Medical Oncology Group of Australia Position Statement
COVID-19 vaccination in adult patients with solid tumours

This position statement has been developed for cancer clinicians and other healthcare professionals caring for people with cancer. The COVID-19 pandemic is constantly evolving and the position statement may be updated with emergence of new evidence. Clinicians should remain cognisant that data is rapidly changing around current vaccines and newer agents, both in terms of positive and negative effects.
Version 15 (8 Jan 2023)

This statement has been endorsed by the Clinical Oncology Society of Australia (COSA).

Summary of Changes from 20 October 2022 version

- *Update on expanded indication for pre-exposure prophylaxis and second bivalent COVID-19 vaccine approval*

Summary of Changes from 29 July 2022 version

- *Update by ATAGI that the Moderna bivalent vaccine can be used as an alternate vaccine for any booster dose in people aged 18 years or older*
- *No changes have been made to ATAGI's current booster recommendations (no extra booster doses advised beyond the second booster dose)*

Summary of Changes from 2 June 2022 version

- *An update in relation to antiviral therapy and monoclonal antibodies for COVID-19 treatment and pre-exposure prevention.*

Summary of Changes from 6 April 2022 version

- *Updated advice from the Australian Technical Advisory Group on Immunisation (ATAGI) on expanded recommendation for winter COVID-19 booster dose.*

Summary of Changes from 21 Jan 2022 version

- *Updated advice from ATAGI with regards to a winter booster dose in immunocompromised individuals and adults aged over 65 years, from 4 months following their first booster dose.*

Summary of Changes from 17 October 2021 version

- *Updated advice from ATAGI with regards to booster (4th) vaccine dose in immunocompromised individuals who received three doses of COVID-19 vaccine as part of their primary course.*
- *Additional advice regarding vaccination after COVID-19 infection.*

Summary of Changes from 17 August 2021 version

- *Updated advice from (ATAGI) with regards to use of a 3rd dose of COVID-19 vaccine in immunocompromised individuals and update of the data available regarding serological response and vaccination in cancer patients.*

Summary of Changes from 21 June 2021 version

- *Updated advice from the ATAGI with regards to interval between COVID-19 vaccine doses in an outbreak setting (13 July 2021) is incorporated. Provisional registration of the Moderna vaccine is also included.*
- *Update with regards to the emerging consideration for additional (third) vaccine dose in immunocompromised people is added.*

Summary of Changes from 27 May 2021 version

- *Updated the preferred minimum interval between receipt of a COVID-19 vaccine and any other vaccine, including influenza vaccine, is 7 days. This is to be consistent with ATAGI Clinical guidance on use of COVID-19 vaccine in Australia version 5 (17 June 2021). The ATAGI advice was based on the current absence of data on the immunogenicity and safety of these vaccines when co-administered, and may change as further information becomes available.*
- *Updated advice from ATAGI on the COVID-19 Pfizer vaccine being the preferred vaccine for those aged 16 to under 60 years.*

Summary of Changes from 21 May 2021 version

- *Updated statement from ATAGI regarding additional groups for whom the Pfizer vaccine is recommended.*

Summary of Changes from 26 April 2021 version

- *Updated advice from the Australasian Society of Clinical Immunology and Allergy to consult an immunologist for people with history of allergic reactions to pegylated drugs.*

Summary of Changes from 13 April 2021 version

- Updated with advice from the *Australasian Society of Clinical Immunology and Allergy with regards to patients with history of hypersensitivity to paclitaxel and other anti-neoplastic agents containing components of COVID-19 vaccine.*

Summary of Changes from 25 March 2021 version

- Updated statement from the *Australian Technical Advisory Group on Immunisation (ATAGI) regarding preference for the Pfizer vaccine in adults under 50 years.*

Summary of Changes from 3 March 2021 version

- *Section regarding expanded skin testing to components of COVID-19 vaccines has been removed. This recommendation was based on the Mass General Brigham allergy expert consensus, however, the reagents for skin testing to PEG, polysorbate-80 are not currently available in Australia.*
- *The Australasian Society of Clinical Immunology and Allergy (ASCIA) guideline (17 Feb 2021) recommends precautions (including immunology consultation) with COVID-19 vaccination in people with generalised allergic reaction to one of the ingredients of the COVID-19 vaccines. Reference to history of immediate (<4 hours) reaction to anti-cancer agents containing COVID-19 vaccine components has been removed for consistency with these guidelines.*

- *TGA reporting is recommended for serious or unexpected side effects from COVID-19 vaccination.*
- *An updated statement from the Australian Technical Advisory Group on Immunisation (ATAGI) regarding vaccination in people with history of clotting condition is provided.*

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Background

The 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 infection 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 and tumour types. There is also variation in the type of systemic anti-cancer therapy used including chemotherapy, endocrine therapy, targeted therapy and immunotherapy. These factors all contribute towards an individual's risk of COVID-19 infection and related complications, with potential implications in their response to vaccination.

As COVID-19 vaccination campaigns are being rolled out globally, additional considerations are relevant for people with cancer. While Australian guidelines exist for haematological malignancies[5] and haematological stem cell transplant and CAR-T cell therapy recipients[6], solid tumour patients 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 cancers in the Australian context.

Is the vaccine safe for people with cancer?

People with cancer were underrepresented in COVID-19 vaccine clinical trials[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[8]. The safety profile of COVID-19 vaccines to date have been favourable[7-9], and while cases of anaphylaxis were observed, these were rare events, with vaccination deemed safe for the majority of the population.

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 agents and have been implicated in allergic reactions[10] (see reference 10 for listing of medications). A recent study found only 3 of 252 patients with a recorded history of PEG (n=202) or polysorbate (n=50) reactions developed mild rash following COVID-19 vaccination (Pfizer and Moderna vaccines)[11]. This finding was reassuring for the safety of patients with past reactions to PEG/polysorbate, including patients with history of paclitaxel reactions, to receive COVID-19 vaccines. On the other hand, patients who developed an acute (within 12 hours) reaction to 1st dose of mRNA COVID-19 vaccine were at greater risk of repeated symptoms following a second dose (reaction occurring in 43 or 44 patients on re-challenge).

The Australasian Society of Clinical Immunology and Allergy (ASCIA) has advised patients with history of hypersensitivity to paclitaxel and docetaxel can still receive either the Pfizer or AstraZeneca COVID-19 vaccine, given the risk of an allergic reaction is low. These patients should be vaccinated in a medical facility with capability to manage anaphylaxis with a lengthened (30 minutes) post-vaccination observation period[12].

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 (Comirnaty) vaccine. Patient with a history of **multiple** drug allergies (where PEG or polysorbate 80 is present in the allergenic drugs) should 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. Please consult local specialist COVID-19 / high risk vaccination clinics for further advice regarding specific patient circumstances.

Vaccination is contraindicated with documented anaphylaxis to one of the COVID-19 vaccine components (Pfizer- PEG or AstraZeneca- polysorbate 80)[13]. 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 patients receiving chemotherapy. The Pfizer Comirnaty BNT162b2 (mRNA) and AstraZeneca ChAdOx1-S (viral vector), Janssen/ Johnson & Johnson Ad26.COV2.S (viral vector), Moderna Spikevax elasomeran (mRNA) and Novavax NVX-CoV2373 (protein subunit) vaccines have received provisional approval by the TGA[14]. None of these vaccines are live vaccines. An important observation for people with cancer following COVID-19 vaccination is the development of lymphadenopathy[7, 8], which needs to be differentiated from disease progression in people with cancer[15]. Similarly, mammogram should be scheduled away from COVID-19 vaccination where possible to avoid false positive findings from vaccination induced lymphadenopathy[16].

People with cancer are at increased risk of venous thromboembolic events. Concerns were initially raised in European nations with regards to venous thromboembolic disorders following vaccination with the AstraZeneca COVID-19 vaccine. However, on review by the European Medicines Agency, the concern is specifically regarding thrombosis with thrombocytopenia syndrome (TTS), rather than thromboembolic events in general[17]. TTS has been associated with thrombosis in unusual locations such as mesenteric vein or cerebral venous sinus thrombosis (CVST). The incidence of TTS varies with age, ranging from 3.1 per 100,000 in people <50 years to 2.7 per 100,000 in people aged 50-59 years[18]. The majority of CVST cases occurred in women aged under 55 years[17].

As of 17 June 2021, the Australian Technical Advisory Group on Immunisation (ATAGI) has advised the use of the Pfizer vaccine, in preference over the AstraZeneca vaccine in adults under 60 years of age [19] . The ATAGI update on 23 May 2021 has advised the Pfizer COVID-19 vaccine to be used in people with a past history of CVST, heparin induced thrombocytopenia, idiopathic splanchnic (mesenteric, portal and splenic) venous thrombosis, antiphospholipid syndrome with thrombosis or TTS following first dose of AstraZeneca COVID-19 Vaccine[20].

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[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[21]:

- Age- per decade increase (OR 1.84)
- Male gender- (OR 1.63)
- Smoking status- former smoker versus never smoker (OR 1.60)
- Comorbidities- two versus none (OR 4.50)
- Eastern Cooperative Oncology Group performance status- 2 versus 0 or 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)[22]
- Advanced stage (OR 5.58 for death from COVID-19 infection)[1]

In general, the priority for vaccination should be for people with active cancer and people on cancer therapy (except if receiving hormonal therapy only). This guideline acknowledges that the definition of people with cancer, for the purpose of vaccination prioritisation, is still an evolving topic under discussion between government and relevant stakeholders.

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 (HR 5.74) compared with patients who were not on any treatment[4]. 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[22]. 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[21]. In this cohort, an increased risk of death was associated with recent chemotherapy (within two weeks of COVID-19 infection), but not seen with longer time interval since chemotherapy administration.

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?

Immunotherapy used for the treatment of cancer include antibodies against programmed cell death protein 1 (PD-1), programmed death-ligand 1 (PD-L1) and cytotoxic T-lymphocyte associated protein 4 (CTLA-4), collectively called immune checkpoint inhibitors. Extrapolating from the experience with influenza vaccines in recipients of immunotherapy,

most studies support vaccine safety with no excessive rates of high grade immune-mediated toxicities[23-26]. These studies, however, are primarily comprised of patients receiving monotherapy with anti-PD(L)1 antibodies, and data for vaccine safety among recipients of combination immunotherapy is scarce. With regards to efficacy, studies support the efficacy of influenza vaccination among people receiving immune checkpoint inhibitors[23, 27], with seroconversion rates of 60-70%[25].

Immune checkpoint inhibitor therapy was not associated with an adverse outcomes from COVID-19 infection in most studies[28-30] except one[31]. In a study of lung cancer patients treated with anti-PD1 antibody, immunotherapy administration showed a trend towards increased risk of hospitalization and death, although the apparent association was lost after adjustment for smoking status[32]. Therefore, the overall body of data supports safety of COVID-19 vaccination of patients on immunotherapy, a practice supported by multiple guidelines including from the National Comprehensive Cancer Network (NCCN)[33] and in the Memorial Sloan Kettering Cancer Center COVID-19 vaccine interim guidelines for cancer patients[34].

What is the impact of other anti-cancer therapies on COVID-19 vaccination?

Other anti-cancer therapies associated with neutropenia and leucopenia include targeted therapy such as cyclin-dependent kinase 4/6 (CDK4/6) inhibitors and poly-ADP-ribose polymerase (PARP) inhibitors[35, 36]. Although the risk of febrile neutropenia with these agents is low, any impact that this may have on COVID-19 infection and vaccination remains unknown. Patients receiving endocrine therapy for breast and prostate cancers, are expected to be at a similar risk level as the general population[28]. Finally, people who have completed anti-cancer therapy with curative intent and are without active cancer have an immunity level similar to the general population of which they should be reassured and considered for vaccination at the same priority level.

Will 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[37]. Lower immunogenicity from influenza vaccination, as measured by seroconversion rate and magnitude of antibody response, has been shown in people with cancer compared with the general population[38, 39]. A single-arm study of 53 patients with solid tumours found that the seroprotection rate decreased by 24 weeks post influenza vaccination[40]. Population-based data suggests a modest vaccination effectiveness of 21% in people with cancer, which is lower than the rate of 42% in a more generalised population[41]. In this study, vaccine effectiveness not influenced by active chemotherapy use[41].

Published rates of clinical effectiveness of COVID-19 vaccines are 95% with Pfizer[8], 94% with Moderna[7], 89% with Novavax[42], 70% with AstraZeneca[9], and 66% with the Johnson & Johnson[43] vaccine. To date, the Johnson & Johnson vaccine is the only vaccine designed for administration by a single dose. The mRNA vaccines encapsulated in lipid carriers maybe taken up in cancer tissues[44]. Theoretically this may reduce vaccine immunogenicity although clinical evidence for this is currently lacking. 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.

Studies presented at the 2021 European Society of Medical Oncology Congress provided reassuring data on the efficacy of COVID-19 vaccination in people with cancer, including those

receiving cancer treatment. The VOICE trial reported on 743 participants including 503 with solid tumours. The proportion of patients with SARS-CoV-2 spike (S1-specific) antibody response following two doses of mRNA-1273 (Moderna) vaccines was non-inferior among patients on immunotherapy, chemotherapy or chemo-immunotherapy, compared with individuals without cancer[45]. However, an inadequate antibody response was found among 6.9% of patients who received immunotherapy, 16.2% of patients who received chemotherapy and 11.2% of patients who had chemo-immunotherapy[45]. The CAPTURE study of 585 patients post two doses of BNT162b2 or AZD1222 COVID-19 vaccines, found 85% seroconversion rate among solid tumour patients[46]. The study found a lower rate of neutralising antibodies generated against variants of concern compared with wild-type SARS-CoV-2[46].

The duration of protection from COVID-19 vaccination among people with cancer remains uncertain. Administration of two doses of influenza vaccination has been shown to induce a superior immune response than one dose among solid cancer patients receiving cytotoxic and/or targeted therapy[39]. As of 12 August 2021, the United States FDA authorised an amendment to the Emergency Use Authorisation for Pfizer-BioNTech and Moderna COVID-19 vaccines, allowing an additional vaccine dose at least 28 days following completion of the initial two doses, for immunocompromised individuals, including individuals on active or recent treatment for solid tumours[47]. This has translated into various jurisdictions (France, Israel, United Kingdom and Germany) announcing a planned third vaccine dose among the immunocompromised population[48].

What is the recommended COVID-19 vaccination schedule among immunocompromised individuals?

As of 7 October 2021, ATAGI has recommended a 3rd primary dose of COVID-19 vaccine in severely immunocompromised population[49]. This includes patients with non-haematological malignancy currently undergoing active treatment such as chemotherapy, whole body irridation or on high dose corticosteroid treatment equivalent to >20mg/day of prednisone for >=14 days in a month. ATAGI does not currently recommend a 3rd primary dose for patients on immune checkpoint inhibitor alone. The third dose is recommended to given 2 – 6 months after the 2nd dose of vaccine. An mRNA vaccine (Pfizer or Moderna) is the preferred vaccine for the 3rd dose, although individuals who have received two doses of AstraZeneca vaccine can receive a 3rd dose of AstraZeneca vaccine in the absence of contraindications. For immunocompromised patients aged 18 years and over, these initial 3 doses of COVID-19 vaccine constitute their primary course of COVID-19 vaccination. These patients are recommended to receive a booster dose (i.e. 4th dose) at 3 months after completion of primary course of vaccination, in line with the general population[50].

From 25 May 2022, ATAGI has expanded the winter booster dose, initially for people aged 16 – 64 years with complex, chronic or severe heath conditions. This includes patients with non-haematological cancer diagnosed within the past 5 years, on or recently completed active treatment (including chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy), or with advanced disease regardless of treatment, and survivors of childhood cancer[51]. For this immunocompromised population, the winter booster dose will constitute their 5th COVID-19 vaccine dose. This additional winter booster dose can be given from 3 months after the first booster dose, or from 3 months after confirmed SARS-CoV2 infection. The Comirnaty (Pfizer), Spikevax (Moderna), Spikevax bivalent or Pfizer bivalent (Original/Omicron BA.1) COVID-19 vaccines are the preferred vaccines for boosters.

The Moderna bivalent vaccine (Spikevax Bivalent Original/Omicron BA.1) received provisional TGA approval on 29 August 2022 and can be used as a booster dose where available[52]. This is applicable to the general population aged 18 years and over, and there is currently no specific advice in relation to immunocompromised individuals with regards to use of the Moderna bivalent vaccine. More recently, the Pfizer bivalent vaccine has also received provisional TGA approval on 27 October 2022[53].

What COVID-19 treatments can cancer patients with COVID-19 receive?

Immunocompromised patients (such as those on chemotherapy in the last 3 months) who develop COVID-19 infection and are within five days of their illness are eligible to receive antiviral therapy to reduce risk of severe illness. Oral antiviral agents (eg nirmatrelvir/ritonavir [Paxlovid] and molnupiravir) have received provisional TGA approval for adults with COVID-19 who do not require supplemental oxygen but are at increased risk of severe disease from COVID-19. There are no published limitations on a time gap to vaccination following use of these antivirals which have short half-lives.

The present eligibility for oral COVID-19 treatments is listed here:
https://www.health.gov.au/health-alerts/covid-19/treatments/eligibility

There are potential drug interactions with Paxlovid (nirmatrelvir/ritonavir). This maybe relevant for patients on cancer therapy, such as CDK4/6 inhibitors for breast cancer. Drug interaction check can be done here:

https://covid19-druginteractions.org/checker

Sotrovimab was previously used for treatment of mild/moderate COVID-19 but no longer in routine use with the emergence of new variants (eg Omicron BA2) and inherent resistance. Patients treated with sotrovimab should not receive COVID-19 vaccination (including booster doses) for the next 90 days as the vaccine is not expected to be effective for that period due to the long half-life of this anti-SARS-CoV-2 monoclonal antibody.

ATAGI has advised that people with past COVID-19 infection can defer vaccination for up to 3 months. However, patients who are significantly immunocompromised and at greater risk of COVID-19 re-infection may proceed with vaccination without delay, providing that they have recovered from the acute illness[54].

Are there any other treatments (aside from vaccination) cancer patients can receive to prevent COVID-19?

Recently, Evusheld (tixagevimab and cilgavimab) has been provisionally approved by the TGA as pre-exposure prevention of COVID-19 in patients who are moderately to severely immunocompromised due to a medical condition, or due to immunosuppressive treatment where they may not mount an adequate immune response to COVID-19 vaccination[55]. Patients who are not recommended COVID-19 vaccination due to a history of severe adverse reaction to COVID-19 vaccine or vaccine component are also eligible. Evusheld is available through the National Medical Stockpile and distributed to states and territories to administer in their health systems[56]. Access was initially prioritised for the highest risk patients (e.g.

recipient of B or T cell depleting therapies). Access has since been broadened in numerous jurisdictions to include solid individuals receiving chemotherapy or whole body radiotherapy. With COVID-19 variants becoming the predominant stains in Australia, efficacy of various COVID-19 therapies against variants and sub-variants will need to be considered[57-59]. Prescribers should also be aware that Evusheld contained polysorbate 80 and there may be cross reactivity to the mRNA vaccines which contain PEG if patients have had an allergic reaction and referral to an immunologist should be considered if patients have a history of a severe allergic reaction to a COVID 19 vaccine[60].

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

People with cancer would ideally receive COVID-19 vaccination at least two weeks prior to their commencement of a course of chemotherapy[31]. If the patient is already receiving chemotherapy, the Memorial Sloan Kettering Cancer Center guidelines recommend COVID-19 vaccination in between chemotherapy cycle and away from the nadir period[34]. This is due to the expectation that that blood count recovery would parallel improved immune function and potentially greater immune response from vaccination. Ultimately, the optimal timing of COVID-19 vaccination in patients undergoing chemotherapy remains uncertain, with some guidelines (e.g. NCCN) recommending administration of the vaccine as soon as available and practical to do so. 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.

There are now four COVID-19 vaccines available in Australia: Pfizer/BioNTech BNT162b2, AstraZeneca AZD1222, Moderna mRNA-1273 and Novavax NVX-CoV2373. These vaccines require administration of two doses, 21 days apart for the Pfizer and Novavax vaccines, 4 weeks apart for Moderna and 12 weeks apart for the AstraZeneca vaccine[61]. However, in the setting of a COVID-19 outbreak, an interval of between 4 – 8 weeks between first and second doses of the AstraZeneca COVID-19 vaccine has been recommended by ATAGI[62]. In people due to commence anti-cancer therapy, both COVID-19 vaccine doses should ideally be completed prior to starting cancer treatment, with the minimum recommended time between the two doses where practical. The commencement of anti-cancer therapy should not be delayed for COVID-19 vaccination.

Summary of Society guidelines

Cancer societies globally have advocated COVID-19 vaccination in people with cancer as the benefits from reducing COVID-19 infection outweigh the possible risks from vaccination. A summary is presented in the table below. In Australia, people with cancer are recommended to receive the COVID-19 vaccine in accordance with the Australian Government COVID-19 vaccine national roll-out strategy: <https://www.health.gov.au/resources/publications/covid-19-vaccination-australias-covid-19-vaccine-national-roll-out-strategy >

Given the impact of vaccination on preventing COVID-19 infection and transmission is unknown, people with cancer and their close contacts (such as families and careers) should continue to practice good hand hygiene, maintain social distancing and wear face masks where appropriate within Australian Government guidance.

Other considerations and pending issues

- <u>Vaccination in people with advanced (incurable) cancer:</u> The impact of COVID-19 vaccination in people with advanced cancer and limited life expectancy remains

unknown. The NCCN guidelines acknowledge that it may be argued that COVID-19 immunisation would be most effective and impactful in other cancer populations such as those who have finished treatment with curative intent and have no evidence of cancer[33]. In Australia, where no vaccine supply shortages are anticipated, this issue may be less pressing. Vaccination in the palliative setting can facilitate patient reunification with loved ones especially where interstate travel is involved. This remains an ethical consideration to be based on a case-by-case decision between individual clinicians, patients and their families at this time.

- Cancer clinical trial participation in the COVID-19 era: The NCCN guideline stipulates that ongoing clinical trials should update protocols to allow COVID-19 vaccination, not to place patients in the position to choose between vaccination and clinical trial participation[33].
- Ongoing pharmacovigilance and data collection of efficacy and adverse outcomes will help inform the optimal strategy for COVID-19 vaccination in our cancer population. In Australia, real-time collection of data for adverse events is occurring through AusVaxSafety.
- Underserved populations: Issues of access and health literacy in underserved populations (such as elderly, rural and remote, first nations people, underprivileged, non-English speaking people with cancer) need to be considered in vaccine roll-out programs. Cold chain issues will be a consideration for regional and remote patients. Although a national program, implementation of the vaccine rollout is state based. At times during the pandemic, border populations have been severely impacted by border closures and we need to ensure unfettered access across borders based on priority and need.
- Impact of vaccination status on treatment delivery in healthcare settings: 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, chemotherapy delivery in open plan infusion day centres may need to take into consideration the vaccination status of patients and the health care workers.
- National guideline for best practice: In Australia, the operation of healthcare facilities is largely state-based leading to variation in practice across states and territories. A unified approach to COVID-19 vaccination and healthcare operational implications would help standardise practice in Australia.

COVID-19 Vaccination	ESMO	ASCO	NCCN	MSKCC
Use in cancer patients	Supports	Supports	Supports	Supports
Safety	No obvious safety concerns are evident for COVID-19 vaccination with antineoplastic therapies.	Immunocompromised individuals may still receive COVID-19 vaccination if they have no contraindications to vaccine components.	No safety concerns are evident in patients undergoing cancer care.	• No contraindication to receipt of COVID-19 vaccine across a range of antineoplastic therapies including chemotherapy • No data to suggest ICI recipients experience complications or exaggerated immune-related adverse events from any viral vaccine
Efficacy	Based on influenza vaccination data, cancer patients are able to mount a protective immune response from COVID-19 vaccination, but level of immunity maybe modulated by factors including cancer type, cancer therapy, timing of vaccination, baseline immune function.	Immunocompromised patients may experience decreased response to the vaccine, but it may still confer some benefit and help to reduce risk or severity of COVID-19 to cancer patients.	Vaccine efficacy in the setting of cancer care and immunosuppression is unknown.	• Antibody response to vaccines generally lower in recipients of cytotoxic chemotherapy • Immune responses to influenza vaccine are more robust in recipients of ICIs than cytotoxic chemotherapy
Priority for vaccination	Patients with cancer have an increased risk of severe COVID-19 (e.g. active advanced solid tumour or history of solid tumour <5 years ago) and should be positioned at high prioritisation.	Cancer has been identified as one of the high-risk medical conditions for phase 1c of CDC's priority group of vaccination but no specific comment regarding prioritisation within the cancer patient population.	• Active cancer on treatment • Planned to start treatment • <6 months post treatment *except* those on only hormonal therapy • Risk factors for severe COVID-19 e.g. age >65, co-morbidities, socio-demographic factors	• Patients with solid tumours should receive the COVID-19 vaccine as stratified by factors such as age • No additional stratification recommendations related to cancer type or stage of disease at this time
Timing of vaccination	Ideally prior to systemic therapy commencement, otherwise vaccinate during therapy.	See below	See below	• Ideally ≥2 weeks prior initiation of antineoplastic therapy • Avoid dosing antineoplastic therapy when vaccine side effects are expected (≤2-3 days of vaccination, more pronounced post 2nd dose)
-Chemotherapy	No specific recommendation	In between cycles of therapy	Whenever vaccine available as optimal timing to chemotherapy cycle unknown	In between chemotherapy cycles and away from nadir period
-Immunotherapy	No specific recommendation	No specific recommendation	Maybe considered on same day as ICI to reduce visits, lack of data on timing of vaccine	No specific timing recommended

ESMO: European Society of Medical Oncology[63]; ASCO: American Society of Clinical Oncology[64]; NCCN: National Comprehensive Cancer Network[33], MSKCC: Memorial Sloan Kettering Cancer Centre[34], ICI: immune checkpoint inhibitor

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, people with non-haematological cancers should be prioritised in Phase 1b, including patients diagnosed within the past 5 years or on recently completed active treatment including chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy, or with advanced disease regardless of treatment.
- 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 minutes of observation, as per ASCIA advice. People with a history of allergy to pegylated drugs such as pegfilgrastim, pegylated liposomal doxorubicin, should be reviewed by an immunologist prior vaccination. Patients with a history of **multiple** drug allergies (where PEG or polysorbate 80 is present in the allergenic drugs) should be reviewed by a clinical immunology/allergy or vaccinology specialist prior to vaccination. Click here for a listing of common injectable medications containing PEG or polysorbate 80. 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 minimum 7-day interval between COVID-19 vaccination and influenza vaccination was previously recommended (eg during the primary vaccination course). However, as of 24 December 2021 ATAGI now advises that it is acceptable to co-administer a COVID-19 booster vaccine dose with other vaccines[50].
- People with cancer and their close contacts (such as families and careers) should continue to practice good hand hygiene, maintain social distancing and wear face masks where appropriate within Australian Government guidance.

Useful resources

Health care professionals

- American Society of Clinical Oncology
- European Society of Medical Oncology

- National Comprehensive Cancer Network
- Memorial Sloan Kettering Cancer Center
- Australasian Society of Clinical Immunology and Allergy

Patients
- Cancer Australia
- Cancer Council

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