



Clinician's guide to COVID-19 vaccination for patients with cancer

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OFFICIAL

COVID-19 vaccines

Patients with malignancy are at increased risk for COVID-19 (1, 2). Cases of COVID-19 in patients with haematological malignancy have been associated with high case fatality ratios of up to 60 per cent (2-4). In addition, COVID-19 positive cancer patients experience more rapid deterioration, have more concurrent infections, have higher rates of intensive care unit admission and need for mechanical ventilation (1, 5).

Australia has secured four COVID-19 vaccines based on different platforms (6). They are the Pfizer-BioNTech (Pfizer) vaccine (mRNA with lipid nanoparticle), AstraZeneca-Oxford ChAdOx1 (AstraZeneca) (non-replicating adenovirus vectored) vaccine, ModernaTX MRNA-1273 (Moderna) vaccine (mRNA) and Novavax NVX-CoV2373 (Novavax) (recombinant protein with adjuvant) vaccine.

COVID-19 vaccination in patients with cancer

Vaccination is an effective strategy to reduce risk and burden of infection in at-risk patients. However, in patients receiving treatment for malignancy, response to vaccination may be impaired due to patient, disease or treatment-related factors (7-13).

Clinical trials of vaccines against SARS-CoV-2 have excluded patients receiving anti-cancer therapies. Pfizer and AstraZeneca vaccines have been rolled out in the United States, United Kingdom and Europe including to patients with cancer. The Pfizer, AstraZeneca, Novavax and Moderna vaccines do not contain live SARS-CoV-2 and as such do not pose a risk of infection to recipients.

There remains inadequate data on immunogenicity of the vaccines in patients with cancer (on/off therapy) and insufficient evidence to guide optimal vaccine choice and timing of vaccination. However, based on evidence extrapolated from use of other inactivated vaccines in patients with cancer, recent reports and guidance provided by the Australian Technical Advisory Group on Immunisation (ATAGI), the following broad principles for COVID-19 vaccination have been developed. Whilst not mandatory, vaccination against COVID-19 is highly recommended.

Guidance for clinicians:

Vaccine type and response

- Patients with cancer are at higher risk for morbidity and mortality associated COVID-19 infection. Therefore, vaccination against COVID-19 is recommended.
- Carers and family members of patients with cancer are encouraged to have the COVID-19 vaccine as soon as it is available to them.

- Vaccines available (and those that will become available) in Australia do not contain live SARS-CoV-2, therefore do not pose an infectious risk to patients.
- Vaccine choice should be guided by the latest [ATAGI](#) advice, taking into account patient age, community outbreaks of COVID-19, risks for severe complications from COVID-19 infection and possible vaccine related adverse events.
- Immune response to COVID-19 vaccination will likely be negatively impacted by underlying disease or therapy and patients should be advised to continue general measures such as hand hygiene, physical distancing and mask wearing. Early investigation of respiratory symptoms for SARS-CoV-2 and other respiratory viruses remain vital.

Adverse events

- Local adverse effect (e.g. pain) is the most common reported adverse effect following vaccination.
- Fever is a less common adverse effect following vaccination. Persistent fever for more than 48 hours after vaccination (or fever in association with concerning symptoms (e.g. sweats, rigors) should prompt medical review and investigation for a cause including testing for COVID-19.
- A rare but serious adverse event, thrombosis with thrombocytopenia syndrome/vaccine-induced immune thrombotic thrombocytopenia, has been linked with use of the AstraZeneca-Oxford vaccine. New or persistent symptoms such as severe headache unresponsive to simple analgesia, beyond 3 days following vaccination should prompt medical review.
- Radiation recall reactions have been noted in patients who have received radiotherapy prior to vaccination. These are usually mild. In addition to symptomatic management (analgesia and barrier creams), if this is suspected, please contact the treating radiation oncology team.
- A serious/severe immediate allergic reaction (e.g. anaphylaxis) to a COVID-19 vaccine or known component (such as polyethylene glycol [PEG] or polysorbate) is a contraindication to vaccination. PEG and polysorbate are also components in some conventional chemotherapeutic drugs (see Table 2 below). Referral for specialised review via the Victorian Specialist Immunisation Service is recommended. Patients should be assessed for whether they have subsequently tolerated other medications containing PEG or polysorbate before referral.

Timing of vaccination

- Where possible, commence vaccination prior to anticipated commencement of myelosuppressive, lymphodepleting therapy or targeted therapies taking into account the need for and timing of second vaccine dose.
- Delaying or interrupting cancer treatment/cycles to potentially improve responses to COVID-19 vaccination is not currently recommended.
- Where possible, avoid COVID-19 vaccination during anticipated periods of immune nadir (e.g. expected neutropenic nadir) or risk period for immune-related adverse event associated with the specific cancer therapy.
- Patients on dual checkpoint inhibitor therapy should discuss with their treating physician about the optimal timing of their COVID-19 vaccine in relation to their cancer therapy.
- If vaccinating during treatment, it would be preferable to vaccinate during the 'off' week during the treatment cycle to avoid potential overlap of treatment-related and vaccine-related adverse events.
- Defer vaccination if severe neutropenia present ($ANC < 0.5 \times 10^9/L$) until anticipated recovery.
- Patients have been able to mount an immune response to vaccination 3-6 months following autologous (as early as 2 months) and allogeneic haematopoietic stem cell transplant (HCT). Patients could be vaccinated from 3 months following HCT.
- Use of inactivated vaccines has not been associated with flares of graft vs. host disease (GvHD) and patients with stable GvHD on therapy could be vaccinated for COVID-19.
- Anti-CD20 antibody therapy is likely to negatively impact response to vaccination. However, with significant risk posed by COVID-19 it would be reasonable to vaccinate during or within 6-months of anti-CD20 with the understanding that protection maybe limited.

Special considerations

- Where possible, avoid COVID-19 vaccination on the same day as intravenous immunoglobulin replacement to minimise confusion around any adverse events.
- Currently, the minimum interval between COVID-19 vaccination and receipt of other vaccines is **1 week**.
- If positron emission tomography (PET) scan is planned, discuss recommended timing of vaccination relative to PET scanning with their treating specialist and ensure receipt of recent vaccination is highlighted/communicated to the PET imaging team.
- Patients who have thrombocytopenia or on oral anticoagulants may develop a haematoma at the injection site. To minimise risk, application of prolonged pressure at injection site recommended.
- Suitability of vaccination in patients receiving end of life care should be evaluated in line with their goals of treatment/care.
- Avoid vaccination in a body area where a patient is receiving or has received radiation therapy to (e.g. use contralateral upper limb).

Safety and follow up

- Currently routine measurement of serological response to COVID-19 vaccination is not recommended as there is no established cut-off value which correlates with protection/response. Consider enrolling patient in available immunogenicity studies.
- Any suspected adverse event following immunisation should be reported to [SAEFVIC](#), the state vaccine safety team based at the Murdoch Children’s Research Institute (MCRI), Parkville.

Table: Common drugs utilised in oncology containing PEG or polysorbate, adapted from Banerji et al.(23)

Common drugs used in oncology containing PEG		
PEG-filgrastim		
Trastuzumab		
Common drugs used in oncology containing polysorbate		
Anidulafungin	Durvalumab	Pembrolizumab
Atezolizumab	Elotuzumab	Ramucirumab
Avelumab	Etoposide	Rituximab (Truxima, Rituxan, Ruxience, Rituxan Hycela)
Bevacizumab	Fosaprepitant	Siltuximab
Belantamab	Inotuzumab	Temozolomide
Brentuximab	Ipilimumab	Tocilizumab
Cemiplimab	Isatuximab	Trastuzumab (Herceptin, Herceptin Hylecta, Herzuma, Herzuma, Kanjinti, Ontruzant, Trazimera)
Daratumumab	Mogamulizumab	Mycophenolate
Denosumab	Nivolumab	Peg filgrastim (Neulasta, Nyvepria, Udenyca)
Docetaxel	Ofatumumab (Kesimpta, Arzerra)	Filgrastim (Neupogen, Nivestym, Granix, Zarxio)

NB: This list is not exhaustive and monoclonal antibodies have been reported to cause immediate systemic symptoms which is not necessarily IgE mediated.

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