of current bowel disease such as 'increase of bowel movements', 'abdominal pain', 'blood in stool' and 'vomiting' were reported by 11.1%, 6.6%, 3.5% and 1.2% of patients, respectively. Globally, GI symptoms were reported by 15.6% (76 of 488) of patients at a mean±SD of 3±3.4 days after the vaccine, with a minimum of 1 day and a maximum of 15 days. However, virtually all cases were mild and self-limiting, and only one patient needed hospitalisation and consequent surgery due to a pre-existing substenotic pouchitis.

According to univariate and multivariate analyses (online supplemental file 1) and in line with a recent survey by Botwin *et al*,[7] AEs are more common among younger patients (OR 0.96, p<0.0005) and in cases of previous COVID-19 infection (OR 2.3, p=0.021). Regarding ongoing therapy, we found azathioprine (OR 0.39) to be inversely correlated to the presence of any AEs, while anti-tumour necrosis factor therapy (OR 2.01) was statistically significant only in the univariate analysis. Moreover, in the multivariate analysis, female gender was found to be a risk factor for developing any AEs (OR 1.96).

Regarding GI symptoms, we observed a higher rate of diarrhoea and abdominal pain compared with that reported by trials in the general population.[6 8] Age (OR 0.97) and disease remission (OR 0.43) inversely correlated with onset of GI symptoms both in the univariate and multivariate analyses (online supplemental file 1). To date, there has been no evidence that COVID-19 vaccination can trigger a flare-up, in accordance with prior experience which did not report any flares after vaccination.[9]

In conclusion, COVID-19 vaccination is highly recommended to patients with IBD and the rate of reported AEs is similar to the general population. In our cohort, a slightly higher rate of GI symptoms was observed, especially in younger patients with a concomitant active disease. However, the course of reported clinical flares is benign and self-limiting and should not discourage vaccine administration. Our findings suggest that in patients with active IBD, the decision to provide or postpone the vaccine in active disease should be tailored to each patient. Moreover, our data were based on a short-term follow-up and further studies on long-term AEs with objective markers are needed to state clearer recommendations.

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