Canadian Society of Transplantation
Société canadienne de transplantation
LEADERSHIP IN CANADIAN TRANSPLANTATION | LEADERSHIP EN TRANSPLANTATION AU CANADA

National Transplant Consensus Guidance on COVID-19 Vaccine

Introduction

The following document provides expert consensus guidance that can be used by provincial organ donation organizations and regional transplant and donation programs to guide the management of COVID-19 vaccination in transplant recipients in light of the pandemic. It is understood that each organization, program, and jurisdiction will develop their own policies.

Since the situation is rapidly evolving, going forward, regular teleconferences will be held with national experts to discuss and update this consensus guidance. These discussions, and the consensus itself, will continue to be informed by recommendations from the Canadian Society for Transplantation, Canadian Blood Services' advisory committees, Health Canada, Public Health Agency of Canada, WHO, provincial agencies, and international partners (including UK and Spain).

This document was last updated on **March 6th, 2021** and will continue to be updated as new evidence and information becomes available.

What do we know about COVID-19 and transplant recipients?

COVID-19 is a disease caused by the SARS-CoV-2 virus that is predominantly a respiratory virus but can cause multi-system disease. Several organ transplant recipients have contracted COVID-19 and symptoms have ranged from mild disease to the need for ICU care and death. Whether COVID-19 is more severe due to immunosuppression is unclear; however, many transplant patients also have other comorbid conditions such as advanced age, chronic kidney disease, diabetes, and heart/lung disease that put them at increased risk of severe COVID-19 disease. Lung transplant patients also seem to be at particularly high risk of severe disease.

What is the status of COVID-19 vaccines in Canada?

There are several formulations of the COVID-19 vaccine in various stages of development and/or approval.

mRNA Vaccines:
Two vaccines (Pfizer/BioNTech and Moderna vaccine) have been authorized for use by Health Canada. Both vaccines are composed of mRNA in a lipid nanoparticle and have specific storage conditions. In total, approximately 70,000 persons participated in placebo-controlled phase 3 trials with these vaccines. The Pfizer vaccine has an efficacy of 95% in immunocompetent persons and is for use in persons 16 years of age and older. The Moderna vaccine has a 94.1% efficacy and is for persons 18 years of age and older. Both vaccines are given as a two dose series.

Adenovirus Vector Vaccines:
Two vaccines (University of Oxford/AstraZeneca and Johnson & Johnson) have been authorized for use by Health Canada. Both vaccines are adenovirus vector vaccines that can be stored at 2-8C similar to standard vaccines. The Oxford/AZ vaccine uses a chimpanzee adenovirus vector to encode spike protein and has 62 to 90% efficacy in a

phase 3 trial. This is given as a 2-dose series 4-12 weeks apart. Due to lack of data in older populations, the National Advisory Committee on Immunization has recommended this vaccine for persons <=65 years of age. The J&J vaccine uses the Ad26 vector to encode spike protein and has 66% overall efficacy with its one dose preparation although has 86% efficacy in preventing severe disease. It is given as a single dose.

Vaccines may have reduced efficacy for circulating variants and therefore efforts are being made to study booster doses of vaccine that could be effective against SARS-CoV-2 variants.

What are the side effects of COVID-19 vaccine?

Local and systemic side effects can occur after any of the four vaccines. These include local tenderness, swelling, and erythema. Relatively common systemic symptoms include fever, myalgias, and headache. In the Pfizer vaccine trial, systemic symptoms were more common in younger age groups and after the second vaccine dose. Similarly, in the Moderna vaccine trial, there were more systemic events after the second dose. Adenovirus vector vaccines appear to have a similar side effect profile to mRNA vaccines. Systemic symptoms are similar to COVID-19 disease so patients receiving vaccine should be counseled on the possibility of these symptoms occurring in the first few days after each vaccine dose.

What data are available about the COVID-19 vaccine in transplant recipients?

Currently, there are no efficacy, immunogenicity, or safety data available for transplant patients with any COVID-19 vaccine. Transplant recipients were not enrolled in phase 3 studies of vaccine. However, with the licensure of vaccine in many countries, more information is expected. A recent publication describing 187 transplant recipients who were vaccinated with Pfizer and Moderna vaccines did not show any unexpected short-term local and systemic side effects of vaccine.

Can transplant patients receive the COVID-19 vaccine?

Although further data are needed, the opinion of experts is that transplant patients may receive any of the authorized COVID-19 vaccines. Experts believe that based on the mechanism of action of mRNA vaccine, there is no reason to suspect that adverse events will be any different than in the general population. Similarly, the adenovirus used in vector vaccines is nonreplicative and therefore, such vaccines can be given to transplant recipients. Therefore, transplant recipients can receive any currently authorized vaccine available to them, if age requirements are met. No data exist on the relative efficacy or immunogenicity in transplant patients. In summary, based on expert opinion, the potential benefits of vaccine likely outweigh theoretical risks. All vaccines lead to a vaccine-specific immune response and the generation of alloimmunity or rejection following vaccination is unlikely based on the mechanisms of the vaccines, and broad experience with other vaccines in the transplant population. For optimum vaccine efficacy, it is suggested that:

- When possible, vaccine be administered in the pre-transplant setting with the final dose at least 1-2 weeks prior to transplant
- It is not necessary to put a patient on hold for transplant while waiting for vaccination
- In post-transplant patients, wait at least 1 month after transplant to provide the vaccine regardless of induction therapy.
- Ideally, the full 2-dose series (Pfizer, Moderna, Oxford/AZ) should be given at the recommended interval. If the patient undergoes transplantation between the first and second doses, provide the second dose at > 1 month after transplant. Additional doses are not recommended.
- Prolonging dosing interval beyond that studied in phase 3 trials is not recommended for transplant recipients since immunogenicity may be lower and wane more quickly.
- In patients undergoing active treatment for acute rejection, vaccination can be deferred for a 1-month period.
- Avoid giving vaccine for at least 3 months after rituximab for improved efficacy
- If a patient has had COVID-19 before, wait 90 days from diagnosis and symptom recovery before giving COVID-19 vaccine.
- Since there are no vaccine coadministration studies, avoid giving other vaccines within 2 weeks of the COVID-19 vaccine dose.
- Vaccine should not be given to patients that have had an anaphylactic reaction to a known component of the vaccine (i.e., polyethylene glycol)
- Since efficacy is expected to be lower than the general population, it is strongly recommended that patients continue to practice infection control measures. In addition, household contacts of the transplant recipient should also be vaccinated when possible.

When will the vaccine be available for transplant patients?

In Canada, the priority groups are currently long-term care residents/workers, healthcare workers, and indigenous populations. Some transplant recipients have received vaccine as part of the priority groups. As of March 2021, vaccine is also being rolled-out by age group and some transplant recipients will be eligible due to age. Some provinces (eg, ON, BC) have also identified organ transplants as a priority population for vaccination and vaccination may begin for all transplant recipients regardless of age group either now or as soon as April 2021. The vaccine given may differ depending on the age of the transplant recipient. Provinces are also extending the interval between doses up to 4 months. One dose of a two-dose regimen is likely to have lower efficacy in transplant recipients compared to the general population. The durability of response to one dose of vaccine is also unclear. Therefore, where possible, transplant recipients should receive vaccine at standard intervals that were studied in clinical trials rather than extended intervals.

What about pediatric transplant patients?

The vaccines are currently not approved for children under 16 years of age, but once approved, we expect similar recommendations to apply to pediatric transplant recipients. Studies are currently ongoing for ages 12 and up.

What are the national and international recommendations?

The CDC Advisory Committee on Immunization Practices (ACIP;U.S.) and the Joint Committee on Vaccination and Immunisation (JCVI; U.K.) has stated that vaccine can be given to immunocompromised population when it becomes available. The JCVI has listed patients with a transplant as being a prioritized vulnerable population. The AST (American Society of Transplantation) and ISHLT (International Society for Heart and Lung Transplantation) have also recommended COVID-19 vaccine to be given to transplant patients when available. Health Canada and FDA have not contraindicated the vaccine for immunocompromised although have stated that there are no data on efficacy and adverse events in this population.

The National Advisory Committee on Immunization in Canada has updated its recommendations and stated that vaccination may be given to immunocompromised patients after considering the risk vs. benefits and letting individuals know that data on efficacy and safety are lacking. Efficacy may be lower in the immunosuppressed state and immunocompromised patients should continue to practice infection control measures against COVID-19.

Summary

Given that: (a) COVID can cause serious illness in a transplant recipient, (b) transplant recipients often have comorbidities, (c) the mechanism of action of vaccine is specific, and (d) transplantation is not a contraindication to COVID vaccine according to Health Canada, we recommend that vaccine may be given to the pre- and post-transplant patient population when it is available to them. Based on expert opinion, we recommend that the potential benefits of vaccine outweigh any theoretical risks or concerns about immunogenicity. *Due to the severity of COVID in this population, we also recommend that transplant patients be prioritized for vaccination.* Transplant patients should be made aware of the lack of safety and efficacy data and encouraged to report any adverse events.

Disclaimer

The guidance provided is not meant to replace clinical judgement. The field is also rapidly evolving and as such the guidance will likely change over time. Any clinical decisions should be made in consideration of the latest available information.

Endorsement

These guidelines were written and are regularly updated by Dr. Deepali Kumar and Dr. Atul Humar, in conjunction with the Transplant Infectious Diseases group at the UHN Ajmera Transplant Center and endorsed by the Canadian Society of Transplantation.

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