Australian Technical Advisory Group on Immunisation (ATAGI)

Provider guide to COVID-19 vaccination of people with immunocompromise

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What has changed

- *Information on 3rd doses in the primary course for severely immunocompromised individuals has been included*

This guide contains information about the COVID-19 vaccines Comirnaty (Pfizer), Spikevax (Moderna), and Vaxzevria (AstraZeneca). Pfizer and Moderna are registered for use in people aged 12 and older. AstraZeneca is registered for use in people aged 18 and older. Pfizer and Moderna are currently the preferred vaccines for people < 60 years. This guide will be updated as further vaccines become available.

Introduction

This guide is aimed at supporting health professionals who are counselling patients with immunocompromise regarding COVID-19 vaccination. People may be immunocompromised due to an underlying medical condition/s and/or because of medical treatment, e.g. chemotherapy, immunosuppressants or immunomodulators.

Many immunocompromising conditions are associated with a higher risk of severe illness and complications from COVID-19. These include solid organ transplantation, blood and solid organ cancers, or their treatments including immune therapy, chemotherapy, radiotherapy, blood/marrow stem cell transplant and CAR-T cell therapy.[1]

The immune response to vaccination may be reduced in people with some immunodeficiencies and people taking some immunosuppressants. Many people with immunocompromise will still develop at least a partial response to vaccination. This includes people in the following categories:

- People with primary or secondary immunodeficiencies
- People with asplenia (anatomical or functional)
- People taking B-cell depleting therapies such as anti-CD20 antibodies and CAR-T cell therapy
- People taking T-cell depleting therapies
- People receiving some chemotherapy
- People receiving high dose corticosteroids (equivalent to ≥20 mg per day)
- People who have undergone a haematopoietic stem cell transplant
- People taking multiple immunosuppressants.

COVID-19 vaccination should be strongly encouraged for people with immunocompromise, however for some patients the optimal timing of vaccination requires special consideration. Consultation with their treating specialist may be required.

Providers can also refer relevant patients to the *COVID-19 vaccination decision guide for people with immunocompromise* .

COVID-19 vaccine safety in people with immunocompromise

- There are no specific safety concerns relating to immunocompromise for people receiving Pfizer, Moderna or AstraZeneca. Pfizer and Moderna are not live vaccines. contains a non-replicating viral vector which cannot spread to other cells, and therefore does not behave like a ‘live vaccine’.
- AstraZeneca is associated with a rare condition called thrombosis with thrombocytopenia syndrome (TTS). There is no evidence that the risk of TTS is higher in people with immunocompromise. Pfizer and Moderna are not associated with TTS.
- Pfizer and Moderna are the preferred COVID-19 vaccines for people under 60 years of age and are the recommended vaccines for people with a past history of cerebral venous sinus thrombosis (CVST), heparin induced thrombocytopenia (HIT), idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis or antiphospholipid syndrome with thrombosis.
- For further information about TTS, refer to: *Information for Immunisation Providers on Thrombosis with Thrombocytopenia Syndrome (TTS) following COVID-19 vaccination.*

- Direct safety data from clinical trials of COVID-19 vaccines is currently not available. Individuals with known or suspected immunodeficiencies (other than HIV below) or who were receiving immunosuppressive treatment were excluded from enrolment.
- In the phase II/III trial of Comirnaty, 120 participants with well-controlled HIV were enrolled and there were no reported differences in safety signals in these participants compared to the general trial population.[2]
- A total of 179 participants with stable, chronic HIV infection were enrolled in the phase III trial of Spikevax, which was 0.6% of the total study population.[3] Numbers of symptomatic SARS-CoV-2 infection in this subgroup were not sufficiently high to perform meaningful analysis of vaccine efficacy (n=1, in placebo group). There were no specific safety concerns in the subgroup of participants with medical comorbidities.[3]
- 54 participants with HIV (all male, median age 42.5 years) were enrolled in the phase II/III trial of COVID-19 Vaccine AstraZeneca.[4] These participants were receiving antiretroviral therapy and had undetectable viral loads and CD4 counts of > 350 cells/μL. No serious adverse events occurred in this cohort, and local and systemic adverse events occurred at similar frequencies to HIV-negative participants.
- As of August 2021, over 4.5 billion doses of COVID-19 vaccines have been administered worldwide, and people with immunocompromise have been given vaccines as a priority group in many countries. So far no safety issues have been identified specific to people with immunocompromise.
- Select populations of people with severe immunocompromise have been recommended to receive an additional dose as part of their primary course. More information can be found in the *ATAGI recommendations on use of a 3rd dose of COVID-19 vaccine in individuals who are severely immunocompromised*.

COVID-19 vaccine effectiveness in people with immunocompromise

All three vaccines have been shown to be effective in healthy adults and adults with well-controlled non-immunocompromising medical co-morbidities. In particular, all vaccines are highly effective at preventing serious illness and hospitalisation. For further information about vaccine efficacy, refer to *ATAGI clinical guidance on COVID-19 vaccine in Australia in 2021*.

Small studies demonstrate that certain groups of immunocompromised individuals mount an immune response to COVID-19 vaccination, although humoral and immune responses may be impaired. Compared to people without immunocompromise, antibody levels have been lower among individuals with higher degree of immunosuppression, such as solid organ transplant recipients [5–8], individuals with haematological malignancies[9,10], and those receiving B-cell depleting therapy[11–13]. Few studies have evaluated T-cell responses among immunocompromised individuals, with some indicating relatively preserved cellular immunity[14], whereas other studies found blunted responses[15] in line with decreased antibody response.

In a cohort of 54 participants with HIV in the phase II/III trial of COVID-19 Vaccine AstraZeneca, there was no significant difference in magnitude or persistence of spike-specific humoral or cellular responses compared with HIV-negative participants.[4] Other small studies have indicated that the immunogenicity of COVID-19 vaccines in individuals with HIV infection is similar to healthy control subjects.[16,17] The immunogenicity and safety data of HIV subjects enrolled in the clinical trials for Pfizer and Moderna is not currently available.

It is uncertain how antibody levels and cellular immunity translate to protection against (a)symptomatic SARS-CoV-2 infection, hospitalisation and death. Vaccine effectiveness studies estimate COVID-19 vaccines to be approximately 70-90% effective at preventing SARS-CoV-2 infection among immunocompromised individuals, as compared to 84-94% among the general population in these same studies.[18–21] Most studies

evaluated Comirnaty (Pfizer) or Spikevax (Moderna). Whitaker et al. estimated Comirnaty and COVID-19 Vaccine AstraZeneca to be 73% (95% CI: 34-89%) and 75% (95% CI: 19-92%) effective against medically-attended PCR-confirmed COVID-19, respectively.[21] Due to the evaluation of the immunocompromised subpopulation among the general population, certainty around the estimated effectiveness is low. Additionally, the estimated vaccine effectiveness in the general immunocompromised population may not be indicative of vaccine effectiveness in specific immunocompromising conditions. All studies did confirm that a two dose COVID-19 vaccine schedule is essential, as protection after one single dose is poor.[20–22]

Data on the potential benefit of additional doses of COVID-19 vaccine (i.e. third dose) on the immune response and vaccine effectiveness among immunocompromised individuals is limited. Additional doses is therefore currently not recommended, and routine serological testing after two doses of COVID-19 in immunocompromised individuals is not required.

Recommendations

- Vaccination is strongly encouraged for people with immunocompromise who are in an eligible age group, since the benefits of vaccination are considered to outweigh any potential risks.
    - Pfizer and Moderna are registered for use in people aged ≥ 12 years
    - AstraZeneca is registered for use in people aged ≥ 18 years
- Pfizer, Moderna and AstraZeneca are considered acceptable for use in people with immunocompromise. Pfizer and Moderna are preferred over AstraZeneca in adults under 60 years of age and are recommended in people with a past history of cerebral venous sinus thrombosis (CVST), heparin induced thrombocytopenia (HIT), idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis or antiphospholipid syndrome with thrombosis. Pfizer and Moderna are also the preferred vaccines for pregnant women.
- People with immunocompromise may have a suboptimal immune response to vaccination and should be counselled to continue other protective measures against COVID-19 even after vaccination, such as physical distancing, wearing a face mask, practicing hand hygiene and isolation or quarantine as advised by public health authorities.
- On first principles, vaccination of household contacts is also recommended, when available, to provide indirect protection to people with immunocompromise.
- The primary course of COVID-19 vaccines (Pfizer, Moderna, and AstraZeneca) is 2 doses. For Pfizer, these doses should be given 3-6 weeks apart and for Moderna, two doses should be given, 4-6 weeks apart. Longer intervals may be recommended in special circumstances. For AstraZeneca, two doses should be given, preferably 12 weeks apart, however the interval can be shortened to as little as 4 weeks if required (e.g. if aiming to vaccinate before starting a new immunosuppressive therapy, or in outbreak settings, where an interval of 4-8 weeks is recommended).
- Severely immunocompromised individuals are recommended to receive a 3rd dose as part of their primary course to address the risk of suboptimal or non-response to the standard 2 dose schedule.
- Definitions of severe immunocompromise and recommendations on the use of the 3rd dose is available in the *ATAGI recommendations for the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised*.
- There is no established serological correlate of protection for COVID-19. Serology should not be used to confirm that an adequate vaccine response has been achieved, including after a 2nd or 3rd dose of COVID-19 vaccine in an immunocompromised individual.

Timing of vaccination

- For most people with immunocompromise, Pfizer, Moderna or AstraZeneca can be given at any time, and the main priority is to be vaccinated as early as possible.
- Active disease is not a contraindication to vaccination, though in those with severe illness, a short delay until the active disease is under control may be advisable to avoid incorrect attribution of vaccine-related adverse events to underlying acute illness and vice versa. As with any other vaccine, vaccination should be deferred in people who are febrile (fever ≥ 38.5°C).
- For people taking immunosuppressive therapies, the timing of vaccination should be discussed with their treating specialist, considering disease severity, characteristics of the immunosuppressive therapy, and patient preferences. In general, maintenance immunosuppression should not be withheld or deferred for vaccination, unless advised by the treating specialist.
- Deferring immunosuppressive therapy or deferring vaccination for a short period may be recommended in some circumstances, e.g., to allow for a better immune response to the vaccine or to reduce the risk of misattribution of adverse events from an immunosuppressive therapy to the vaccine or vice versa.
- Discuss the optimal timing of vaccination in people taking immunosuppressive therapy (particularly B-cell depleting therapies such as rituximab) with their treating specialist, to maximise the immune response to vaccination.
- For people taking immune checkpoint inhibitors, discuss the timing of vaccination with their treating specialist, to minimise the theoretical risk of immune-related adverse events being triggered by vaccination.
- For people who will be commencing a new immunosuppressive treatment that is likely to impair the immune response to vaccination, the vaccine course should ideally be completed 2-4 weeks prior to initiation of the immunosuppression. If required, the interval between doses can be reduced to 21 days for Pfizer and Moderna, and 28 days for AstraZeneca, to facilitate this.
- Allow at least 3 days of spacing if possible and avoid vaccination on the same day as a regular infusion (e.g., immunoglobulin replacement therapy, immunosuppressant infusion), to avoid incorrect attribution of vaccine-related adverse events to the infusion treatment or vice versa.
- Avoid vaccination during anticipated periods of neutropenia, or during periods of confirmed severe neutropenia (ANC < 0.5 x 10^9/L). This is to avoid fever, which may result in additional investigations being required to rule out other differential diagnoses (such as sepsis).
- Consider temporary deferral of vaccination or use additional precautions during periods of severe thrombocytopenia (e.g., platelet count < 50 x10^9/L). After vaccination, the injection site should not be rubbed, and firm pressure should be applied for 5-10 minutes. If a collection of blood develops, immobilise the area and apply an ice pack.
- For further information on the optimal timing of vaccination in people with immunocompromise, including recipients of solid organ or haematopoietic stem cell transplants, refer to the *Australian Immunisation Handbook: Vaccination for people who are immunocompromised.*

Younger children with immunosuppression

- There are no COVID-19 vaccines approved for use in children aged under 12 years in Australia at this time.
- Children are generally at low risk of severe illness from COVID-19, and off-label use of COVID-19 vaccines in this age group is not recommended.

Further reading

- ATAGI – Shared decision making guide for people with immunocompromise
- ATAGI recommendations on the use of a 3rd

A number of specialty societies have released statements with advice relating to COVID-19 vaccines specific for their patients, including:

- *The Haematology Society of Australia and New Zealand*
- *Australia and New Zealand Transplant and Cellular Therapies Ltd*
- *Gastroenterological Society of Australia*
- *Australian Rheumatology Association*
- *Cancer Australia*
- *The Australian and New Zealand Association of Neurologists and MS Australia*

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