INTERNAL MEDICINE JOURNAL

RACP Specialists. Together

doi:10.1111/imj.15339

POSITION PAPER

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

Yada Kanjanapan [1,2] Prunella Blinman,[3,4] Craig Underhill [5,6] Deme Karikios [4,7] Eva Segelov [8,9] and Desmond Yip [1,2]

[1]Department of Medical Oncology, The Canberra Hospital, and [2]ANU Medical School, Australian National University, Canberra, Australian Capital Territory, [3]Department of Medical Oncology, Concord Repatriation General Hospital, [4]Sydney Medical School, The University of Sydney, and [7]Medical Oncology, Nepean Cancer Care Centre, Nepean Hospital, Sydney, [5]Border Medical Oncology, Albury-Wodonga Health, and [6]University of NSW Rural Medical School, Albury, New South Wales, and [8]Department of Oncology, Monash Health, and [9]School of Clinical Sciences, Monash University, Melbourne, Victoria, Australia

Key words
COVID-19, cancer, vaccination, immunosuppression.

Correspondence
Yada Kanjanapan, Department of Medical Oncology, The Canberra Hospital, Yamba Drive, Garran, ACT 2605, Australia.
Email: yada.kanjanapan@act.gov.au

Received 17 March 2021; accepted 7 April 2021.

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 malignancies[5] 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

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. Please refer to http://www.moga.org for the latest update of the guideline.

Funding: None.

Conflict of interest: None.

Desmond Yip- Stock ownership in CSL Limited, manufacturer of AZD1222 vaccine in Australia.

the time. Infectious diseases consultation was sought with no additional comments made. The statement was subjected to peerreview 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.[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 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.[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.[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.[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:[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)[13]
- Advanced stage (OR 5.58 for death from COVID-19 infection)[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.[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.[13] 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.[12]

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.[14,15] 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.[16]

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.[17] 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.[17]

Published rates of clinical effectiveness of COVID-19 vaccines are 95% with Pfizer,[8] 94% with Moderna,[7] 89% with Novavax,[18] 70% with AstraZeneca[9] and 66% with the Johnson & Johnson[19] 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 pegfilgrastim, 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.[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 optimal timing of COVID-19 vaccination in patients undergoing chemotherapy remains uncertain, with some guidelines recommending administration of the vaccine as soon as available and practical to do so.[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 vaccine.[22] In people due to commence anti-cancer therapy, both doses should ideally be completed at least 2 weeks prior to starting treatment.[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 vaccination 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 scientific evidence.

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 vaccination 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 chemotherapy 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).

References

1 Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z *et al*. Patients with cancer appear more vulnerable to SARS-COV-2: a multicenter study during the COVID-19 outbreak. *Cancer Discov* 2020; **10**(6): 789–791.

2 Ribas A, Sengupta R, Locke T, Zaidi SK, Campbell KM, Carethers JM *et al*. Priority COVID-19 vaccination for patients with cancer while vaccine supply is limited. *Cancer Discov* 2020: **11**(2): 233–236.

3 Mehta V, Goel S, Kabarriti R, Cole D, Goldfinger M, Acuna-Villaorduna A *et al*. Case fatality rate of cancer patients with COVID-19 in a New York hospital system. *Cancer Discov* 2020; **10**: 935–41.

4 Russell B, Moss C, Papa S, Irshad S, Ross P, Spicer J *et al*. Factors affecting COVID-19 outcomes in cancer patients: a first report from Guy's Cancer Center in London. *Front Oncol* 2020; **10**: 1279.

5 Haematology Society of Australia and New Zealand. COVID-19 Vaccination in Haematology Patients: An Australia and New Zealand Consensus Position Statement. 2021 [updated 2021 Feb 2; cited 2021 Feb 28]. Available from URL: https://www.hsanz.org.au/news/10054698

6 Australia and New Zealand Transplant and Cellular Therapies. COVID19 Vaccination Consensus Position Statement. 2021 [cited 2021 Feb 2]. Available from URL: https://anztct.org.au/wp-content/uploads/2021/02/FINAL-ANZTCT-COVID19-Vaccination-Position-Statement-Version2-2-Feb-2021.pdf

7 Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2020; **384**: 403–16.

8 Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S *et al*.

Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**: 2603–15.
9 Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021; **397**: 99–111.
10 Banerji A, Wickner PG, Saff R, Stone CA Jr, Robinson LB, Long AA *et al*. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. *J Allergy Clin Immunol Pract* 2020; **9**(4): 1423–37.
11 Australasian Society of Clinical Immunology and Allergy. Allergy Immunodeficiency, Autoimmunity and COVID-10 Vaccination Position Statement. 2021 [cited 2021 Mar 3]. Available from URL: https://www.allergy.org.au/hp/papers/ascia-hp-position-statement-covid-19-vaccination
12 Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR *et al*. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020; **395**: 1907–18.
13 Jee J, Foote MB, Lumish M, Stonestrom AJ, Wills B, Narendra V *et al*. Chemotherapy and COVID-19 outcomes in patients with cancer. *J Clin Oncol* 2020; **38**: 3538–46.
14 Lee LY, Cazier JB, Angelis V, Arnold R, Bisht V, Campton NA *et al*. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020; **395**: 1919–26.
15 Pinato DJ, Zambelli A, Aguilar-Company J, Bower M, Sng C, Salazar R *et al*. Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients. *Cancer Discov* 2020; **10**: 1465–74.
16 Chong CR, Park VJ, Cohen B, Postow MA, Wolchok JD, Kamboj M. Safety of inactivated influenza vaccine in cancer patients receiving immune checkpoint inhibitors. *Clin Infect Dis* 2020; **70**: 193–9.
17 Rousseau B, Loulergue P, Mir O, Krivine A, Kotti S, Viel E *et al*. Immunogenicity and safety of the influenza A H1N1v 2009 vaccine in cancer patients treated with cytotoxic chemotherapy and/or targeted therapy: the VACANCE study. *Ann Oncol* 2012; **23**: 450–7.
18 Novavax. COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial. 2021 [cited 2021 Mar 18]. Available from URL: https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3
19 Johnson & Johnson. Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of Its Phase 3 ENSEMBLE Trial. [cited 2021 Feb 3]. Available from URL: https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial
20 Memorial Sloan Kettering Cancer Center. MSK COVID-19 Vaccine Interim Guidelines for Cancer Patients. 2021 [cited 2021 Mar 8]. Available from URL: https://www.asco.org/sites/new-www.asco.org/files/content-files/covid-19/2021-MSK-COVID19-VACCINE-GUIDELINES.pdf
21 National Comprehensive Cancer Network. Preliminary Recommendations of the NCCN COVID-19 Vaccination Advisory Committee. [cited 2021 Mar 18]. Available from URL: https://www.nccn.org/covid-19/
22 Therapeutics Goods Administration. COVID-19 Vaccines. 2021 [cited 2021 Mar 14]. Available from URL: https://www.tga.gov.au/collection/covid-19