
UK Chemotherapy Board

Clinician Frequently Asked Questions (FAQs) and guidance on COVID-19 vaccine for patients receiving Systemic Anti-Cancer Therapy

This document has been endorsed by the UK chemotherapy board member organisations.

The document was based on guidelines from Guy's & St Thomas' NHS Foundation Trust¹ published 17 December 2020, and has been updated on 21 January 2021 to include information for the Pfizer/BioNTech COVID-19 vaccine, Oxford University/AstraZeneca vaccine and in anticipation of Moderna vaccine, and updated guidance in the "Green Book".

Disclaimer

The information contained in this document is based on evidence available until 21 January 2021. It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance processes. Care has been taken in the preparation of the information contained within the FAQ; nonetheless, any person seeking to use the information is expected to use independent, personal medical and/or clinical judgement in the context of the individual clinical circumstances, or to seek out supervision of a qualified clinician. The UK Chemotherapy Board makes no representation or guarantee of any kind whatsoever regarding the content or its use or application and disclaim any responsibility for its use or application in any way.

Purpose:

This document has been produced in response to questions raised by cancer health care professionals relating to the administration of the Pfizer/BioNTech COVID-19 vaccine, Moderna COVID-19 vaccine and the Oxford University/AstraZeneca COVID-19 vaccine in patients receiving systemic anti-cancer therapy (SACT).

Scope:

This FAQ document covers all tumour groups receiving chemotherapy and is relevant to all clinical staff involved with the management of patients within these tumour groups.

Introduction

- This document has been produced in response to questions raised by cancer health care professionals relating to the administration of the Pfizer/BioNTech, Moderna and Oxford University/AstraZeneca COVID-19 (CV-19) vaccines in patients receiving systemic anti-cancer therapy (SACT).
- The Pfizer/BioNTech CV-19 and Moderna CV-19 vaccines are not live vaccines. The Oxford University/AstraZeneca vaccine is a recombinant replication deficient adenovirus which should not be considered as a live vaccine in terms of the risks of SACT co-administration. However, none of the vaccines have been trialled in patients receiving SACT.
- Cancer patients receiving / or about to receive SACT, will fall into the clinically extremely vulnerable category and therefore the overall consensus is that the benefits of the CV-19 vaccine will potentially outweigh the risks.
- If there is sufficient time between the decision to start treatment and the start date, **vaccination should take place during this window when the patient has intact immune function.**
Local services and vaccination hubs should establish efficient pathways for rapid referral of these patients. Where timing (e.g. in planned adjuvant chemotherapy) would allow both doses (i.e. the second dose given at week 3 or 4 depending on the product) to be given **before** commencing chemotherapy this is encouraged, rather than waiting the 8-12 weeks generally being recommended for routine vaccination by JCVI. This is consistent with the updated advice in the Green Book (January 21st).
- All considerations of CV-19 vaccine risk in the SACT patient needs to be balanced with the risk of COVID-19 infection in the intervening period (e.g. if deciding to postpone vaccination).
- It is recommended that all patients receiving SACT are considered for CV-19 vaccination, providing they meet the eligibility criteria in the latest national protocol.
- Where possible, treatment should not be deferred or delayed due to CV-19 vaccination.
- The only specific contraindication to the vaccines are hypersensitivity to the active substance or to any of the excipients
- The most up to date national protocol for Pfizer/BioNTech CV-19 vaccine contains details on allergies and exclusions can be found here:
[National protocol for COVID-19 mRNA vaccine BNT162b2 \(Pfizer/BioNTech\)](#)
- The National protocol contains useful information from The British Society for Allergy and Clinical Immunology (BSACI).
 - For example, BSACI have advised that Individuals with a history of immediate onset-anaphylaxis to multiple classes of drugs or an unexplained anaphylaxis **should not** be vaccinated with the Pfizer BioNTech vaccine¹. The AstraZeneca vaccine can be used as an alternative (if not otherwise contraindicated)

¹ The Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 contains polyethylene glycol (PEG). Although not yet available yet in the UK, PEG is also an excipient in the Moderna mRNA COVID-19 vaccine; individuals who have a systemic allergic reaction to the Pfizer-BioNTech vaccine should not be given a dose of the Moderna vaccine, and vice versa.

- Information on the currently approved vaccines can be found here:

Vaccine Manufacturer	Pfizer	AstraZeneca	Moderna
MHRA Links	Regulatory approval of Pfizer/BioNTech vaccine for COVID-19	Regulatory approval of COVID-19 Vaccine AstraZeneca	Regulatory approval of COVID-19 Vaccine Moderna
	Information for Healthcare Professionals on Pfizer/BioNTech COVID-19 vaccine	Information for Healthcare Professionals on COVID-19 Vaccine AstraZeneca	Information for Healthcare Professionals on COVID-19 Vaccine Moderna

- Any queries regarding the vaccine should refer to the “Green Book” as with all other vaccination questions within the UK. The relevant chapter is – Chapter 14a, and can be accessed here: [COVID-19: the green book, chapter 14a](#)
- Myelosuppressive effects of chemotherapy especially thrombocytopenia may be a minor consideration due to the need for intra muscular delivery of the vaccine.

FAQ 1: What is an “immune suppressing systemic anti-cancer therapy”?

- The Green Book does not define this.
- It would be reasonable to assume this includes any SACT with a potential to cause immunosuppression, in particular regimens containing a cytotoxic agent. Whilst some monoclonal antibodies may cause B-cell or T-cell suppression, these are not deemed to be a contra-indication to receiving the vaccination.
- For the purpose of this document, systemic anti-cancer therapies have been separated out into the following categories:
 1. Cytotoxic chemotherapy (e.g. regimens containing ‘traditional’ cytotoxic drugs such as docetaxel, cisplatin, cyclophosphamide etc.)
 2. Monoclonal Antibodies (e.g. bevacizumab, cetuximab, rituximab, trastuzumab)
 3. Immunotherapy (e.g. atezolizumab, avelumab, ipilimumab, nivolumab, pembrolizumab)
 4. Small molecule tyrosine/protein kinase inhibitors (TKIs) (e.g. alectinib, imatinib, sunitinib)
 5. Immunomodulatory (IMiDs) (e.g. lenalidomide, thalidomide, pomalidomide)
 6. Proteasome Inhibitors (e.g. bortezomib, ixazomib)
 7. PARP inhibitors (e.g. olaparib, rucaparib)
 8. CDK4/6 inhibitors (e.g. abemaciclib, ribociclib, palbociclib)

FAQ 2: Should Immunotherapy patients receive the vaccine?

Immunotherapy (IO) (i.e. checkpoint inhibitors such as pembrolizumab and ipilimumab) encourage an enhanced immune response, which can result in auto-immune effects. IO can be given either alone or in combination with chemotherapy. The Green Book does not provide advice for these patients. A small observational study [Bayleet *al*, 2020] of influenza vaccine in France given to patients receiving IO suggests that the treatment is safe and effective. There is a small risk that IO-toxicity could be exacerbated by CV-19 vaccination (similar to seasonal flu vaccine) particularly for those patients receiving anti-CTLA4 therapy. However, the evidence is weak and the benefit of vaccination should be weighed against risk.

Recommendation: Yes, patients receiving immune checkpoint inhibition (whether anti-CTLA4 or PD-1/PD-L1) should receive the CV-19 vaccine at any point during the treatment cycle. (It may be practical to schedule this during a routine hospital visit in order to avoid additional attendances).

FAQ 3: Should SACT Clinical Trial patients receive the vaccine?

Unless vaccination is contra-indicated (or excluded) in a clinical trial of SACT, patients in such trials should be considered for CV-19 vaccination.

FAQ 4: “Timing of Treatment” – Is there an optimal time to administer the CV-19 vaccine relative to the SACT cycle?

Immunosuppression may reduce the immune response to the vaccine. It may be impractical/inappropriate to delay starting SACT until after CV-19 vaccination. In addition, delaying CV-19 vaccination until completion of SACT may be inappropriate.

Many clinicians have given empirical advice for other vaccines (such as seasonal flu vaccine), to have the vaccine when the full blood count is at the highest. However, seroconversion takes several weeks and for patients on cyclical SACT, the immunity will cycle. There is a small study of influenza vaccine which suggests that administration of the vaccine on the day of chemotherapy reduces effectiveness compared with the nadir [Loulergue *et al*, 2011]. It is unknown if the same effect will be seen in patients receiving the CV-19 vaccine.

As a suggestion, patients could receive the vaccine when they attend for a pre-chemotherapy outpatient appointment (if this is different to the day of SACT administration).

The table below highlights suggested timings of the CV-19 vaccine as a guide for clinicians for patients on existing treatment. The suggestion to “avoid on same day as chemotherapy” is based on extrapolated data (from influenza vaccine) on efficacy of the vaccine rather than safety.

	Suggested Timing of CV-19 vaccine
Cytotoxic chemotherapy	Avoid on same day of chemotherapy. *If patient is known to have low platelets – see FAQ 5
Monoclonal Antibodies (single agent) Should not be a contraindication	No specific timing issues. *If patient is known to have low platelets – see FAQ 5
Monoclonal Antibodies (with cytotoxic chemotherapy)	Avoid on same day of chemotherapy. *If patient is known to have low platelets – see FAQ 5
Immunotherapy (IO) (single agent)	No specific timing issues. *If patient is known to have low platelets – see FAQ 5
Immunotherapy (IO) (with cytotoxic chemotherapy)	Avoid on same day of chemotherapy. *If patient is known to have low platelets – see FAQ 5
Small molecule protein kinase inhibitors (TKIs)	No specific timing issues. *If patient is known to have low platelets – see FAQ 5
Immunomodulatory (IMiDs)	No specific timing issues. *If patient is known to have low platelets – see FAQ 5
Proteasome Inhibitors (e.g. bortezomib, ixazomib)	Avoid on same day of chemotherapy. *If patient is known to have low platelets – see FAQ 5
PARP inhibitors (e.g. olaparib, rucaparib)	No specific timing issues. *If patient is known to have low platelets – see FAQ 5
CDK4/6 inhibitors (e.g. abemaciclib, ribociclib, palbociclib)	No specific timing issues *If patient is known to have low platelets – see FAQ 5
Hormone treatments and other supportive treatments	No specific timing issues *If patient is known to have low platelets – see FAQ 5
Bladder instillations (BCG, mitomycin, gemcitabine, epirubicin etc) (small chance of systemic absorption)	No specific timing issues *If patient is known to have low platelets – see FAQ 5
Talimogene laherparepvec (T-VEC)	Avoid on same day for first dose. For subsequent treatments - ok to receive on same day. *If patient is known to have low platelets – see FAQ 5
Radiotherapy	No specific timing issues. *If patient is known to have low platelets – see FAQ 5

Chemo-Radiotherapy	<p>Intravenous chemotherapy e.g. carboplatin, cisplatin, mitomycin: Avoid on same day of chemotherapy.</p> <p>Continuous capecitabine, temozolamide: No specific timing issues.</p> <p>If possible, try to give the vaccine before starting chemo-radiotherapy course</p> <p>*If patient is known to have low platelets – see FAQ 5</p>
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For patients receiving continuous treatment (e.g. tyrosine kinases) or treatment with short treatment breaks that allow recovery from toxicity (e.g. capecitabine), there is no evidence to suggest a treatment interruption is beneficial, indeed waiting to give the vaccine at a planned treatment interruption will increase the time the patient is left without any protection and may prove logistically challenging given the scale and urgency of the current pandemic.

All currently approved vaccines require a second dose. For the Pfizer/BioNTech COVID-19 vaccine this dose should be given at least 3 weeks after the first vaccine. No data has been published to confirm how long this vaccine can be delayed. The second dose of the Moderna Vaccine should be given at least 4 weeks after the first vaccine. For the Oxford University/AstraZeneca vaccine the second dose should be *at least* 4 weeks after the first vaccine dose but can be delayed up to 12 weeks. An exploratory analysis suggests that immunogenicity increases when the interval is between 8 and 12 weeks. The current Department of Health Guidance is to delay the second dose for up to 12 weeks to allow greater capacity for uptake of the first dose of the vaccine.

There is no evidence for changing between vaccine preparations.

FAQ 5: What about SACT patients with bleeding disorders and anti-coagulation?

SACT patients with bleeding disorders may be vaccinated intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk, vaccines or similar small volume intramuscular injections can be administered safely.

In the SACT treated population, thrombocytopenia (due to SACT) and anticoagulation (due increased VTE risk in cancer) are relatively common and these need considered and addressed as appropriate before pursuing intramuscular vaccination.

Firm pressure should be applied to the injection site for at least 5 minutes after injection, and patients should be warned of the risk of haematoma.

For thrombocytopenia there is no consensus on an adequate platelet count for a single IM injection but likely the count would preferably be $>20 \times 10^9/L$.

The British Society for Haematology (BSH) statement "COVID-19 Vaccine in patients with haematological disorders", contains more instructive advice within the appendix "*Advice from haematology groups on specific haematological conditions*": [Link](#)

FAQ 6: What about neutropenia and CV-19 vaccination?

Ideally injection should be avoided in a patient who is unwell with neutropenia until neutrophil counts have recovered to $>1 \times 10^9/L$ (without growth factor support) and the patient is well. Some patients have chronic neutropenia in which case the patient should receive the vaccine without delay.

FAQ 7: What about patients who have recently undergone an autologous or allogeneic stem cell transplant?

The British Society of Blood and Marrow Transplantation & Cellular Therapy (BSBMTCT) have produced COVID vaccine information found here: [Link](#)

Bloodcancer.org.uk have produced useful advice for patients on "Covid vaccine and cancer treatment" found here: [Link](#)

FAQ 8: What about patients planned for CAR T therapy undergoing lymphodepletion or who have received a CAR T product?

The European Society for Blood and Marrow Transplantation (EBMT) have produced COVID vaccine information found here: [Link](#)

FAQ 9: What about effectiveness of the vaccination in patients receiving SACT?

Patients receiving SACT may not mount as robust an immune response to such vaccination so vaccination of their close contacts may be particularly appropriate. Also, it should be emphasised that protective measures including hand washing, mask wearing and social distancing ("hands, face, space") continue to be recommended to reduce risk of transmission of infection.

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[COVID-19: the green book, chapter 14a. Last updated 31 December 2020](#), Last updated 21 January 2021 (accessed 21 January 2021)

[National protocol for COVID-19 mRNA vaccine BNT162b2 \(Pfizer/BioNTech\)](#), Last updated 10 January 2021 (accessed 21 January 2021)

Change Log		
Date	Version	Changes
21.01.21	2.0	<ul style="list-style-type: none"> • Updated Allergy advice • Moderna Vaccine reference • Revised recommendation for CDK4/6 inhibitors • Bladder instillation added • Introduction – suggestion for patients awaiting to start SACT • Introduction – points rearranged • FAQ 1 – amended wording for monoclonal antibodies • References to “When blood counts have maximally recovered (towards end of cycle)” and “(providing FBC is within normal/acceptable range)” removed • T-VEC, Radiotherapy, Chemo-Radiotherapy added to table • Immunomodulatory (iMiDs) – suggested timings changed • Updated to reflect option to give both dose of vaccine prior to starting SACT if timing allows.