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 Trust[1] published 17 December 2020, and has been updated to include information for the Oxford University/AstraZeneca vaccine on 31st December 2020.

Disclaimer

The information contained in this document is based on evidence available until December 31st 2020. 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 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 and Oxford University/AstraZeneca COVID-19 (CV-19) vaccines in patients receiving systemic anti-cancer therapy (SACT).

- All considerations of CV-19 vaccine risk 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.

- The Pfizer/BioNTech CV-19 vaccine is not a live vaccine. 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, neither vaccine has been trialled in patients receiving SACT.

- However many cancer patients receiving 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.

- Furthermore, treatment should not be deferred or delayed due to CV-19 vaccination.

- The only specific contraindication is hypersensitivity/anaphylaxis to either the vaccine or any excipients.
  In addition, the following MHRA advice issued on 9 December 2020 should be adhered to: "Any person with a history of anaphylaxis to a vaccine, medicine or food should not receive the Pfizer/BioNTech vaccine. A second dose should not be given to anyone who has experienced anaphylaxis following administration of the first dose of this vaccine". Specific advice for the Oxford University/AstraZeneca vaccine has not been so prescriptive, however, patients with a history of anaphylaxis or angioedema were excluded from clinical trials.

- In the first instance, 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: https://www.gov.uk/government/publications/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 potential to cause immunosuppression, in particular regimens containing a cytotoxic agent.
  Tyrosine Kinase Inhibitors (TKIs) and most monoclonal antibody treatments do not cause significant immune suppression.

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. Proteosome 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.

Table 1: Suggested timings of the CV-19 vaccine as a guide for clinicians for patients on existing treatment.

	Suggested Timing of CV-19 vaccine
Cytotoxic chemotherapy	When blood counts have maximally recovered (towards end of cycle) – but avoid on same day of chemotherapy.
Monoclonal Antibodies (single agent) Should not be a contraindication	No specific timing issues (providing FBC is within normal/acceptable range).
Monoclonal Antibodies (with cytotoxic chemotherapy)	When blood counts have maximally recovered (towards end of cycle) – but avoid on same day of chemotherapy.
Immunotherapy (IO) (single agent)	No specific timing issues (providing FBC is within normal/acceptable range).
Immunotherapy (IO) (with cytotoxic chemotherapy)	When blood counts have maximally recovered (towards end of cycle) where possible avoid on same day of chemotherapy.
Small molecule protein kinase inhibitors (TKIs)	No specific timing issues (providing FBC is within normal/acceptable range).
Immunomodulatory (IMiDs)	When blood counts have maximally recovered (towards end of cycle) – but avoid on same day of chemotherapy.
Proteosome Inhibitors (e.g. bortezomib, ixazomib)	When blood counts have maximally recovered (towards end of cycle) – but avoid on same day of chemotherapy.
PARP inhibitors (e.g. olaparib, rucaparib)	No specific timing issues (providing FBC is within normal/acceptable range).
CDK4/6 inhibitors (e.g. abemaciclib, ribociclib, palbociclib)	When blood counts have maximally recovered (towards end of cycle – but avoid on same day of chemotherapy.
Hormone treatments and other supportive treatments	No specific timing issues

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.

Both 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. 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 x 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 x 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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