Clinical Guidance on COVID-19 Vaccines for People with Solid Cancers

This guidance is intended for healthcare providers and is based on known evidence as of April 18, 2023.

This document relates to patients with solid tumours. For information on patients with hematological malignancies and those who have undergone hematopoietic stem cell transplant or CAR-T-cell therapy, please refer to the other guidance document for that patient population. For general information, please refer to BCCDC Guidance and information COVID-19 vaccines for providers.

Is COVID-19 immunization recommended for people with solid cancers?

COVID-19 vaccines should be encouraged for people with solid cancers and are not contraindicated, including those who have had COVID-19 infection. This recommendation is based on the following review:

• The National Advisory Committee on Immunization (NACI) recommends that immunosuppressed individuals be offered the vaccine if the benefits of vaccines outweigh the potential risks.1
• Patients with cancer have an increased risk of death related to COVID-19 infection.2-4
• The United Kingdom, the United States, France, and Australia have prioritized patients with cancer for COVID-19 immunizations, highlighting that this population is considered as having an increased COVID-19 risk.4-6

Is the COVID-19 vaccine efficacious and safe in patients with solid cancers?

There are data to suggest that the currently available COVID-19 vaccines have efficacy in patients with cancer or undergoing therapy for their cancer (cytotoxic chemotherapy, endocrine therapy, targeted therapy, immunotherapy) and/or radiation therapy (external-beam, brachytherapy, or systemic), while there may still be uncertainty as to the timing of immunization in relation to their cancer treatments.7-18

As with most vaccines, there may be a blunted immune response in individuals who are immunocompromised due to their disease or treatment. Patients with active cancer or undergoing active cancer treatment seemed to be generally excluded from the COVID-19 vaccine trials.19-21 However, in the COMIRNATY (Pfizer-BioNTech) vaccine trial, 3.9% of enrolled participants had a malignancy.22

There is one study that suggests that a third dose of COVID-19 vaccine in immunocompromised patients can increase
antibody levels. Small studies on third doses of the mRNA COVID-19 vaccines have shown that immunogenicity (immunity measured in the blood) may increase with a third dose. However, it is unclear how much antibody is needed for protection and/or the role of other immunological responses.

The frequency and severity of adverse events following vaccination with an mRNA COVID-19 vaccine in these populations were comparable to that of non-immunosuppressed individuals in these studies and what was reported in clinical trials. Safety data in these populations following vaccination with a viral vector vaccine is not available.

Informed consent should include discussion about the possibility that individuals who are immunosuppressed may have a diminished immune response to any of the authorized COVID-19 vaccines.

**Are there any specific contraindications or exceptions for people with solid cancers?**

Individuals who have had a severe allergic reaction to an ingredient of one type of COVID-19 vaccine are still able to receive future doses of the other type of vaccine. BCCDC has a list of the individual components and their purpose in the vaccines. For a complete list of components in the vaccine, consult the vaccine monographs found at: [www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19](http://www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19).

People with a history of anaphylaxis without known or obvious cause, and those with suspected hypersensitivity or non-anaphylactic allergy to COVID-19 vaccine components, are advised to consult with an allergist prior to immunization. Healthcare providers with patients with a history of severe allergic reactions should refer to the vaccine monographs to review the complete list of components. If there is a specific concern about a possible allergy to a component of the COVID-19 vaccine being administered, an extended period of observation for 30 minutes post-vaccination may be warranted. Alternatively, the vaccine can be administered in an emergency room setting with an extended observation period.

Potential allergens known to cause type I hypersensitivities include polyethylene glycol (PEG) in the mRNA vaccines and polysorbate 80 in the viral vector vaccines:

<table>
<thead>
<tr>
<th>Polyethylene glycol (PEG)</th>
<th>Polysorbate 80</th>
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<tbody>
<tr>
<td>COMIRNATY, COMIRNATY Bivalent(^{28,29}) (Pfizer-BioNTech)(^{19})</td>
<td>VAXZEVRIA (AstraZeneca)(^{21})</td>
</tr>
<tr>
<td>SPIKEVAX, SPIKEVAX Bivalent(^{30}) (Moderna)(^{20})</td>
<td>JCOVDEN (Janssen)(^{31})</td>
</tr>
<tr>
<td>NUVAXOVID (Novovax)(^{32})</td>
<td></td>
</tr>
</tbody>
</table>

Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.

Currently, it is recommended that COVID-19 vaccines can be given concomitantly with, or any time before or after any other indicated vaccine including the seasonal influenza vaccine.\(^{33-36}\)
Are there specific recommendations or considerations for safe and/or most effective administration?

There are no known studies regarding the timing of COVID-19 vaccine in relation to systemic therapy for cancer. The current vaccines reviewed in this clinical guidance are given as two doses (COMIRNATY, COMIRNATY Bivalent [Pfizer-BioNTech], SPIKEVAX, SPIKEVAX Bivalent [Moderna], VAXZEVRIA [AstraZeneca]). For the two-dose vaccines, optimal protection assumed after the second dose for the general population. The efficacy and duration of immunity after the first dose of a two-dose vaccine are continuously being evaluated and recommendations are evolving rapidly. The optimal protection and degree of protection, if any, in immunosuppressed individuals are currently unknown. Therefore, patients should be vaccinated following the current advice from the BC Centre for Disease Control.

The general recommendation for patients on cancer therapy is to proceed with COVID-19 immunization, with considerations outlined below in Table 2 and under Special Considerations for Immunotherapy. Patients with cancer who are undergoing chemotherapy or other cancer treatments that affect the immune system will be offered vaccination according to B.C.’s COVID-19 Immunization Plan. In general, it is preferred that patients complete immunization before starting immunosuppressive therapy if possible, ideally with at least 14 days after the second dose of the vaccines. However, there is emerging evidence that significant protection against severe illness and death is obtained even after the first dose of the two-dose vaccines. BCCDC recommends a third dose of vaccine at least 28 days after the second dose for immunocompromised.  

*However, life-saving or -prolonging therapy should not be delayed solely to complete immunization

Any other timing would require case-by-case assessment based on:

a. Risk of morbidity related to COVID-19 infection (including local incidence of the pandemic, cancer type, comorbidities that confer higher risk in the general population, etc.)

b. Cancer-related morbidity due to delay of active treatment, and

c. Suboptimal immunity protection due to insufficient time window between immunization and immunosuppressive therapy.

Recommendations for timing of COVID-19 immunization for patients aged 12 and above with solid malignancies starting or already receiving treatment (outside the setting of bone marrow, hematopoietic stem cell transplant, or CAR-T) are listed in Table 2 below.

Special considerations for immunotherapy:

The general recommendation for patients on immunotherapy is to proceed with COVID-19 immunization.*

a. Rituximab and other anti-CD20 monoclonal antibodies

Of note, patients receiving these agents may have a reduced immune response to vaccines in general that can extend up to 6 months following treatment completion. These patients may benefit from a 3rd dose of vaccine as per BCCDC guidance, to be given at least 28 days after the second dose.
b. **Checkpoint inhibitors**

Previous studies have not signalled an increased risk of complications of COVID-19 disease for patients on checkpoint inhibitors such as CTLA-4 inhibitors (e.g., ipilimumab), PD-1 inhibitors (e.g., nivolumab, pembrolizumab, cemiplimab) and PD-L1 inhibitors (e.g., atezolizumab, avelumab, durvalumab). There have been theoretical concerns of an enhanced immune reaction to COVID-19 vaccines, particularly with CTLA-4 inhibitors.

*Given the seriousness of COVID-19 infection, COVID-19 immunization is recommended with consideration of both the patient’s risk profile and immunotherapy regimen.*

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**Table 2. Suggested timing of vaccine injection and therapy for cancer**

<table>
<thead>
<tr>
<th>Population</th>
<th>When should patients receive COVID-19 vaccine?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunosuppressive therapy</strong>*</td>
<td>This follows the general vaccination guidelines for immunocompromised patients38-40:</td>
</tr>
</tbody>
</table>
| - **Before starting active treatment** | *First dose of two-dose vaccines (single dose if single-dose vaccine) at least 2 weeks before treatment*  
*For two-dose vaccines, second dose at least two weeks before treatment* |
| - **During cyclical treatment** | *In general, it is preferred that patients complete immunization before starting immunosuppressive therapy if possible, based on the timing of the treatments and the availability of vaccines at the time. However, life-saving or -prolonging therapy should not be delayed solely to complete immunization. Some immunity may be achieved following the first dose of the two-dose vaccines.*  
*For patients who received 2 doses while on or shortly after active treatment, a third dose is advised.* |
| - **During maintenance or non-cyclical treatment (e.g., rituximab given every 3 months)** | *First dose of two-dose vaccines (or single dose if single-dose vaccine) in the week before next treatment as this is when counts are likely to be the highest.*  
*For patients who received 2 doses while on or shortly after active treatment, a third dose is advised. This should also be given in the week before the next treatment.*  
*Note: Avoid on same day as treatment*  
*At any time during treatment* |
<table>
<thead>
<tr>
<th>Treatment/Condition</th>
<th>Timing</th>
</tr>
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<tbody>
<tr>
<td>Endocrine therapy, targeted therapy (including PARP inhibitors)</td>
<td>At any time during treatment</td>
</tr>
<tr>
<td>Systemic corticosteroids†</td>
<td>Ideally, systemic corticosteroids (at daily doses 20 mg or higher of prednisone or equivalent for 1 month or longer) should be avoided or completed at least 28 days before commencing the first vaccine dose when possible. If it is not possible, immunization should proceed. For patients who received 2 doses while on or shortly after this treatment, a third dose is advised.</td>
</tr>
<tr>
<td>Patients due to start radiation therapy</td>
<td>If immunization is pending, and it is possible to delay radiation therapy without compromising outcomes, radiation therapy should be postponed until anticipated immunity is achieved before commencing radiation therapy. Life-saving or prolonging therapy should not be delayed solely to complete immunization. For patients who received 2 doses while on or shortly after active treatment, a third dose is advised.</td>
</tr>
<tr>
<td>Patients on radiation therapy‡</td>
<td>At any time during treatment while blood counts are near normal range, ideally as early in the course of radiation therapy as possible.</td>
</tr>
<tr>
<td>Patients who have completed a course of radiation therapy or during a regimen of cyclical radio-isotope therapy‡</td>
<td>Radiation therapy can suppress lymphocyte counts for months to years after treatment in a dose- and volume-dependent fashion. As it is not known what level of WBC counts would alter vaccine efficacy, there is no specific blood count level to target for vaccine delivery; however, if the radiation therapy regimen§ is expected to cause transient myelosuppression for up to eight weeks, immunization should start at least one week after the nadir of myelosuppression.</td>
</tr>
</tbody>
</table>

* Immunosuppressive therapy – including but not limited to cytotoxic chemotherapy, rituximab, obinutuzumab, alemtuzumab
† This recommendation does not relate to inhaled, nebulized, intra-articular, intrabursal or topical corticosteroids, which have no bearing on immunization timing.
‡ Injection should be given on the opposite side if unilateral radiation treatment is, or was, given to area of injection site
§ Myelosuppression on radiation therapy regimens varies with dose, fractionation, and patient factors but typically examples of suppressive regimens include hemi-body, total body, total marrow, whole abdominal, craniospinal, or total skin radiation.
References


34. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 - Biological Products. SPIKEVAX. Updated 8 August 2022. Available at: www.bccdc.ca/health-
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