**Medical Oncology Group of Australia position statement: COVID-19 vaccination in patients with solid tumours**

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**Abstract**

People with cancer are vulnerable to increased morbidity and mortality from the coronavirus disease 2019 (COVID-19). COVID-19 vaccination is key to protecting the population of people with cancer from adverse outcomes of SARS-CoV-2 infection. The Medical Oncology Group of Australia aimed to address the considerations around COVID-19 vaccination in people with cancer, in particular, safety and efficacy of vaccination. The assessment of patients with generalised allergic reaction to anti-cancer therapy containing vaccine components and practical implementation of vaccination of people on active anti-cancer therapy are also discussed.

**Introduction**

The coronavirus disease 2019 (COVID-19) pandemic has caused significant morbidity and mortality worldwide. People with cancer are at greater risk of serious complications and death from SARS-CoV-2 infection.1,2 People with cancer have high case-fatality rates from COVID-19 with reported rates of 21–25% from the United States and United Kingdom,3,4 compared with 1–4% in the general population.3

People with cancer comprise a heterogeneous population at different points of the cancer disease trajectory. There are differences in patients’ age, comorbidities, tumour types and the type of systemic anti-cancer therapy. These factors all contribute towards an individual’s risk of COVID-19 infection and related complications, with potential implications in their response to vaccination.

While Australian guidelines on COVID-19 exist for haematological malignancies5 and haematological stem cell transplant and chimeric antigen receptor T-cell (CAR-T cell) therapy recipients,6 people with solid tumours are, by comparison, generally less immunocompromised from their treatment and underlying cancer. This position statement discusses key issues relevant to COVID-19 vaccination for people with solid tumours in the Australian context.

**Methods**

Representative members from the Medical Oncology Group of Australia (MOGA) convened a working group to produce this position statement. Key questions relevant to the solid tumour population were identified. The authors reviewed the existing literature in order to address these questions using the available evidence of
the time. Infectious diseases consultation was sought with no additional comments made. The statement was subjected to peer review by the MOGA Executive Committee prior to endorsement. A full version of the statement was subsequently first uploaded online on 15 March 2021. In version 2 of the full position statement available online, there was input from the Australasian Society of Clinical Immunology and Allergy. Acknowledging the rapidly evolving nature of the topic, this was intended to be a live document with updates as new information arise, with version 2 uploaded online on 26 March 2021. This statement also received endorsement by the Clinical Oncology Society of Australia on 29 March 2021.

Is the vaccine safe for people with cancer?

People with cancer were under-represented in COVID-19 vaccine clinical trials.\textsuperscript{7–9} Even in the phase III trial of the BNT162b2 (Pfizer) vaccine, in which 1395 people (3.7% of study population) with a history of malignancy were included (and 733 (3.9%) received the vaccine), people with active malignancy receiving systemic immunosuppressive therapy were excluded.\textsuperscript{8} The safety profile of COVID-19 vaccines to date have been favourable,\textsuperscript{7–9} and while cases of anaphylaxis were observed, these were rare events, with vaccination safe for the majority of the general population. While specific evidence regarding COVID-19 vaccines in people with cancer is limited, there is no scientific rationale for a heightened risk of vaccine-related toxicities.

Concerns have been raised about the active constituents of the Pfizer and Moderna mRNA vaccines (polyethylene glycol (PEG); and AstraZeneca and Johnson & Johnson vaccines (polysorbate 80), which are active components of many anti-cancer therapies and have been implicated in allergic reactions.\textsuperscript{10} The Australasian Society of Clinical Immunology and Allergy (ASCIA) has advised people with cancer and a history of generalised allergic reaction to anti-cancer agents containing polysorbate (e.g. docetaxel) or polyoxyl 35 castor oil (e.g. paclitaxel) remain eligible for vaccination in a medical facility with capability to manage anaphylaxis and a lengthened (30 min) post-vaccination observation period.\textsuperscript{11} Patients with a history of generalised allergic reaction and/or anaphylaxis to pegylated liposomal doxorubicin or pegfilgrastim should be referred to an immunologist for COVID-19 vaccination, due to high risk of cross-reactivity with the Pfizer vaccine. Patients with a history of multiple drug allergies (where PEG or polysorbate 80 is present in the allergenic drugs) should also have a review or discussion by an immunologist prior to COVID-19 vaccination to consider skin prick testing and assess the risk/benefit of vaccination for each patient. Vaccination is contraindicated with documented anaphylaxis to one of the COVID-19 vaccine components (Pfizer-PEG or AstraZeneca- polysorbate 80). These patients may still be able to receive a different COVID-19 vaccine not containing the allergenic component. Any serious or unexpected reaction to COVID-19 vaccination should be reported to the Therapeutics Goods Administration (TGA) in Australia. Live vaccines are contraindicated for immunocompromised patients including those receiving cytotoxic therapy. Of the two TGA-approved (Pfizer BNT162b2 (mRNA) and AstraZeneca AZD1222 (viral vector)) vaccines, neither are live vaccines.

Is there a priority ranking for COVID-19 vaccination?

People with cancer who are immunosuppressed from anti-cancer therapy should be prioritised for vaccinations, due to their risk of an adverse outcome from COVID-19 infection.\textsuperscript{2} Additionally, risk factors for cancer overlap with many risk factors for adverse outcome from COVID-19, including increased age or comorbidities such as chronic pulmonary disease. Among people with cancer, risk factors for increased risk of complications from COVID-19 infection are listed below, with the odds ratio (OR) for 30-day mortality:\textsuperscript{12}

- Age: per decade increase (OR 1.84)
- Male: (OR 1.63)
- Smoking: former smoker versus never smoker (OR 1.60)
- Comorbidities: two versus none (OR 4.50)
- Eastern Cooperative Oncology Group performance status: 2 versus 0/1 (OR 3.89)
- Active cancer: progressing versus in remission (OR 5.20)

Other reported risk factors identified in literature include:

- Lung cancer (hazard ratio (HR) 2.0 for severe COVID-19)\textsuperscript{13}
- Advanced stage (OR 5.58 for death from COVID-19 infection)\textsuperscript{1}

What is the impact of cytotoxic chemotherapy on COVID-19?

A series of 156 cancer patients from Guy’s Cancer Center in London, United Kingdom, found patients receiving systemic therapy in the non-curative setting had an
increased risk of death from COVID-19 infection (HR 5.74) compared with patients not on treatment. However, recent chemotherapy has not been associated with a severe or critical COVID-19 event in a series of 309 cancer patients with COVID-19 infection from the Memorial Sloan Kettering Cancer Center, New York. Chemotherapy was also not significantly associated with 30-day all-cause mortality in cancer patients with COVID-19 infection in the COVID-19 and Cancer Consortium (CCC19) cohort study of 1035 patients from the United States, Canada and Spain.

The contrasting findings from these studies means the impact of chemotherapy on outcome from COVID-19 infection remains uncertain. In the Australian context, with minimal local COVID-19 transmission, interruption of chemotherapy is not generally recommended. This remains a clinical benefit/risk assessment by clinicians for their patients, taking into consideration the local epidemiology of COVID-19 at the time, given that the risk of adverse COVID-19 outcomes from chemotherapy is not established.

Are there specific considerations for immunotherapy?

Immune checkpoint inhibitor treatment was not associated with adverse outcome from COVID-19 infection in the majority of studies. There are currently no published data on the immunogenicity of COVID-19 vaccination among recipients of immunotherapy. However, studies support the efficacy of influenza vaccination among checkpoint therapy recipients.

Will the COVID-19 vaccination be effective in people with cancer and for how long?

People with cancer on cytotoxic chemotherapy are immunosuppressed and may mount an inferior immune response from vaccination. Lower immunogenicity from influenza vaccination, as measured by seroconversion rate and magnitude of antibody response, has been shown in people with cancer on chemotherapy compared with the general population.

Published rates of clinical effectiveness of COVID-19 vaccines are 95% with Pfizer, 94% with Moderna, 89% with Novavax, 70% with AstraZeneca and 66% with the Johnson & Johnson vaccine. The duration of protection from COVID-19 vaccination among people with cancer, and whether those immunosuppressed by antineoplastic therapy require future ‘booster’ injections currently remains unknown. Given people with cancer have an attenuated response to immunisation, they should ideally be prioritised for the higher efficacy vaccines. However, the choice of vaccine candidate may ultimately be dictated by supply.

When should people with cancer receive their COVID-19 vaccine?

People with cancer receiving chemotherapy can receive COVID-19 vaccination in between chemotherapy cycles

Box 1 Recommendations for COVID-19 vaccination of people with cancer in the Australian context

- People with cancer should receive COVID-19 vaccination in the absence of contraindications such as anaphylaxis to vaccine components.
- Live vaccines are contraindicated in immunocompromised patients. All of the following are not live vaccines: Pfizer/BioNTech (BNT162b2), AstraZeneca/Oxford (AZD1222), Moderna (mRNA-1273), Novavax (NVX-CoV2373) and Johnson & Johnson/Janssen (Ad26.Cov2.S) COVID-19 vaccines.
- In line with the Australian Government COVID-19 vaccine national roll-out strategy, cancer patients should be prioritised in Phase 1b among adults with an underlying medical condition.
- Anti-cancer therapy including cytotoxic chemotherapy, immune checkpoint inhibitor therapy and targeted therapy should not inhibit vaccination; these patient should also be vaccinated.
- People with a history of generalised allergic reaction (without anaphylaxis) to COVID-19 vaccine components including polysorbate 80 (e.g. docetaxel) or polyoxyl castor oil (e.g. paclitaxel) can still receive COVID-19 vaccination (Pfizer or AstraZeneca), followed by 30 min of observation, as per ASCIA advice. Patients with a history of generalised allergic reaction and/or anaphylaxis to pegylated liposomal doxorubicin or pegiligrastim, or have multiple drug allergies (where PEG or polysorbate 80 is present in the allergenic drugs) require immunologist review prior to vaccination. Vaccination is contraindicated with documented anaphylaxis to one of the COVID-19 vaccine components (Pfizer-PEG or AstraZeneca-polysorbate 80). These patients may still be able to receive a different COVID-19 vaccine not containing the allergenic component. In general, patients should be vaccinated at the earliest opportunity. Clinicians may elect to time vaccination in between chemotherapy cycle, avoiding the nadir period where possible. Vaccination concurrently at the time of immune checkpoint inhibitor dosing can be considered to minimise hospital visits.
- A 2-week interval between COVID-19 vaccination and influenza vaccination is recommended given the overlap in the approaching winter influenza vaccine rollout in the southern hemisphere.
- People with cancer and their close contacts (such as families and carers) should continue to practise good hand hygiene, maintain social distancing and wear face masks where appropriate within Australian Government guidance.
and ideally away from the nadir period.\textsuperscript{20} This is due to
the expectation that blood count recovery would parallel
improved immune function and potentially greater
immune response from vaccination. Ultimately, the op-
timal timing of COVID-19 vaccination in patients under-
going chemotherapy remains uncertain, with some
guidelines recommending administration of the vaccine
as soon as available and practical to do so.\textsuperscript{21} As COVID-
19 vaccination side-effects such as fever are expected at
2–3 days post-vaccination with potential intensification
of side-effects following the second dose, systemic anti-
cancer therapy should be avoided at this time.

As of 20 February 2021, two vaccines are approved by
the Australian TGA: Pfizer/BioNTech BNT162b2 and
AstraZeneca AZD1222 vaccines. Both vaccines require
administration of two doses, 21 days apart for the Pfizer
vaccine and 12 weeks apart for the AstraZeneca vac-
cine.\textsuperscript{22} In people due to commence anti-cancer therapy,
both doses should ideally be completed at least 2 weeks
prior to starting treatment.\textsuperscript{20} The commencement of
anti-cancer therapy should not be delayed for COVID-19
vaccination.

**What is the impact of vaccination status on
cancer care delivery?**

COVID-19 vaccination is voluntary under the Australian
Government national roll-out strategy. The impact of
non-vaccinated individuals (due to contraindications or
personal choice) on healthcare delivery currently
remains uncertain. Of particular relevance to oncology,
the delivery of anti-cancer therapy in open plan infusion
centres may need to take into consideration the vaccina-
tion status of patients and healthcare workers. Clinicians
need to make individual patient risk–benefit assessment
regarding COVID-19 vaccination, and should address
any vaccine hesitancy in people with cancer using sci-
centific evidence.

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**Box 2 Useful resources**

**Healthcare professionals**

- American Society of Clinical Oncology: https://www.asco.org/asco-coronavirus-resources/covid-19-vaccines-patients-cancer
- European Society of Medical Oncology: https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination
- National Comprehensive Cancer Network: https://www.nccn.org/covid-19/
- Memorial Sloan Kettering Cancer Center: https://www.asco.org/sites/new-www.asco.org/files/content-files/covid-19/2021-MSK-COVID19-VACCINE-GUIDELINES.pdf
- Australasian Society of Clinical Immunology and Allergy: https://www.allergy.org.au/hp/papers/ascia-hp-position-statement-covid-19-vaccination

**Patients**

- Cancer Australia: https://www.canceraustralia.gov.au/affected-cancer/covid-19-and-cancer/covid-19-vaccines-and-cancer/FAQs

**Conclusions**

People with cancer are at an increased risk for adverse outcomes from SARS-CoV-2 infection. COVID-19 vacci-
nation is key to protecting this vulnerable population.
This MOGA position statement outlines evidence
supporting COVID-19 vaccination in people with cancer,
including those on anti-cancer therapy such as chemo-
therapy and immunotherapy. It considers vaccinations
of people with generalised allergic reaction to anti-cancer
therapy containing vaccine components who may
require additional precautions in COVID-19 vaccination.
The statement aims to assist cancer clinicians in their
individual patient decision-making regarding COVID-19
vaccination. It is intended as a resource for all healthcare
professionals caring for people with cancer to facilitate
discussion around and encourage uptake of
COVID-19 vaccination (Boxes 1, 2).
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