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.

SARS-CoV-2 vaccination for patients with inflammatory bowel disease

We read with interest the position statement of the British Society of Gastroenterology Inflammatory Bowel Disease (IBD) section and IBD Clinical Research Group.[1] Although we largely agree with the key messages that SARS-CoV-2 vaccination should be strongly supported for patients with IBD and that the anticipated risks are low, we wish to raise a few relevant remarks based on previously published studies on vaccination for other pathogens in this patient group. Alexander and colleagues[1] rightfully argue that the response to pneumococcal, influenza, and hepatitis A vaccination in patients with IBD receiving immunosuppressive agents is diminished compared with that in control individuals. However, we disagree that the response to vaccination in patients receiving anti-tumour necrosis factor (anti-TNF) agents is lower than that in patients receiving conventional immunomodulators. In a systematic review and meta-analysis of 17 studies, we showed that patients with IBD using anti-TNF agents were more likely to seroconvert after the first dose of hepatitis A vaccine (OR 12·1, 95% CI 2·14–68·2) than were patients using conventional immunomodulators.[2] Regarding pneumococcal vaccination, a study involving 141 patients with IBD showed that the response to pneumococcal vaccination was not inferior (63%) in patients receiving anti-TNF therapy compared with patients receiving conventional immunomodulators (60%).[3] Patients on combination therapy had a significantly lower response (52%) than did those receiving either anti-TNF therapy or conventional immunomodulators. A systematic review on pneumococcal vaccination comprising 2077 participants found a superior response in patients using an anti-TNF treatment compared with those using conventional immunomodulators. One explanation could be that anti-TNF agents cause a more specific inhibition of the immune system than do conventional immunomodulators.[4]

It should be noted that approved SARS-CoV-2 vaccines are very different from the currently licenced vaccines that were previously tested in patients with IBD. Both the mRNA and adenovirus vector vaccines encode the production of SARS-CoV-2 spike protein, leading to the production of neutralising antibodies and virus-specific T-cell responses.[5] We agree that, in the current absence of immunogenicity studies and the unfortunate situation of vaccine paucity, patients with IBD should accept whichever approved vaccine is offered to them. However, we hypothesise that mRNA vaccines might prove to be the better option for patients with IBD using immunosuppressants than might adenovirus vector vaccines for two reasons. First, the licenced adenovirus vector vaccines (ie, Janssen or Oxford/AstraZeneca) are less effective than mRNA vaccines (ie, Pfizer/BioNTech or Moderna) in healthy individuals. Thus, effectiveness in immunocompromised individuals is expected to be lower as well, even though optimal protection of this susceptible population is needed. Second, the adenovirus vector formulation might generate adenovirus-specific immunity, which might limit the effectiveness of booster doses that could be necessary for immunocompromised individuals.[5]

We declare no competing interests.

*Hannah M Garcia Garrido, Martin P Grobusch, Geert R A M D'Haens, *Abraham Goorhuis*
a.goorhuis@amsterdamumc.nl

Centre of Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Amsterdam Institute for Infection and Immunity (HMGG, MPG, AG) and Department of Gastroenterology and Hepatology (GRAMD), Amsterdam UMC, University of Amsterdam, Amsterdam 1105 AZ, Netherlands

1 Alexander JL, Moran GW, Gaya DR, et al. SARS-CoV-2 vaccination for patients with inflammatory bowel disease: a British Society of Gastroenterology Inflammatory Bowel Disease section and IBD Clinical Research Group position statement. *Lancet Gastroenterol Hepatol* 2021; **6:** 218–24.
2 Garcia Garrido HM, Veurink AM, Leeflang M, Spijker R, Goorhuis A, Grobusch MP. Hepatitis A vaccine immunogenicity in patients using immunosuppressive drugs: a systematic review and meta-analysis. *Travel Med Infect Dis* 2019; **32:** 101479.
3 van Aalst M, Garcia Garrido HM, van der Leun J, et al. Immunogenicity of the currently recommended pneumococcal vaccination schedule in patients with inflammatory bowel disease. *Clin Infect Dis* 2020; **70:** 595–604.
4 van Aalst M, Langedijk AC, Spijker R, de Bree GJ, Grobusch MP, Goorhuis A. The effect of immunosuppressive agents on immunogenicity of pneumococcal vaccination: a systematic review and meta-analysis. *Vaccine* 2018; **36:** 5832–45.
5 Teijaro JR, Farber DL. COVID-19 vaccines: modes of immune activation and future challenges. *Nat Rev Immunol* 2021; **21:** 195–97.

Authors' reply

We thank Garcia Garrido and colleagues for their comments on the British Society of Gastroenterology Inflammatory Bowel Disease (IBD) and IBD Clinical Research Group section position statement[1] and the studies cited in their Correspondence, including the valuable meta-analysis of the impact of immunosuppression on pneumococcal vaccination.[2] However, the results of this meta-analysis should be interpreted with caution in patients with IBD, as most of the studies included (18 of 22) were from patients with other immune-mediated inflammatory diseases (mostly rheumatoid arthritis), in which the only conventional immunomodulator reported was methotrexate. Additionally, in the few IBD studies included, anti-TNF treatment significantly impaired vaccine responses, whereas immunomodulators did not. The 2020 study by van Aalst and colleagues[3] also substantiates impaired pneumococcal vaccine (PCV13) responses in patients receiving anti-TNF agents. The key message is that there is clear evidence of impaired pneumococcal vaccine responses in patients with IBD taking

anti-TNF therapy, with less clear or conflicting evidence available for conventional immunomodulators.

We agree that any impact of immunosuppression is likely to be specific to vaccines. Fortunately, data are now emerging on the effects of immunosuppressive therapies on anti-SARS-CoV-2 vaccine immunogenicity in patients with IBD. Results from 1283 patients with IBD in the CLARITY IBD study have shown that rates of seroconversion are lower after the first dose of both the BNT162b2 (Pfizer/BioNTech) and ChAdOx1 nCoV-19 (Oxford/AstraZeneca) vaccines in patients treated with infliximab than in patients treated with vedolizumab.[4] Anti-TNF monotherapy and immunomodulator monotherapy were not compared; however, the combination of infliximab and immunomodulator therapy was associated with the lowest rates of seroconversion with both vaccines. Whether any particular vaccine should be favoured in patients with IBD is more contentious. No major serological differences were observed in CLARITY IBD between the two vaccines, but there are conceptual reasons to suspect that adenovirus vector vaccines might elicit favourable T-cell responses, which could be important for durable immunity. Data regarding the effects of immunosuppressive therapies on T-cell responses are eagerly anticipated.

Important unanswered questions remain. Although early data from small cohorts of patients with IBD treated with anti-TNF agents completing two doses of mRNA vaccination in CLARITY IBD and in the USA[5] report robust vaccination responses, larger studies, including those incorporating data on adenovirus vector vaccines, are urgently needed. Furthermore, the effects on vaccine immunogenicity of other immunosuppressive regimens used in IBD are yet to be systematically investigated.

JLA reports sponsorship from Vifor Pharma for accommodation and travel to British Society of Gastroenterology 2019. NAK reports personal fees from Dr Falk, Janssen, Takeda, and Tillotts; and grants and personal fees from Pharmacosmos. TA reports grants from F Hoffmann-La Roche AG, Janssen, and Galapagos; grants and personal fees from Biogen, Celltrion, and Celgene; non-financial support from AbbVie and Tillotts; personal fees from Arena, Adcock Ingram, Gilead, Pfizer, and Genentech; and grants, personal fees, and non-financial support from Takeda. CWL reports grants and personal fees from Gilead; and personal fees from AbbVie, Takeda, Janssen, Ferring, Trellus Health, Pfizer, Galapagos, and Iterative Scopes. NP reports serving as a speaker for Allergan, Bristol Myers Squibb, Falk, Ferring, Janssen, Pfizer, Tillotts, and Takeda, and as a consultant and/or an advisory board member for AbbVie, Allergan, Celgene, Bristol Myers Squibb, Ferring, and Vifor Pharma.

*James L Alexander, Nicholas A Kennedy, Charlie W Lees, Tariq Ahmad, *Nick Powell, on behalf of the British Society of Gastroenterology Inflammatory Bowel Disease section and IBD Clinical Research Group*
nicholas.powell@imperial.ac.uk

Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK (JLA, NP); Department of Gastroenterology, Imperial College Healthcare NHS Trust, London, UK (JLA, NP); Department of Gastroenterology, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK (NAK, TA); Exeter Inflammatory Bowel Disease and Pharmacogenetics Research Group, University of Exeter, Exeter, UK (NAK, TA); Institute of Genetic and Molecular Medicine, University of Edinburgh, Edinburgh, UK (CWL); Department of Gastroenterology, Western General Hospital, Edinburgh, UK (CWL)

1 Alexander JL, Moran GW, Gaya DR, et al. SARS-CoV-2 vaccination for patients with inflammatory bowel disease: a British Society of Gastroenterology Inflammatory Bowel Disease section and IBD Clinical Research Group position statement. *Lancet Gastroenterol Hepatol* 2021; **6:** 218–24.

2 van Aalst M, Langedijk AC, Spijker R, de Bree GJ, Grobusch MP, Goorhuis A. The effect of immunosuppressive agents on immunogenicity of pneumococcal vaccination: a systematic review and meta-analysis. *Vaccine* 2018; **36:** 5832–45.

3 van Aalst M, Garcia Garrido HM, van der Leun J, et al. Immunogenicity of the currently recommended pneumococcal vaccination schedule in patients with inflammatory bowel disease. *Clin Infect Dis* 2020; **70:** 595–604.

4 Kennedy NA, Lin S, Goodhand JR, et al. Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD. *Gut* 2021; published online April 26. https://doi.org/10.1136/gutjnl-2021-324789.

5 Wong SY, Dixon R, Pazos VM, et al. Serological response to mRNA COVID-19 vaccines in IBD patients receiving biological therapies. *Gastroenterology* 2021; published online April 19. https://doi.org/10.1053/j.gastro.2021.04.025.

Stent insertion for incurable oesophageal carcinoma: what is the optimal treatment?

We read with great interest the Article by Douglas Adamnson and colleagues in *The Lancet Gastroenterology & Hepatology*[1] assessing the outcomes of patients with incurable oesophageal cancer who had received external beam radiotherapy (EBRT) after stenting with self-expanding metal stent (SEMS) versus receipt of usual care in the ROCS trial. They concluded that the EBRT increased the cost of treatment without any improvement in overall survival, dysphagia deterioration-free survival, relief of dysphagia, and quality of life. We believe that this multicentre, randomised, controlled trial is a landmark study examining the merits of EBRT following SEMS, and congratulate Adamson and colleagues for their valuable study.

In our previous prospective study in patients with incurable oesophageal carcinoma,[2] we showed that EBRT conferred no survival benefit, but that it increased the cost of treatment in hospital.[2] Zhu and colleagues[3] presented results showing that BRT can better relieve dysphagia and prolong patient survival when compared with SEMS. The findings from the ROCS trial are consistent with our work. In the ROCS trial, many patients experienced distant or lymph node metastasis, which might be a leading cause of death in this patient population. Theoretically, the addition of EBRT might not improve survival because EBRT provides radiotherapy only to tumour lesions and has no effect on disease metastases. Furthermore, the dose of radiation from EBRT in the oesophageal lumen was too difficult to precisely measure and control. Generally, there is a risk of perforation during continuous radiotherapy.

Overall survival in this patient population in previous studies