
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 9th May 2021 to include updated information for the Pfizer/BioNTech COVID-19 vaccine, Oxford University/AstraZeneca vaccine and Moderna vaccine, reflecting updated guidance from JCVI and the MHRA.

Disclaimer

The information contained in this document is based on evidence available until 9th May 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.**
- Ideally all oncology and haematology-oncology patients should receive 1st dose of COVID-19 vaccine at least 2 weeks prior to start cycle 1, day 1 of SACT, at time of diagnosis/pre- or post-surgery where possible.
- The second dose of the COVID-19 vaccination (i.e. vaccine booster) should be offered at the recommended minimum for that vaccine (three or four weeks from the first dose) or as soon as practically possible following the first dose, pending availability of vaccine, scheduling of subsequent SACT cycle and disease specific advice/individual patient considerations.
- There is emerging data to suggest the efficacy of vaccination, particularly in haemato-oncology patients, is uncertain and therefore all patients receiving vaccination in combination with SACT must be counselled appropriately, including shielding requirements according to government guidelines. All adult household members of SACT patients should also be offered the COVID-19 vaccination in accordance with national government recommendation.
- Local services and vaccination hubs should establish efficient pathways for rapid referral of these patients. This is consistent with the updated advice in the [Green Book/JCVI](#) (updated 7th May, 2021).
- 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)
- Refer to FAQ 10 for specific guidance on vaccine choice for patients who have had a reaction to SACT or its excipients.

¹ The Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 contains polyethylene glycol (PEG). 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 CV-19 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 [[Bayle et 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. A recent case series, using the Pfizer vaccine, in combination with immunotherapy provides some reassurance that there is no current evidence to suggest an increase in immune related adverse events [[Waissengrin et al, 2021](#)].

Therefore, 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.

FAQ 3 Should SACT Clinical Trial patients receive the CV-19 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 ** See FAQ 12 for anti-CD20 monoclonal antibodies
Monoclonal Antibodies (with cytotoxic chemotherapy)	Avoid on same day of chemotherapy.** *If patient is known to have low platelets – see FAQ 5 ** See FAQ 12 for anti-CD20 monoclonal antibodies
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 ** Refer to FAQ 6 regarding concerns with thrombosis and hormonal treatments
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	Intravenous chemotherapy e.g. carboplatin, cisplatin, mitomycin: Avoid on same day of chemotherapy.

Suggested Timing of CV-19 vaccine	
	<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>

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](#)

Refer to FAQ 6 for thrombosis with AZ vaccine

FAQ 6 What about the risk of thrombosis with the AZ CV-19 vaccine?

In light of evolving data which suggests there may be an association between unusual blood clotting and the AZ vaccine ([Link](#)), the JCVI have recommended that alternative vaccines are used in patients under 40 years of age. There is currently no evidence of a link between other factors affecting blood clots (e.g. co-morbidities or medication, including tamoxifen) to suggest other groups should be selected to give one vaccine in preference to another.

Thrombocytopenia has been observed in patients who have developed these unusual blood clots. However there is no indication that there would be any value in checking platelet levels prior to administration. Contra-indications and special precautions for use can be found in the AZ CV-19 vaccine summary of product characteristics. ([Link](#)).

FAQ 7 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 8 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 9 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-19 vaccine information found here: [Link](#)

FAQ 10 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.

FAQ 11 What about patients who have had a reaction to SACT or its excipients?

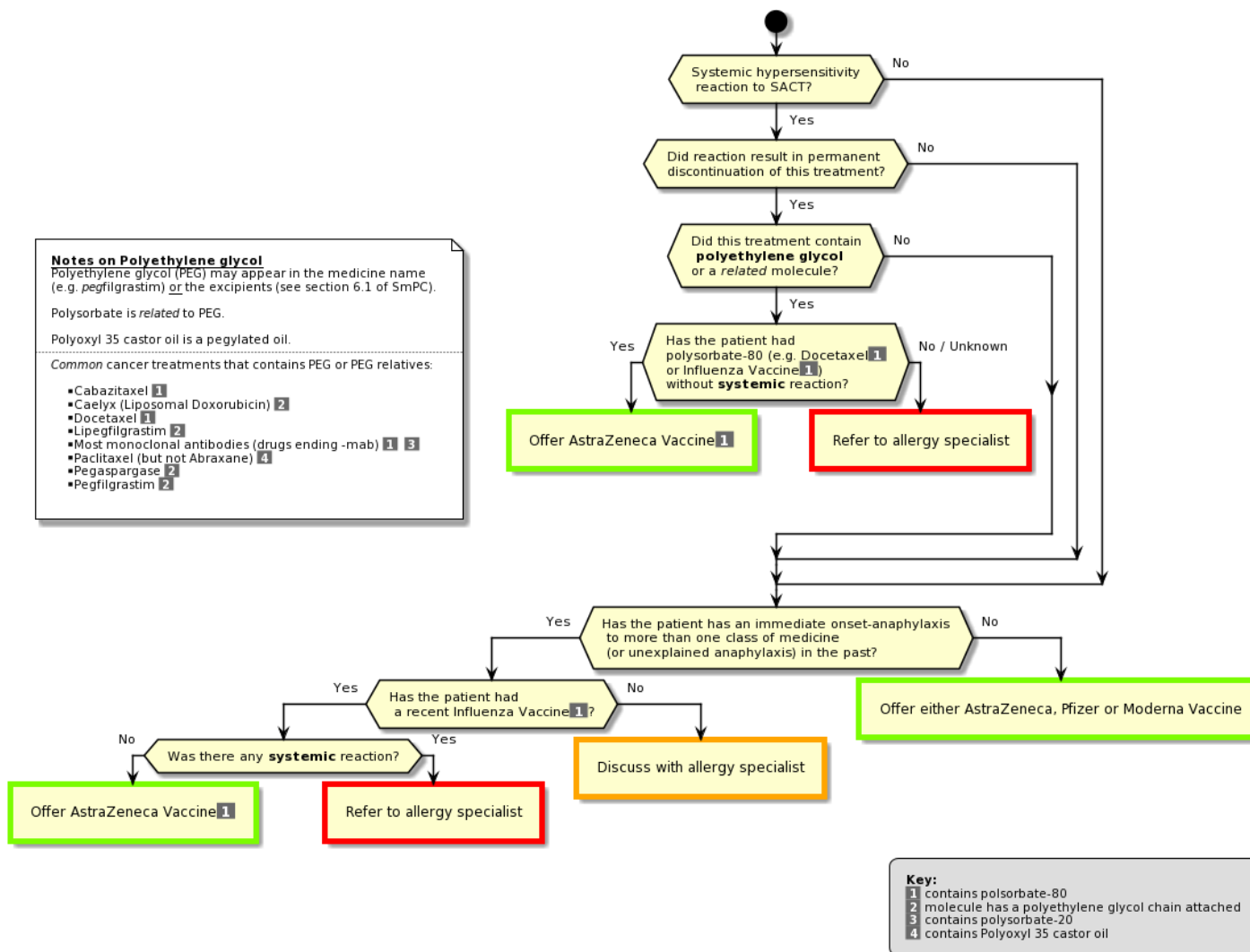
(Acknowledgement: Dr Annette Wagner & Allergy Colleagues at GSTT Adult Allergy Department)

Some SACT excipients (similar to those found in Covid-19 vaccines) are thought to cause adverse effects and/or hypersensitivity following intravenous infusion. Allergy to the polymers (Polyethylene glycol (PEG), Polysorbate or Polyoxyl 35) - contained in SACT products and/or certain vaccines - are very rare and cross-reactivity patterns have not been firmly established, due to limited data.

Patients who had an identified anaphylaxis to any of these excipients (PEG, Polysorbate or Polyoxyl 35) should be seen by an allergist, tested and depending on results, given the most suitable vaccine. The AZ vaccine may not be suitable in all cases.

The decision aid below, gives clinicians a pragmatic approach to identifying the best choice of vaccine, in patients with a history of hypersensitivity reaction(s) to SACT or its excipients.

Decision aid for selection of coronavirus vaccine in patients with a history of allergic reaction to Systemic Anti-Cancer Therapies (SACT)



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Further notes

Polysorbate seems to be less allergenic than PEG and far fewer cases of anaphylaxis have been published. It is also thought that higher molecular weight polymers seem to be more allergenic than lower molecular weight ones. Patients who have had a systemic reaction to SACT containing PEG or a PEG derivative, but have safely received Influenza Vaccine which contains polysorbate-80 (all Influenza Vaccines in the 2019/20 and 2020/21 UK vaccine campaign contain polysorbate-80) are unlikely to react to the polysorbate-80 in the AstraZeneca Vaccine.

Taxanes

Patients who had a hypersensitivity reaction to paclitaxel and switched successfully to docetaxel (which contains polysorbate-80) therapy, would also be expected to tolerate the AstraZeneca Vaccine.

Note: Abraxane™ (nab-paclitaxel) does not contain a pegylated surfactant.

Monoclonal antibodies

Characterisation of SACT infusion reactions is often challenging and few patients will undergo extensive IgE testing. Patients who have had an “infusion reaction” to monoclonal antibodies such as trastuzumab, rituximab and cetuximab but have been able to continue receiving further doses of treatment are unlikely to have had an IgE mediated reaction and so could be considered for vaccination unless they have other contra-indications.

Platinum based therapies

Platinum based chemotherapies (cisplatin, carboplatin and oxaliplatin) also commonly cause hypersensitivity reactions however these products do not contain these excipients and therefore, unless the patient has had a reaction to another class of medicine (causing immediate onset-anaphylaxis), either vaccine is deemed appropriate.

Other liposomal products (not identified in above diagram)

Identified hypersensitivity to other liposomal products used as part of SACT therapy e.g. Vyxeos™ (liposomal daunorubicin/cytarabine), liposomal amphotericin, etc. should be referred to allergist for advice on choice of vaccine.

Please note: reporting of any adverse events to the vaccines, must be reported in the usual way through the Coronavirus Yellow Card Scheme (<https://coronavirus-yellowcard.mhra.gov.uk/>).

FAQ 12 What about T and B cell depleting therapies? E.g. rituximab, obinutuzumab, bendamustine

There is conflicting opinion within the international haemato-oncology community regarding the expected efficacy of the vaccine within 6 months of receiving anti-CD20 monoclonal antibodies. The current BSH recommendation is in favour of vaccination, whilst EBMT recommend delaying for 6 months.

Administration of the vaccine is unlikely to be harmful during the first six months after antibodies and therefore we have recommended vaccination as soon as possible, but clearly patients need to be carefully counselled.

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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.
09.02.21	3.0	<ul style="list-style-type: none"> • New FAQ 11 - What about patients who have had a reaction to SACT or its excipients?
09.05.21	4.0	<ul style="list-style-type: none"> • New FAQ 12 – explaining rationale for vaccination with anti-CD20 monoclonal antibodies • New FAQ 6 regarding concerns about unusual thrombosis with AZ CV-19 vaccine & updated JCVI recommendation that alternative vaccines are used in patients under 40 years of age • FAQ 2 - updated with new data • FAQ 11 - Decision aid updated to add Moderna Vaccine, Note presence of Polysorbate 80 as well as 20 in in some monoclonal antibodies, and revise colour use for better legibility for those with reduced colour vision • Introduction - Updated in line with JCVI to recommend vaccination of household contacts and receiving second dose 3-4 weeks later depending on vaccine.(updated 16/04/21) • Some FAQs have been renumbered. The change log reflects their current FAQ number