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.

BNT162b2 Messenger RNA COVID-19 Vaccine Effectiveness in Patients With Inflammatory Bowel Disease: Preliminary Real-World Data During Mass Vaccination Campaign

A 2-dose regimen of the BNT162b2 messenger (m) RNA COVID-19 vaccine (Pfizer-BioNTech; Pfizer, New York, NY) has demonstrated 95% efficacy in preventing COVID-19 in a phase III placebo-controlled randomized clinical trial[1] and in real-world data analyses.[2,3]

Patients with inflammatory bowel disease (IBD) treated with immune-modifying agents are considered partially immunosuppressed, and thus, the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) recommends that patients with IBD should be vaccinated against COVID-19 and that vaccination should not be deferred in patients receiving immune-modifying therapies.[4] Because patients with immune conditions (including IBD) were excluded from the COVID-19 vaccine clinical trials, it is important to describe accumulating real-world data.[5]

In Israel, patients with IBD were given priority for early vaccination in the campaign, which is, as of June 23, 2021, the most extensive worldwide (63.6% of the total population received at least 2 doses, and 59.5% of the population was fully vaccinated).[6]

This study is a preliminary report of the effect of mass vaccination in patients with IBD.

This retrospective cohort study was conducted using data from the Maccabi Healthcare Services (MHS) central computerized database. MHS is the second largest state-mandated health care provider in Israel, covering >2.5 million members (25% of the population) and is a representative sample of the Israeli population.

To evaluate vaccine effectiveness, this study included individuals from the MHS IBD registry aged ≥16 years who received the BNT162b2 mRNA COVID-19 vaccine and matched patients (1:3) who were vaccinated between December 19, 2020 and March 10, 2021. Individual matching was performed based on sex, birth year, coexisting comorbidities, and month of the first vaccination dose. IBD status was defined according to the MHS IBD registry based on physician diagnosis and dispensed medications.[7]

The analysis excluded patients with a history of a positive polymerase chain reaction (PCR) result or a diagnosis of COVID-19 any time before the first BNT162b2 vaccination. All eligible patients were required to have a minimum of 30 days of follow-up after the second vaccine dose date, referred to as the "index date," to observe study outcomes. Retrospective follow-up lasted from the index date until April 11, 2021 (details are provided in the Supplementary Text). The MHS Ethics Committee approved the study protocol.

The study included 12,231 patients with IBD and 36,254 matched patients. Overall, 50.0% were women, and the mean age was 47 ± 17 years in both groups. Follow-up was a median of 71 days (interquartile range, 52–80 days), and the interval between vaccines was a median of 21 days (interquartile range, 20–21 days). Baseline characteristics and positive PCR result by disease type and treatment are presented in Supplementary Table 1.

Breakthrough infection rates >7 days after the second dose were 0.19 % in patients with IBD and 0.15% in matched patients and after >14 days after the second dose were 0.14% and 0.10%, respectively. The calculated relative risk (RR) for IBD was 1.21 (95% confidence interval [CI], 0.74–1.97) >7 days after the second dose and 1.26 (95% CI, 0.71–2.23) >14 days after the second dose. The Mantel-Cox log-rank test from the Kaplan-Meier survival analysis (Figure 1*A*) was not statistically significant ($P = .430$). Of 23 patients with IBD who had a positive PCR result >7 days after the second dose, 9 had symptoms, 2 were hospitalized, and 1 died (details in Supplementary Table 2*a*).

Compared with their matched patients, patients with Crohn's disease (CD) were at a greater risk for breakthrough infection ($P = .055$), while no significant difference ($P = .310$) was shown among patients with ulcerative colitis (UC) (Figure 1*B* and *C*). The RR for CD and matched patients was 1.52 (95% CI, 0.69–3.28) >7 days after the second dose and 1.82 (95% CI, 0.69–4.79) >14 days after the second dose, whereas for UC and matched patients, the RR was 0.53 (95% CI, 0.18–1.58) >7 days after the second dose and 0.95 (95% CI, 0.28–3.81) >14 days after the second dose.

In multivariable Cox proportional hazard models, patients with CD had an elevated risk for breakthrough infection compared with patients with UC >7 days and >14 days after the second dose, with hazard ratios of 3.56 (95% CI, 1.29–9.83) and 3.38 (95% CI, 1.07–10.64), respectively. No increased risk was demonstrated for patients treated with immune-modifying therapies (Supplementary Table 2*a* and *b*).

In this study, we describe the effectiveness of the BNT162b2 mRNA COVID-19 vaccine in patients with IBD. As demonstrated in the general population, the vaccine is highly efficient, with a very low absolute breakthrough infection rate (0.1%) for fully vaccinate patients.

Our large cohort allowed us to explore the effect of immune-modifying treatments in patients with IBD on the risk for COVID-19 infection after vaccination. A publication by the IOIBD recommended that patients with IBD vaccinated against COVID-19 be counseled that vaccine efficacy may be decreased when receiving systemic corticosteroids.[4] Despite the wide use of immune-modifying medications,

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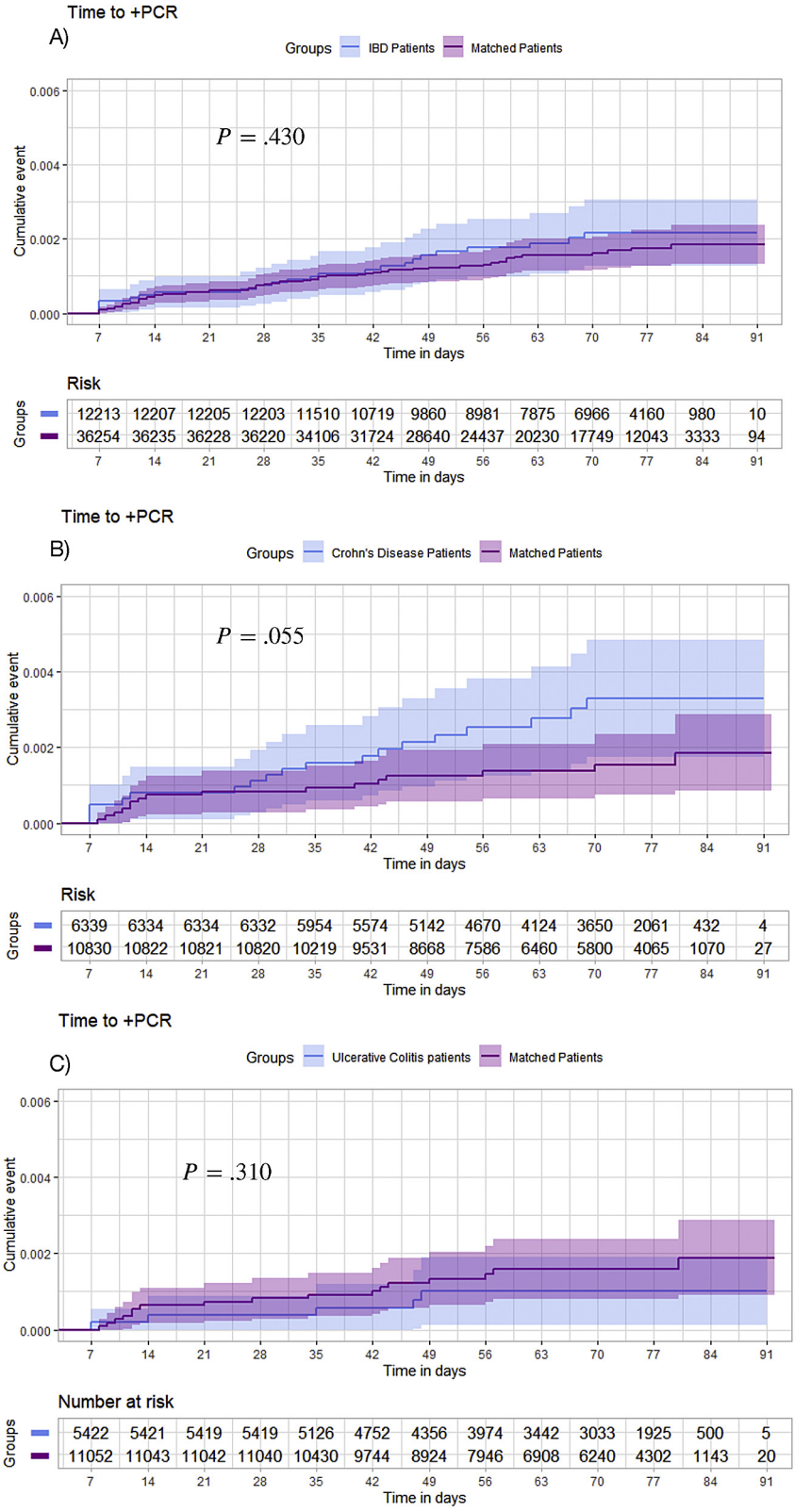

Figure 1. Kaplan Meier survival curves of matched patients with and without (*A*) IBD, (*B*) Crohn's disease, and (*C*) ulcerative colitis showing days to positive polymerase chain reaction (>7 days after the second COVID-19 vaccine). The *shaded areas* indicate the 95% confidence interval.

vaccine effectiveness in our study cohort was high. A recent publication by Wong et al[8] demonstrated that a protective serologic response after mRNA vaccine administration developed in all patients with IBD in their cohort, where most patients were treated with immune-modifying treatments. Their findings support our results.

A trend toward an increased risk for breakthrough infection compared with matched patients was observed

among patients with CD but not among patients with UC. If validated by other and larger cohorts, these findings suggest that patients with CD may have an increased risk for breakthrough infection.

In conclusion, to the best of our knowledge, this is the one of the first reports of real-world COVID-19 vaccine effectiveness in patients with IBD. Overall vaccine effectiveness was excellent and comparable to the reference population.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2021.06.076.

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Supplementary Text

Patient characteristics such as age, sex, vaccine month, and incident COVID-19 infections are described in Supplementary Table S1. Study outcomes were measured by the first positive reverse-transcription polymerase chain reaction SARS-CoV-2 test result or incident diagnosis of COVID-19 (from community care or hospitalization) occurring >7 days and >14 days after the index date. Outcomes were evaluated with Kaplan-Meier curves and relative risk (RR) to analyze patients with inflammatory bowel disease and their matched patients and then evaluated separately for patients with Crohn's disease and those with ulcerative colitis with their matched patients.

In a secondary analysis, internal comparisons were made among patients with inflammatory bowel disease. Cox's regression analyses were performed and evaluated positive polymerase chain reaction outcomes >7 days and >14 days after the second vaccine dose. Covariates in the models included age, sex, type of inflammatory bowel disease, and whether patients were on immunosuppressive treatment (binary variable) 3 months before the index date.