Serological responses to three doses of SARS-CoV-2 vaccination in inflammatory bowel disease

We read with interest the article by Kennedy et al, which demonstrated adequate serological responses to two-dose regimens of SARS-CoV-2 vaccination in individuals with IBD. However, a decay in antibody levels has been shown in the IBD population after two vaccine doses, with anti-tumour necrosis factor (anti-TNF) therapies associated with a more rapid decline. Despite recommendations for three-dose vaccine regimens for individuals with IBD, the uptake has been low in this population. We examined the serological response following three doses of mRNA SARS-CoV-2 vaccines in persons with IBD, the factors associated with antibody titres and the decay of antibody titres over time.

Adults aged 18 years or older with a confirmed diagnosis of IBD who received three doses of an mRNA SARS-CoV-2 vaccine (Pfizer-BioNTech BNT162b2 mRNA (Comirnaty) or NIH-Moderna mRNA-1273 (Spikvax)) were recruited from 25 June 2021 to 6 January 2022. Serum samples were drawn at least 1 week following the third dose of vaccine and processed by Alberta Precision Laboratories using the Abbott SARS-CoV-2 IgG II Quant assay to detect antibodies to the S1 subunit of the spike protein (anti-S). The threshold for seroconversion was defined as ≥50 AU/mL for anti-S antibodies. Age, sex, vaccination date and type, IBD type, and IBD medications at time of vaccination were collected through medical chart review. Vaccine schedule between second and third vaccine doses was defined as ‘scheduled’ for 4–18 weeks between dose administration and ‘delayed’ for >18 weeks. Prior history of COVID-19 was defined by either nucleocapsid seroconversion or molecular-confirmed diagnosis of SARS-CoV-2 infection via PCR.

Geometric mean titres (GMTs) with associated 95% CIs were used to report anti-S concentrations. Multivariable linear regression was used to determine the effect of independent predictors determined a priori on log-transformed anti-S concentration. Exponentiated coefficients represented the fold change (FC) associated with each binary covariate and the FC in log anti-S concentration per unit change for continuous variables.

In total, 232 participants (mean age 52.7 years; 42.7% male) with IBD and three doses of an mRNA vaccine were included (table 1). The seroconversion rate among this sample was 99.6% and the GMT was 14 569 AU/mL (95% CI 12 846 to 16 472 AU/mL). Multivariable linear regression identified significantly increased log anti-S concentration for prior SARS-CoV-2 infection (FC: 1.97 (95% CI 1.22 to 3.18)) and decreased log anti-S concentration for corticosteroid use (FC: 0.07 (95% CI 0.03 to 0.20)) (table 1). Antibodies decayed by 12% per week (95% CI 1.22 to 3.18) following third-dose vaccination (figure 1). Age, sex, IBD type, vaccine type and vaccine schedule were not associated with anti-S concentration. Our data can be viewed in an online dashboard (https://kaplan-gi.shinyapps.io/COVID_Serology) using the Shiny: Web Application Framework for R package.

A three-dose SARS-CoV-2 vaccination regimen for individuals with IBD has been proposed based on impaired serological responses to two-dose regimens. Our study demonstrates near complete seroconversion and high antibody titres following a three-dose mRNA vaccine regimen, similar to an American cohort of individuals with IBD that demonstrated a robust antibody response following an extra dose from the initial vaccine series. Antibody responses following three doses are consistently high across all IBD therapies for maintenance of remission, including biologic and immunomodulator therapies. In contrast, prednisone use at the time of vaccine dosing was associated with lower antibody responses.

Our study also indicated significant decay of antibody titres over time following third-dose vaccination at a rate of 12% per week. While these data support widespread implementation of a three-dose vaccine regimen, future studies are necessary to determine if...
additional doses will be required to maintain sufficient antibody levels over time.

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Contributors GGK has full access to all data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. GGK, CM, IQ, JK, GT, RP conceived and designed the study. GGK, CM, RR, NS, MH, RJ, AM were responsible for clinical data. JK, GT, were responsible for serological data. JQ, GGK, SC, LH analysed the data. JQ and GGK drafted the manuscript. All authors interpreted the data and provided critical revisions of the manuscript for important intellectual content. All authors have approved the final draft of the manuscript.


Competing interests GGK has received honoraria for speaking or consultancy from AbbVie, Janssen, Pfizer, Amgen and Takeda. He has received research support from Ferring, Janssen, AbbVie, GlaxoSmith Kline, Merck and Shire. He has been a consultant for Gilead. He shares ownership of a patent: TREATMENT OF INFLAMMATORY DISORDERS, AUTOIMMUNE DISEASE, AND PBC. UTI Limited Partnership, assignee. Patent WO2019046959A1. PCT/CAN2018/051098. 7 Sept. 2018. CNB is supported by the Bingham Chair in Gastroenterology. CNB has served on advisory Boards for AbbVie Canada, Amgen Canada, Avir Pharmaceuticals, Bristol Myers Squibb Canada, Roche Canada, JAMP Pharmaceuticals Canada, Janssen Canada, Sandoz Canada, Takeda Canada and Pfizer Canada; Consultant for Mylan Pharmaceuticals and Takeda; Educational grants from AbbVie Canada, Pfizer Canada, Takeda Canada, and Janssen Canada. Speaker’s panel for Abbvie Canada, Janssen Canada, and Takeda Canada. Received research funding from Abbvie Canada, Amgen Canada, Sandoz Canada and Pfizer Canada. CM has received consulting fees from AbbVie, Aliments, Amgen, AVIR Pharma Inc, BiJAMP, Bristol Myers Squibb, Celtrion, Ferring, Galapagos Kabi, Janssen, McKesson, Mylan, Takeda, Penderopharm, Pfizer, Roche; speaker’s fees from AbbVie, Amgen, AVIR Pharma Inc, Aliments, Ferring, Janssen, Takeda, and Pfizer; research support from Ferring, Pfizer. RP has received consulting fees, speaker fees and research support from AbbVie, Abbott, Aliments (formerly Roberts), Amgen, Arena Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Celtrion, Cosmos Pharmaceuticals, Eisai, Eli Lilly, Ferring, Fresnius Kabi, Galapagos, Genentech, Gilead Sciences, Glaxo-Smith Kline, Janssen, Merck, Mylan, Opplian Pharma, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Satisfi Health, Sandoz, Schering-Plough, Shire, Sublimity Therapeutics, Theravance Biopharma, UCB and Takeda Pharmaceuticals. EIB has acted as a legal consultant for Hoffman La-Roche Limited and Peabody & Arnold LLP for matters unrelated to a medication used to treat IBD.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the University of Calgary’s Conjoint Health Research Ethics Board (REB20-1082). Participants gave informed consent to participate in the study before taking part.

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