

## **British Society of Gastroenterology Inflammatory Bowel Disease section and IBD Clinical Research Group position statement on SARS-CoV2 Vaccination**

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The Inflammatory Bowel Disease (IBD) Section of the BSG and the IBD Clinical Research Group have agreed the following key recommendations:

- 1. We strongly support SARS-CoV2 vaccination for patients with IBD.**
- 2. The risks of SARS-CoV2 vaccination in IBD patients are anticipated to be very low.**
- 3. In IBD patients taking immunosuppressive drugs, including biologics and small molecule inhibitors, the key concerns are related to the theoretical risk of sub-optimal vaccine responses rather than vaccine side effects.**
- 4. We recommend that IBD patients accept whichever approved SARS-CoV2 vaccination is offered to them, in accordance with UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency (MHRA) guidance.**
- 5. It is important that patients with IBD are offered consistent and unbiased advice. This will be disseminated through the BSG and Crohn's & Colitis UK.**

#### **Position Statement Review**

On 30/12/2020, the Oxford/AstraZeneca *ChAdOx1 nCoV-19* vaccine was given MHRA approval for deployment in the UK. It is anticipated that other vaccines may receive approval in the coming weeks and guidance may change accordingly. Consequently, this Position Statement will be reviewed frequently. The next date for review is 6<sup>th</sup> January 2021.

## Introduction

- The COVID-19 pandemic has caused significant mortality across the globe, with wide-ranging impacts across all sectors of society.
- Patients with IBD may have increased susceptibility to infectious diseases.
- The introduction of SARS-CoV2 vaccines is the first opportunity to suppress the virus over the long term and to protect individual patients from COVID-19.
- Several SARS-CoV2 vaccines are in advanced clinical development, and currently there are three that are approved/awaiting approval in the UK (see table 1). It is likely that additional vaccines will become available in the future.
- The BNT162b2 vaccine (Pfizer/BioNTech)<sup>1</sup> and the ChAdOx1 nCoV-19 (Oxford/AstraZeneca)<sup>2</sup> have been given authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency under Regulation 174 of the Human Medicine Regulations 2012<sup>a,b,c</sup>.
- The mRNA-1273 (Moderna)<sup>3</sup> vaccine is currently under review by the MHRA and an authorisation decision is imminently anticipated.

<sup>a</sup><https://www.legislation.gov.uk/ukxi/2012/1916/contents/made>

<sup>b</sup><https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/information-for-healthcare-professionals-on-pfizerbiontech-covid-19-vaccine>

<sup>c</sup><https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca/information-for-healthcare-professionals-on-covid-19-vaccine-astrazeneca>

Table 1: Overview of SARS-CoV2 vaccines

	<b>Pfizer/BioNTech</b>	<b>Moderna</b>	<b>Oxford/AstraZeneca</b>
Name	<i>BNT162b2</i>	<i>mRNA-1273</i>	<i>ChAdOx1 nCoV-19</i>
Dosing schedule	2 doses, between 3 weeks and 12 weeks apart	2 doses, between 4 weeks and 12 weeks apart	2 doses, between 4 weeks and 12 weeks apart
Mechanism	mRNA encoding a genetically modified SARS-CoV2 spike protein	mRNA encoding a genetically modified SARS-CoV2 spike protein	Non-replicating adenovirus vector, containing SARS-CoV-2 spike protein
Storage (long term)	-80°C to -60°C	-20°C	+2°C to +8°C

Reported efficacy	95%	94.5%	70%*
Safety	No serious concerns. Two anaphylactoid reactions since MHRA approval and roll-out.	No serious concerns	No serious concerns

\*pooled data from two trials - 62% efficacy in one study and 90% in another study in which first vaccination was given at half dose.

### Vaccination logistics in IBD patients

- The Joint Committee on Vaccination and Immunisation (JCVI) is responsible for advising which sectors of society are prioritized in national vaccination programmes. As of 30<sup>th</sup> December 2020, priority sequencing is based on providing protection to the persons most at risk of morbidity and mortality from COVID-19<sup>d</sup>. Since mortality from COVID-19 increases exponentially with age, the initial JCVI prioritisation is primarily age-based. The order of priority for phase 1 of the vaccination programme is listed as:
  1. Residents in a care home for older adults and their carers
  2. All those 80 years of age and over and frontline health and social care workers
  3. All those 75 years of age and over
  4. All those 70 years of age and over, and clinically extremely vulnerable individuals
  5. All those 65 years of age and over.
  6. All individuals aged 16 years to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality
  7. All those 60 years of age and over
  8. All those 55 years of age and over
  9. All those 50 years of age and over

<sup>d</sup><https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-30-december-2020/joint-committee-on-vaccination-and-immunisation-advice-on-priority-groups-for-covid-19-vaccination-30-december-2020>

- In keeping with the BSG risk grid<sup>4</sup>, it is anticipated that IBD patients who are under the age of 65 years and in the moderate BSG risk category will fall into **category 6**. IBD patients in the BSG high risk category will fall into **category 4**.

- Irrespective of their position in the BSG risk grid, IBD patients who are residents in care homes (**category 1**), are frontline health and social care workers (**category 2**), or are aged 75 years or older (**category 3**) will be further prioritized.
- In the context of the rapidly worsening epidemiology of COVID-19 in the UK in late 2020, and given data indicating high efficacy from the first dose of both the BNT162b2 vaccine (Pfizer/BioNTech) and the ChAdOx1 nCoV-19 vaccine (Oxford/AstraZeneca), the JCVI is prioritising the delivery of the first dose of vaccine to as many eligible individuals as possible. The second dose of vaccine can be delivered between 3 to 12 weeks after the first dose of the Pfizer/BioNTech vaccine, and between 4 to 12 weeks after the first dose of the Oxford/AstraZeneca vaccine<sup>d</sup>.
- JCVI further advises that the same vaccine should be used for both doses and that switching between vaccines or missing the second dose is not advised.

### **Concerns of the IBD patient community**

Patients with IBD will have many questions regarding vaccination and specific data to inform many of these concerns are not yet available. However, there are several factors that can offer some reassurance:

- There is a robust and comprehensive regulatory process in place and approval is only given when there are compelling safety data.
- Standards for testing and monitoring of vaccines are generally higher than for most other medical interventions due to their intended use in healthy individuals, in whom the level of acceptable risk is lower.
- The SARS-CoV2 vaccines have been tested in tens of thousands of patients with safety profiles comparable to other vaccines commonly used in IBD patients.

### **Frequently asked questions**

In collaboration with Crohn's & Colitis UK, we have identified a number of questions that are commonly asked about vaccination against COVID-19. We would recommend that patients are directed to the Crohn's & Colitis UK webpage ([www.crohnsandcolitis.org.uk](http://www.crohnsandcolitis.org.uk)). Healthcare providers can help to answer such questions and we have provided some answers below:

#### **1. Can patients with IBD have vaccination against COVID-19?**

*Yes. Although MHRA guidance will be given separately and independently for each of the vaccines, at the time of writing the Pfizer/BioNTech BNT162b2 vaccine and the Oxford/AstraZeneca ChAdOx1 nCoV-19 vaccine have received approval from the MHRA. Importantly, for both vaccines immunosuppression is not a contraindication.*

## **2. Are there any groups of IBD patients who will not be eligible to receive SARS-CoV2 vaccination?**

*Yes, there are some groups of patients in whom vaccination is not yet approved. These include those aged under 16 years. Although routine use of the Pfizer-BioNTech or AstraZeneca SARS-CoV2 vaccines is not recommended in pregnancy, vaccination should be considered in women in whom the risk of exposure to SARS-CoV2 is high and unavoidable, or in women with underlying health conditions that put them at very high-risk of serious complications of COVID-19. In these cases, risk/benefit should be discussed with individual patients. The JCVI advises that breastfeeding is not a contraindication to vaccination. The clinical need for immunisation should be considered and women informed about the absence of safety data for the vaccine<sup>d</sup>.*

## **3. Are the SARS-CoV2 vaccines safe in IBD patients?**

*Although there are no safety data regarding SARS-CoV2 vaccination in IBD patients, MHRA approval is based on safety data generated from monitoring over 19,000 vaccine recipients for at least two months after their second dose (serious side effects from vaccines are very rare beyond this point). Side effect profiles from SARS-CoV2 vaccines are in line with events observed with other commonly used vaccines. Data from the BNT162b2 phase 3 trial, which enrolled >40,000 subjects, and the ChAdOx1 nCoV-19 phase 3 trials, which enrolled >23,000 subjects, demonstrated that mild local injection site reactions (e.g. pain, redness and swelling) and systemic features (fatigue, headache, chills) were common, but serious adverse events were rare<sup>2, 5</sup>. For instance, there were 4 serious adverse events in BNT162b2 recipients (shoulder injury related to vaccine administration, right axillary lymphadenopathy, ventricular arrhythmia, and right leg paraesthesia). Serious adverse events occurred in 79 participants who received ChAdOx1 nCoV-19, and 89 in those who received placebo. Very rare events of neuroinflammatory disorder have been reported with the ChAdOx1 nCoV-19 vaccine, but a causative role has not been established. There were 2 deaths in BNT162b2 recipients and 4 deaths in placebo recipients, which were considered to be unrelated to the vaccine or placebo. There were four non-COVID-19 related deaths in ChAdOx1 nCoV-19 trials, three in controls and one in the vaccine recipients. All were considered unrelated.*

## **4. What effect does immunosuppression have on SARS-CoV2 vaccines?**

*Although the MHRA does not list immunosuppression as a contraindication to the BNT162b2 vaccine or the ChAdOx1 nCoV-19 vaccine, it does indicate that there is a theoretical possibility that immunosuppressive drugs could reduce the effectiveness of the vaccines. This is likely to be based on evidence from studies looking at the impact of immunosuppression on the*

immunogenicity of other commonly used vaccines. Infliximab monotherapy is linked to impaired induction of protective immunity following hepatitis B<sup>6</sup>, hepatitis A<sup>7</sup>, pneumococcal<sup>8, 9</sup> and influenza<sup>10-12</sup> vaccination, which may be more pronounced when anti-TNF therapy is combined with immunomodulators including thiopurines or methotrexate<sup>13, 14</sup>. Vedolizumab, however, which has a gut specific mechanism of action, does not hinder hepatitis B or influenza vaccination, but is associated with impaired antibody responses to cholera toxin, administered orally<sup>15</sup>. There is a lack of data for some of the newer drugs used in IBD, although lessons have been learned in other immune-mediated inflammatory diseases. For instance, in psoriasis, antibody responses to pneumococcal and tetanus vaccines are preserved, and possibly even enhanced in patients treated with ustekinumab, a monoclonal antibody that blocks the p40 subunit of IL12 and IL23<sup>14</sup>. In rheumatoid arthritis, tofacitinib results in diminished induction of protective immune responses to pneumococcal vaccination, but responses to influenza vaccination are maintained<sup>16</sup>. Now that the UK SARS-CoV2 vaccination program has started, observational studies need to be implemented in order to quantify immunity and efficacy in IBD patients. SARS-CoV2 vaccine responses in IBD patients receiving infliximab or vedolizumab will be assessed in the CLARITY IBD study (<https://www.clarityibd.org>).

#### **5. Are there specific data on the effect of SARS-CoV2 vaccines on patients with IBD?**

To date, there are no studies reporting the effect of any SARS-CoV2 vaccine specifically in IBD patients, as these patient groups have been excluded from the phase 3 vaccination studies. Nevertheless, insights into how different IBD therapies impact host immunity can be inferred from serological responses to other vaccination programs, as discussed in question 4. Notably, other commonly used vaccines (e.g. influenza, HBV, HAV, etc) are also very low risk in IBD patients, although they were never specifically trialled in IBD patients prior to approval.

#### **6. When will people with IBD get SARS-CoV2 vaccination?**

IBD patients will be vaccinated based on the phase 1 prioritization list defined by the JCVI (see above).

#### **7. Will vaccination have any effect on Crohn's disease or ulcerative colitis?**

At this stage it is not possible to answer this question directly as none of the SARS-CoV2 vaccines have been tested in patients with IBD. No serious gastrointestinal side-effects to SARS-CoV2 vaccinations have yet been reported. Furthermore, data from other commonly employed vaccination programs are reassuring, with no serious gastroenterological side-effects and low rates of increased IBD disease activity reported<sup>8, 10, 17</sup>.

**8. Should the SARS-CoV2 vaccination be timed around IBD treatment (e.g. biologic infusions)?**

*The main priority with timing is delivery of the vaccine at the earliest opportunity. This is especially important with the NHS under considerable strain during vaccine roll out and we would recommend accepting the first available vaccine appointment if/when offered. Neither IBD disease activity, nor the timing of subcutaneous/intravenous IBD medications should delay vaccination. There is some evidence with annual influenza vaccination that the timing of anti-TNF administration does not significantly impact on vaccination immunogenicity<sup>18</sup>. High dose systemic corticosteroids, particularly in combination with other immunosuppressants, may reduce vaccine immunogenicity, as has been observed with annual influenza vaccination<sup>14</sup>. Where possible, SARS-CoV2 vaccination should be administered whilst patients are taking the lowest dose of systemic corticosteroid.*

**9. What should be done about vaccination in people who have had COVID-19 already?**

*We advise that IBD patients should receive SARS-CoV2 vaccination at invitation, even if they have previously been affected by COVID-19. This is because data on whether individuals acquire sufficient immunity following COVID-19 are currently lacking, as are data on the duration and strength of any acquired immunity. The MHRA advises waiting at least four weeks after onset of COVID-19 symptoms or four weeks from the first PCR positive specimen in those who are asymptomatic<sup>e</sup>.*

**10. Will vaccines be effective against the new COVID variant (VUI-202012/01)?**

*There are no data available regarding the effectiveness of different vaccines against VUI-202012/01. Although this variant does harbour mutations in the spike protein (the 3 main vaccines all use the spike protein to elicit immune responses), current expert opinion is that the vaccines are likely to offer protection from this, and other identified variants<sup>19</sup>.*

**11. Is vaccination safe in those with a history of allergy or adverse reactions to IBD medication?**

*For the approved BNT162b2 vaccine, the MHRA guidance<sup>f</sup> states that “any person with a history of immediate-onset anaphylaxis to a vaccine, medicine, or food should not receive the Pfizer/BioNTech vaccine”. This includes IBD patients who have had severe immediate-onset anaphylaxis following biologic treatment. Other drug-related side effects, including mild to moderate infusion reactions should not be considered contraindications to vaccination. The MHRA states that the ChAdOx1 nCoV-19 vaccine is contraindicated if there is a history of*

*hypersensitivity to the active substance or any of the vaccine excipients. Guidance on allergies for other SARS-CoV2 vaccines will be issued by the MHRA as the vaccines are approved.*

**12. For those who were previously in a high-risk group and receive the vaccine, what does that mean for their occupational risk?**

*The JCVI statement on priority groups for vaccination advises that clinically extremely vulnerable groups should continue to follow Government advice on reducing their risk of infection after vaccination<sup>d</sup>. Further Government guidance is anticipated during vaccine rollout.*

**13. Can patients have both the flu vaccine and SARS-CoV2 vaccine and can they be administered together?**

*IBD patients should be encouraged to have both the annual influenza and the SARS-CoV2 vaccinations. The MHRA advises against co-administration of SARS-CoV2 vaccines with other vaccines, and instead administration of different vaccines should be scheduled at intervals of at least seven days<sup>e</sup>.*

<sup>e</sup>[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/943663/Greenbook\\_chapter\\_14a\\_v3.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/943663/Greenbook_chapter_14a_v3.pdf)

<sup>f</sup><https://www.gov.uk/government/news/confirmation-of-guidance-to-vaccination-centres-on-managing-allergic-reactions-following-covid-19-vaccination-with-the-pfizer-biontech-vaccine>

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