

Cell Therapy Transplant Canada
Position Statement on COVID-19 Vaccination

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There are currently four Health Canada approved vaccines for COVID-19, two based on mRNA technology (BNT162b2/tozinameran, developed by Pfizer/BioNTech, and mRNA-1273, developed by Moderna), and two based on non-replicating adenoviral vectors (ChAdOx1, developed by AstraZeneca, and Ad26.COV2.S, developed by Janssen). All four vaccines are authorized in Canada for individuals aged 18 and older, and the Pfizer/BioNTech vaccine can also be used for children aged 12 and older. Supplies are currently adequate, and individual provinces have been vaccinating eligible individuals based on the priority-based recommendations from the National Advisory Committee on Immunization (NACI). As such, recipients of stem cell transplantation and cellular therapy were included among the highest priority and by this time many may have already received their full course of a particular (or mixed doses of) COVID-19 vaccine.

COVID-19 infection in patients with hematologic malignancies, recipients of hematopoietic stem cell transplant (HSCT), or cellular therapies is associated with a high risk of poor outcomes and an overall mortality rate of 22-36% in adults,¹⁻³ and 6.6% in children.² These data highlight the importance of protecting recipients of stem cell transplantation and cellular therapy.

Immunocompromised patients were not included in the pivotal phase III trials that provided the basis for approval of any of these four vaccines.⁴⁻⁷ There are no studies currently ongoing specifically evaluating this patient population, and no studies are likely to be completed in the near future. Despite the lack of data, there is no evidence that these vaccines are more harmful than other inactivated (non-live) vaccines we currently administer to these patients. In addition, there is no risk of developing COVID from these vaccine products. In general, other vaccine products have not shown a risk of worsening acute or chronic graft versus host disease. These products have now been given to many immunocompromised patients, without any signal of significant toxicities.

Vaccine hesitancy may be an issue for some patients. Both AstraZeneca and Janssen vaccines have been associated with a very small risk of thromboembolic events (vaccine induced prothrombotic immune thrombocytopenia, or VIPIT). The evidence to date suggests this risk is incredibly small and there is no data that suggests the risk of VIPIT is higher in cancer patients or immunocompromised patients. Pediatric patients aged 12 and older are authorized to receive the Pfizer/BioNTech vaccine, and Moderna has published results and is seeking Canadian authorization to use the mRNA-1273 vaccine in adolescents

aged 12-17.⁸ In addition, both Pfizer and Moderna are currently running large pediatric trials to study the safety and effectiveness of using their COVID-19 mRNA vaccines for children under 12.

Patients that are immunocompromised typically do not develop the same immunologic response to the vaccine and might not benefit to the same degree as a member of the general public. That said, in most patients, given the very significant risk associated with COVID infection, the potential benefit associated with the vaccine is likely greater than any risks. Given that the immune response to the vaccine might be impaired in these patients, a strategy that includes vaccinations of caregivers of stem cell transplant and cellular therapy patients is also critical, to mitigate any risk of transmission within the household. Recent evidence in solid organ recipients showed increased antibody responses after a third dose of the Moderna vaccine.⁹ The province of Ontario has recently approved a third COVID-19 vaccine dose for vulnerable people, including transplant recipients and patients with hematological cancers, and has mandated vaccination policies for high-risk settings. Quebec has also implemented a policy to require all health-care workers to be vaccinated.

Based on the above premises, we have the following recommendations. Our recommendations for vaccination are aligned with recommendations issued by the American and European cellular therapy societies.^{10,11}

We recommend:

1. Physicians should discuss the risks and benefits of COVID vaccines with their patients and weigh the potential risks and benefits of vaccination. It is expected that in most circumstances, the recommendation will be to proceed with vaccination, given the probable safety of vaccination and the very significant risks of COVID-19 infection.
2. For patients in the first 3-6 months following allogeneic stem cell transplant, autologous cell transplant, CAR-T therapy, or on active immunosuppression, the timing of vaccination should be considered on a case-by-case basis. A more potent immune response will be obtained if the vaccine is administered at a minimum of 3 months post transplant.
3. For patients in the first 3-6 months following allogeneic stem cell transplant or CAR-T therapy, or on active immunosuppression, given uncertainty about the vaccine efficacy, vaccination of the health care teams providing care for them should be mandated. We also recommend encouraging caregivers and household contacts to get vaccinated. Household transmission is the most common mechanism for acquisition of COVID-19,

and a similar strategy as is used in long-term care facilities (vaccination of all those residing with high-risk patients) should be employed.

4. Eligible transplant and cellular therapy patients that have already received a full vaccination course should get a booster shot where available, to increase immunological response.
5. In general, most of the recommendations above could also apply to patients with other hematologic malignancies on active therapy, given their comparable risk.

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