Commission on Excellence and Innovation in Health.

COVID-19 vaccines for people with cancer

Information for health care professionals

People with cancer are high risk for severe COVID-19 infection

Available evidence indicates that people with active cancer who developed COVID-19 infection have a high fatality rate from increased risks of developing severe infection. Those people with active haematological malignancies are at the highest risk as they have a limited immune response to control an infection as well as people with lung cancer (1). Similarly, there is emerging evidence that those on certain types of cancer treatment may have an increased risk for fatal outcomes from COVID-19 infection (1). Moreover, some people who do not mount a strong immune response against COVID-19 are likely to shed the virus for a longer time and be a source of continued unintended exposure infecting other persons. These data indicate that all people with: a current cancer diagnosis; those who are on active treatment cancer; and those who are recovering from a recent cancer treatment, would be considered for early access for COVID-19 vaccination.

Approved COVID-19 vaccines in Australia

Currently, there are two vaccines approved in Australia – Pfizer/BioNTech SARS-Cov-2 vaccine and Astra Zeneca ChAdox1 nCOV-19 vaccine. There are other vaccines currently in clinical trials around the world. Pfizer/BioNTech SARS-Cov-2 vaccine is a m-RNA vaccine. Importantly, the phase 3 trial of this vaccine included 1,395 patients with cancer and 76 patients with leukaemia or lymphoma. These patients responded with similar efficacy as non-cancer patients. Astra Zeneca ChAdox1 nCOV-19 vaccine is a replication deficient adenoviral vectored vaccine and there is no published information on its effectiveness in immunocompromised patients. Common acute side effects associated with candidate SARS-CoV-2 vaccines reported to date include low-grade fever, myalgias, headache, nausea, fatigue and soreness/redness at the injection site. These acute side effects were more pronounced after the booster dose (2nd vaccine dose) in some of the trials. Long-term side effects have not been defined for SARS-CoV-2 vaccines.

It is important to remember that there is limited information on the safety and effectiveness of the vaccines in people with cancer or on active cancer treatment. As the vaccines may have reduced protection, all patients should continue to practice COVIDSafe measures including optimal public health protective measures. Masks and social distancing work in real time to protect

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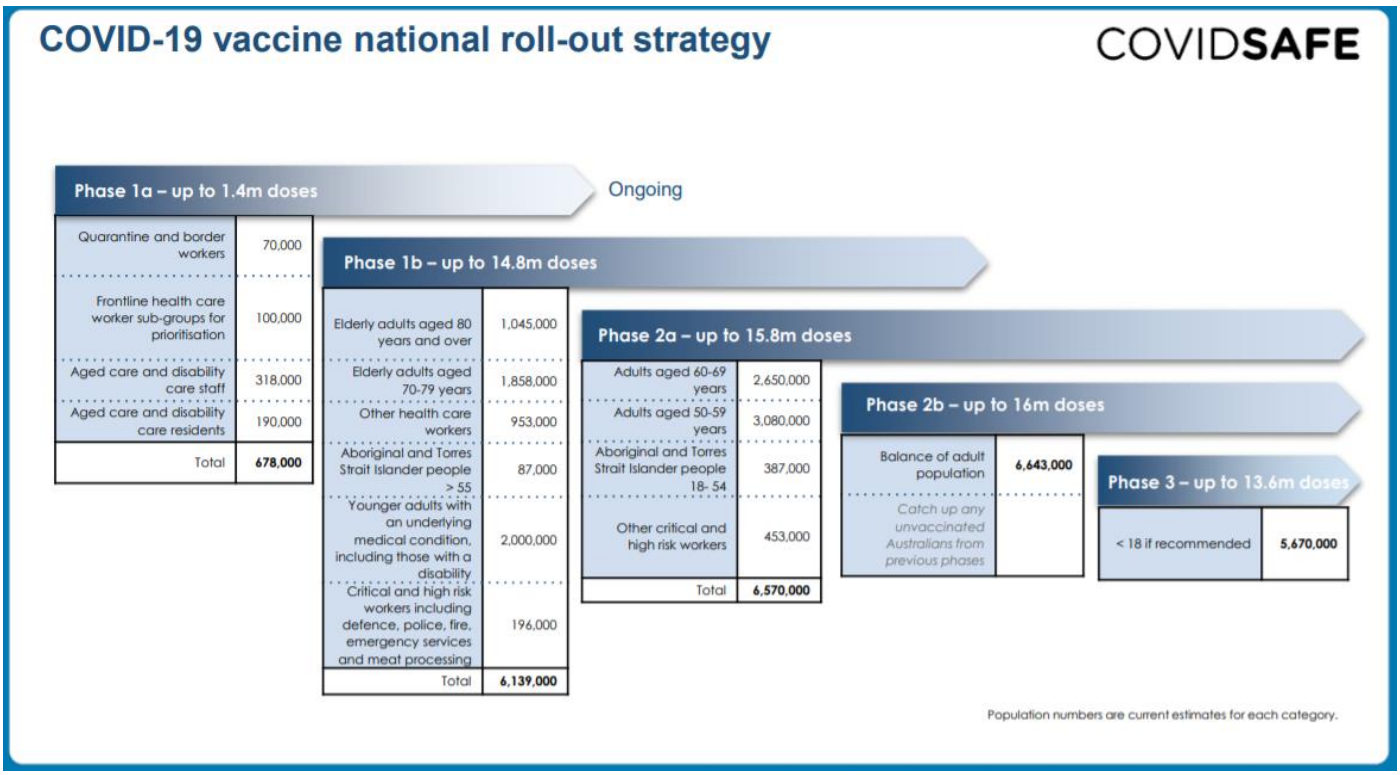
patients with compromised immunity against any strain of SARS-CoV-2. In contrast, COVID-19 vaccines do not provide immediate protection, and none are 100% effective.

Australia's COVID-19 national roll-out strategy

The Australian government has released a COVID-19 vaccination policy and national roll-out strategy (2). As per this plan, there are three priority population groups – those with increased risk of exposure, those increased risk of severe disease, or those working in services critical to societal functioning (Figure).

Figure: COVID-19 vaccine roll-out strategy



Who are those adults with an underlying medical condition, including those with a disability at increased risk for severe COVID?

"These at-risk medical conditions include, but are not limited to, immunocompromised, multiple comorbidities, chronic lung disease, diabetes, cardiovascular disease and severe obesity" (2)

As per Australia's COVID-19 vaccine national roll-out strategy, most people with active cancer will be offered COVID-19 vaccines as part of Phase 1b group (2). Cancer patients on active treatment (except those only on hormonal therapy and no comorbidities e.g. young people with CML in remission on kinase inhibitors, young women on adjuvant hormonal therapy without comorbidities) or those not on active treatment, but with comorbidities or immunosuppressed (e.g. post stem cell transplantation) – fall under Phase 1b cohort. Those free of cancer/cancer survivors without comorbidities/others such as young people without comorbidities on adjuvant non-immunosuppressive therapy (e.g hormonal therapy) and had the diagnosis made more than five years will be offered vaccination in Phase 2a or 2b.

Immunocompromised people and COVID-19 vaccine

The current understanding is that the following immunocompromised people could have attenuated or absent response to a SARS-CoV-2 vaccine (3):

- Immunodeficiencies involving adaptive immunity
- Splenectomy or functional asplenia (sickle cell disease)
- B cell directed therapies against CD20 or CD22, bispecific agents (like blinatumomab), CD19 or CD22-directed CAR-T cell therapies and BTK inhibitors
- T cell directed therapies (calcineurin inhibitors, antithymocyte globulin, alemtuzumab)
- Many chemotherapy regimens

- High-dose corticosteroids (>2 mg/kg/day daily prednisone or equivalent)
- Stem Cell Transplant patients - especially within the first 3-6 months after autologous transplantation and often longer after allogeneic transplantation.
- Underlying aberrant immunity (e.g. Graft-vs.-host disease (GVHD), Llw white blood cell counts. (neutropenia ANC<0.5 x 10^9/L, lymphopenia ALC<0.2 x 10^9/L)

Clinical practice guidance for COVID-19 vaccination

The following recommendations are general guide to health care professionals based on information gleaned from the limited evidence in the literature, national and international guidelines and expert opinion (4).

Is there a preferred vaccine?

mRNA vaccines (Pfizer vaccine and the currently unapproved Moderna vaccine) do not contain live virus or alter the recipient's DNA. Hence, these vaccines are considered to be safe for people with cancer or survivors who are over 16 years of age. Acknowledging the lack of data for efficacy and safety in cancer patients, the Pfizer/BioNTech SARS-Cov-2 vaccine being highly effective in the general population, it is the only vaccine with (albeit limited) data in patients with haematological malignancy. Astra Zeneca ChAdox1 nCOV-19 vaccine utilises the replication deficient adenoviral vector. There is no published literature on its use in people with cancer.

COVID-19 vaccines should not be administered to people who have severe allergic reactions to the first dose or any of its components (including polyethylene glycol). Those allergic to polyethylene glycol may preferentially be given the Astra Zeneca ChAdox1 nCOV-19 vaccine.

What is the most appropriate timing of vaccine administration in relation to cancer therapy?

Patients currently receiving chemotherapy, immunotherapy, CAR-T-cell therapies, hormonal therapies or stem cell transplants can still receive the vaccine. As a general principle, it is recommended that the vaccines should be administered around the period when the patient is least likely to be neutropenic or lymphocytopenic (5-7).

Avoid unnecessary delays with vaccination or cancer treatment.

Vaccination is recommended at least 2-4 weeks prior to the planned immunosuppressive therapy, transplantation or splenectomy.

Preferable to start the first dose 2 weeks prior to the first dose of cytotoxic chemotherapy. Immunomodulators (IMiDs) or cdk4/6 inhibitors.

For those already on treatment with chemotherapy when used alone or in combination with other agents such as immunotherapy, avoid administration of the vaccination on the same day of treatment; preferably, administer the vaccination towards the end of the cycle when the blood counts have recovered.

For those on IMiDs or CDK4/6 inhibitors – administer vaccines when the blood counts have maximally recovered.

For monotherapy with either immunotherapy, kinase inhibitors, monoclonal antibodies, or hormonal therapy – no specific timing issues are required.

Patients for whom for stem cell transplants or CAR-T-cell therapies (TCT) are planned, vaccination should be administered as soon as feasible prior to TCT and without deferral of TCT. Clinicians should consider recommending vaccination 3-6 months post TCT in patients aged older than 16 years who have no known contraindications to the vaccines.

Patients undergoing cancer surgery, it is recommended to wait for at least 10-14 days after the surgery to receive the first dose of vaccine.

Patients undergoing radiotherapy, there is no specific recommendation. If significant is immunosuppression expected from radiotherapy, consider administering vaccination 2-4 weeks prior to the start of radiotherapy.

Pfizer/BioNTech SARS-Cov-2 vaccine is a two-dose course with the second dose given 3-12 weeks after the first dose. Astra Zeneca ChAdox1 nCOV-19 vaccine is also a two-dose course with the second dose given 4-12 weeks after the first dose. The second dose can be timed according to the above recommendations.

Any precautions for the site of vaccination?

COVID-19 vaccines are generally administered intramuscularly in the deltoid region.

For people with breast cancer – consider administering the vaccine in the opposite arm to the primary site where nodal clearance was performed.

For people undergoing radiotherapy – consider avoiding the vaccine administration to the arm that directly drains through the nodes in the radiation field or previously irradiated.

Considerations for imaging?

Enlarged lymphadenopathy can be seen post vaccination. Diagnostic imaging post vaccination – consider delaying imaging for 6-10 weeks to avoid reactive lymph node enlargement from the vaccine being confused with cancer growth.

Clinical trial participation?

Those participating in clinical trials (8) – check the treatment protocol for trial specific guidance regarding the timing of vaccination. In general, avoid the investigational product for at least 2-4 weeks after vaccination if it has any potential to cause cytokine storm.

If the trial involves proven anticancer drugs with known benefits, this delay might be challenging for patients with progressing advanced cancers, and the risks and benefits of the delay must be carefully considered with the patient.

It is recommended that patients avoid receiving their vaccine on days of parenteral dosing of the investigational product (and receive it at a time as distanced as possible from investigational product dosing) and the dose-limiting toxicity period if administration of the SARS-CoV-2 vaccine is mandated while the patient is still participating in an early phase trial.

Do health care workers and caregivers require vaccination?

Healthcare workers caring for people with cancer should be prioritised in receiving vaccination to minimise nosocomial transmission. Healthcare workers will fall under the category of phase 1a or 1b under the national roll-out plan. It is recommended all health care providers be vaccinated unless contraindicated due to allergic/anaphylactic reactions.

It is recommended that caregivers and household/close contacts be vaccinated when possible. However, the caregivers and household contacts may fall under any of the priority groups in the national roll-out plan; hence they should be vaccinated when they are eligible.

Monitoring and research?

Close surveillance and monitoring of patients with cancer is required after COVID-19 vaccination to assess potential adverse events and measure clinical outcomes as limited data exists in this population. Measuring immune response with antibodies will not be routinely performed.

What about children with cancer?

Based on the current data, both vaccines were given to people aged 16 years or more. Hence, the vaccines are limited only to people older than 16 years of age.

What about COVID-19 and other vaccines?

The safety of multiple vaccines administered simultaneously has not been established. Consider giving other vaccines (e.g. influenza) at least 2 weeks before or after the COVID-19 vaccines.

References

1. Ribas et al. Priority COVID-19 Vaccination for Patients with Cancer while Vaccine Supply Is Limited. Cancer Discovery Feb 2021 - DOI: https://doi.org/10.1158/2159-8290.CD-20-1817

2. COVID-10 vaccination policy and national roll-out strategy - https://www.health.gov.au/sites/default/files/documents/2020/12/COVID-19-vaccination-australian-COVID-19-vaccination-policy.pdf; https://www.health.gov.au/sites/default/files/documents/2021/01/COVID-19-vaccination-australia-s-COVID-19-vaccine-national-roll-out-strategy.pdf

3. American Society of Haematology - https://www.hematology.org/COVID-19/ash-astct-COVID-19-and-vaccines

4. Cancer Australia repository for cancer vaccine information - https://www.canceraustralia.gov.au/affected-cancer/COVID-19-and-cancer/health-professionals/COVID-19-vaccines-and-cancer

5. NCCN: Cancer and COVID-19 vaccination - Preliminary Recommendations of the NCCN COVID-19 Vaccination Advisory Committee – version 1.0 22nd January 2021 - https://www.nccn.org/COVID-19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf.

6. UK chemotherapy board - Clinician Frequently Asked Questions (FAQs) and guidance on COVID-19 vaccine for patients receiving Systemic Anti-Cancer Therapy - https://b-s-h.org.uk/media/19241/clinician-faqs-and-guidance-on-COVID19-vaccine-for-patients-receiving-sa_.pdf

7. MSK COVID-19 vaccine guidelines - https://www.asco.org/sites/new-www.asco.org/files/content-files/2021-MSK_COVID19_VACCINE_GUIDELINES_final_V.2.pdf

8. Yap et al. SARS-Cov-2 vaccination and phase 1 cancer clinical trials. The Lancet Oncology Feb 2021 – advanced online - DOI: https://doi.org/10.1016/S1470-2045(21)00017-6

Additional resources

- https://www.health.gov.au/initiatives-and-programs/COVID-19-vaccines
- https://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/conditions/infectious+diseases/COVID-19/vaccine/COVID-19+vaccinations
- https://www.canceraustralia.gov.au/COVID-19-vaccine-and-cancer
- www.COVIDvaccine.sa.gov.au

CMI for vaccines

- Pfizer vaccine - https://www.tga.gov.au/sites/default/files/cmi-comirnaty-bnt162b2-mrna.pdf
- AstraZeneca vaccine - https://www.tga.gov.au/sites/default/files/cmi-approved-COVID19-vaccine-az.pdf

Acknowledgments

- This Document was developed by the State Wide Cancer Clinical Network (SCCN) and endorsed by the Clinical Advisory Group, COVID-19 Vaccination, DHW. Release Date 12th March 2021.