

COVID-19 vaccination advice for cancer patients

1. General information for cancer patients

Patients with cancer are at higher risk of morbidity and mortality following COVID-19 infection than patients with no comorbid conditions.

During the early stages of the COVID-19 pandemic, international oncology societies published guidance on the management of cancer patients during the COVID-19 pandemic and recommended the benefit/risk ratio may need to be reconsidered in some patients. Many guidelines consider patients recently or currently receiving chemotherapy to be at risk. Decisions for starting or continuing cancer therapy should be discussed for both patients who do not have COVID-19 infection, and those who do have COVID-19 infection but are asymptomatic and are still fit and willing to be treated after explanation of the risks and benefits. The priority for cancer treatment will require continual review on an individual patient level depending on the pandemic scenario locally and nationally.

International societies, cancer networks, and government agencies, including ASCO, ESMO, NCCN, ANZTCT, HSNZ, MOGA and the CDC, have released position statements and guidelines recommending that individuals with cancer and on anti-cancer therapies may still receive COVID-19 vaccination if they have no contraindications to vaccination, however, they should be counselled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, as well as the potential for reduced immune responses and the need to continue to follow all current guidance to protect themselves against COVID-19.

Patients with solid organ cancers, blood cancers and post-transplant patients have a higher risk of morbidity and mortality from COVID-19. Data from other vaccine preventable illnesses suggest a protective effect and reduction in morbidity with vaccination in cancer patients. However, responses to vaccines are historically lower in patients receiving cytotoxic chemotherapy, and humoral responses in patients receiving anti-B cell monoclonal antibodies and CD19 CAR-T therapy are minimal. There is no current evidence that patients receiving Immune Checkpoint Inhibitors (ICIs) are at higher risk of immune-related adverse events (irAEs) with COVID-19 vaccination. Data from influenza vaccination suggests that humoral and cell-mediated immune responses to vaccination are more robust in patients treated with ICIs than those treated with cytotoxic chemotherapy.

Types of COVID-19 vaccinations available

There are currently two COVID-19 vaccines authorized by the Therapeutic Goods Administration in Australia for use against COVID-19:

- BioNTech Pfizer vaccine
- Oxford AstraZeneca vaccine.

Both vaccines have been shown to be safe and effective for the general population in clinical trials and there was no evidence that they would not be safe for most cancer patients, however patients receiving immunosuppressive and anti-cancer therapies including cytotoxic and immunomodulatory treatments were excluded from participation in the vaccine trials to date so there is limited data on the safety and efficacy of both vaccines in cancer patients.

Scheduling of COVID vaccination with other vaccinations and therapies

The optimal timing of vaccination in relation to cytotoxic chemotherapy or immunotherapy is not established with conflicting data, therefore when there is opportunity to choose, vaccination at the furthest possible time point away from the cytotoxic treatment effect during a given cycle is recommended. There is no contraindication to receipt of COVID-19 vaccine across the broad range of therapies that patients with cancer may receive. **Therefore, it would be recommended that patients with cancer should receive the COVID-19 vaccine, as stratified by factors such as age and clinicians should not hold or pause cancer directed therapy for vaccination and only if feasible.**

time first dose of vaccine in between chemotherapy cycles, and away from nadir period.

Systemic side effects with the COVID-19 vaccine tend to occur within 2-3 days of the vaccine and may be more pronounced with the second dose. If possible, avoid scheduling immunotherapy or other chemotherapeutic infusions when vaccine side effects are expected. **Routine scheduling and giving a flu vaccine with a COVID-19 vaccine on the same day is not recommended and the recommended interval between seasonal flu vaccine and COVID-19 vaccine is 14 days.**

Benefit of vaccination

The primary benefit of vaccination is protection against illness from COVID-19, and protection against severe illness and death. It is currently unclear to what extent COVID-19 vaccines prevent asymptomatic infection or transmission of SARS-CoV-2 from a vaccinated person to others and in the population. This may also vary between different vaccines. **Even after completing vaccination, all people must continue to practice public health measures to reduce their personal risk of infection with SARS-CoV-2 and of passing the virus to others, such as physical distancing, hand washing, wearing a face mask, COVID-19 testing and quarantine or isolation as required.** As population-level immunity to the virus increases over time following widespread uptake of vaccination, these public health measures may be able to be eased, but only as advised by the local public health authorities.

Side effects

Some side effects to the vaccine may occur. Most side effects are mild and transient. Reactions at the injection site and some systemic reactions, like headaches, fever and fatigue, are very common within the first 48 hours. Very rarely, anaphylaxis has been reported, occurring in the USA at a rate of about 5 cases per 1 million doses (as of January 2021).

In clinical trials, the most reported adverse events in the first week after vaccination were: Injection site pain (84.1 per cent); fatigue (62.9 per cent); headache (55.1 per cent); muscle pain (38.3 per cent); chills (31.9 per cent); joint pain (23.6 per cent); fever (14.2 per cent); and injection site swelling (10.5 per cent).

The potential for other rare or unanticipated side effects to emerge over time is low, but is being closely monitored, as for any vaccine or medicine. Most side effects start within 24 hours of vaccination and will resolve in 1–2 days on their own. To reduce discomfort, paracetamol or ibuprofen can be taken. Some of the expected vaccine side effects overlap with the symptoms of SARS-CoV-2 infection, such as fever. However, a key differentiating factor is that respiratory symptoms (e.g. cough, runny nose etc.) are not known to be associated with COVID-19 vaccinations. Therefore, local public health guidance on criteria for SARS-CoV-2 testing should always be followed. People who have typical non-respiratory side effects (e.g. injection site pain, fever, lethargy) within the first 48 hours after vaccination with a complete absence of any respiratory symptoms may not need to get a COVID-19 test or isolate. Vaccine recipients should be advised to seek medical attention if they are concerned about a symptom, have new or unexpected symptoms, or if they have symptoms which have not resolved after several days.

2. Response to vaccination

Preliminary data from King's College London (pre-print) highlights the potential limited immune responses to COVID vaccination in patients with blood cancer. In 205 patients, including 151 with solid organ cancers and blood cancers, antibody responses at 3 weeks post initial (single dose) Pfizer vaccination occurred in 9 per cent, 39 per cent and 13 per cent of patients with no cancer, solid cancer and blood cancer respectively; at 5 weeks post initial (single dose) Pfizer vaccination antibody responses were 100 per cent, 43 per cent and 8 per cent respectively.

Although preliminary, this data suggests a need to avoid delay in the second vaccine dose in cancer patients, especially in patients with blood cancers. It also raises questions around potential need for assessment strategies of post-vaccine responses in some patient groups. Potential approaches to vaccine response assessment are being considered at both state and national levels.

3. Specific contra-indications

Confirmed allergic reactions to vaccines are not frequently attributed to the active ingredients, but rather to the inactive ingredients, or excipients. Efforts to specifically decrease well-known excipients in vaccines such as egg and gelatin have been highly successful in reducing allergic reactions. Other excipients, such as polyethylene glycol (PEG) and polysorbate, are used to improve water solubility in drugs and vaccines. First-dose reactions to vaccines containing PEG or polysorbates may occur

because of previous sensitization from PEG or polysorbate, which are active components of many anti-cancer agents and have been implicated in allergic reactions.

The Pfizer-BioNTech COVID-19 mRNA vaccine is not formulated with any food, drugs, or latex, but does contain excipient PEG for the purpose of stabilizing the lipid nanoparticle containing the mRNA. The specific PEG in this vaccine is different from the PEG used most commonly in other health care products, both in molecular weight and due to its coformulation as a stabilizing portion of a liposome.

The AstraZeneca (and Johnson & Johnson) COVID-19 vaccine does not contain PEG but instead contains the excipient polysorbate 80.

Polyoxyl 35 castor oil, an excipient in some medications including Paclitaxel, may also cause sensitization to PEG-related excipients.

People with cancer and a history of generalized allergic reaction (without anaphylaxis) to anti-cancer agents containing PEG, polysorbate (eg. docetaxel) or polyoxyl 35 castor oil (eg. paclitaxel) warrant involvement of an immunologist to assess risk/benefit for each patient (see MOGA statement in links below). Patients with positive skin tests to PEG or polysorbate will need to be directed to receive the vaccine without the allergenic component. **Any reaction to COVID-19 vaccination should be reported to the Therapeutics Goods Administration (TGA) in Australia.**

4. **Links to references / guidelines:**

- <https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination>
- <https://perspectives.esmo.org/news/covid-19-vaccination-in-patients-with-cancer-esmo-releases-ten-statements>
- <https://www.asco.org/asco-coronavirus-resources/covid-19-patient-care-information/covid-19-vaccine-patients-cancer>
- <https://www.canceraustralia.gov.au/affected-cancer/covid-19-and-cancer/covid-19-vaccines-and-cancer/FAQs>
- <https://anztct.org.au/anztct-covid-19-vaccination-position-statement/>
- <https://www.moga.org.au/all-position-statements/covid-19-vaccination-in-patients-with-solid-tumours>
- <https://www.sciencedirect.com/science/article/pii/S2213219820314112>

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