Background and Context

As of December 23, 2020, Health Canada has given interim authorization to two vaccines, Pfizer-BioNTech (BNT162b2)\(^1\) and Moderna (mRNA-1273)\(^2\) for the prevention of COVID-19 disease caused by the SARS-CoV-2 virus.

The risk of mortality from COVID-19 disease appears to be higher in patients with cancer.\(^3,4\) However, patients with cancer were generally excluded from the COVID-19 vaccine trials if they were immunosuppressed by disease or treatment;\(^5\) although 3.9% of patients in the Pfizer-BioNTech vaccine trial had a malignancy.\(^6\)

Therefore, there are uncertainties as to whether COVID-19 vaccine is efficacious and safe 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), as well as the timing of immunization in relation to their cancer treatments.
Is the COVID-19 vaccine recommended for patients with cancer or undergoing cancer therapy?

B.C. Cancer recommends that COVID-19 vaccines should not be withheld from individuals who meet criteria for immunization per B.C.’s COVID-19 Immunization Plan, including those who have had COVID-19 infection.

This recommendation is based on the following:
- The National Advisory Committee on Immunization (NACI) recommends that immunosuppressed individuals may be offered the vaccine if the benefits of vaccine outweigh the potential risks.\(^7\)
- Patients with cancer have an increased risk of death related to COVID-19 infection.\(^3,4\)
- The United Kingdom, the United States, France, and Australia have prioritized patients with cancer for COVID-19 immunizations.\(^5\)

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

It is unknown if the currently available COVID-19 vaccines are efficacious in patients with cancer or undergoing systemic therapy. As with most vaccines, there is a potential for diminished immune response in individuals who are immunocompromised due to their disease or treatment.\(^1,2\) In addition, patients with active cancer or undergoing active treatment for cancer seemed to be generally excluded from the COVID-19 vaccine trials, although the Pfizer-BioNTech vaccine trial included 3.9% of patients with a malignancy.\(^6\)

The above noted COVID-19 vaccines are likely safe in patients with cancer or undergoing therapy for cancer as they are NOT live or attenuated. There are currently no known factors that would predispose these individuals to adverse events associated with the vaccines.\(^1,2\) At the time of authorization, there are no known serious warnings or precautions associated with the vaccines in patients with cancer.\(^1,2\)

Individuals should not receive the vaccines if they have a history of severe allergic reaction to a component of the vaccines,\(^7\) including non-medicinal ingredients (see Table 1).\(^1,2\) Polysorbate (which is closely related to polyethylene glycol) is a common ingredient in multiple medications but any clinical implications of potential cross-allergic reactions are unknown.\(^9\) Patients who have had a previous anaphylactic reaction to any medicine should be counselled about the risk of a reaction to the vaccine against the benefits of immunization. Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.
Table 1. Non-medicinal ingredients\(^{12,7}\)

<table>
<thead>
<tr>
<th>Pfizer-BioNTech (BNT162b2)</th>
<th>Moderna (mRNA-1273)</th>
</tr>
</thead>
<tbody>
<tr>
<td>polyethylene glycol</td>
<td>polyethylene glycol</td>
</tr>
<tr>
<td>• ALC-0159 = 2-[[polyethylene glycol]-2000]-N,N-ditetradecylacetamide</td>
<td>• PEG2000 DMG 1,2-dimyristoylracglycerol, methoxy-polyethyleneglycol</td>
</tr>
<tr>
<td>1,2-distearoyl-sn-glycero-3-phosphocholine</td>
<td>1,2-distearoyl-sn-glycero-3-phosphocholine</td>
</tr>
<tr>
<td>ALC-0315 = (4-hydroxybutyl) azanediyl) bis(hexane-6,1-diy)bis(2-hexyldecanoate)</td>
<td>Lipid SM-102</td>
</tr>
<tr>
<td>Dibasic sodium phosphate dihydrate</td>
<td>Acetic acid</td>
</tr>
<tr>
<td>Monobasic potassium phosphate</td>
<td>Sodium acetate</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>Tromethamine</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>Tromethamine hydrochloride</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Sucrose</td>
</tr>
<tr>
<td>Water for injection</td>
<td>Water for injection</td>
</tr>
</tbody>
</table>

When should patients receive the COVID-19 vaccine?

There are no known studies regarding the timing of COVID-19 vaccine in relation to systemic therapy for cancer. Both vaccines are given as two injections with optimal protection assumed after the second dose of the Moderna vaccine and seven days after the second dose of the Pfizer-BioNTech vaccine for the general population. However, optimal protection and degree of protection, if any, in immunosuppressed individuals are currently unknown. The efficacy and duration of immunity after only one dose are unclear. Therefore, patients should be vaccinated with two injections as approved by Health Canada until further information is available.

According to B.C.’s COVID-19 Immunization Plan, COVID-19 vaccines will be offered to people who are deemed clinically extremely vulnerable starting from April 2021, including patients with cancers who are undergoing chemotherapy or other cancer treatments that can affect the immune system. 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. This should ideally be at least 14 days after the second dose of either vaccine, Pfizer BioNTech or Moderna.
This guidance is intended for oncologists and other health-care providers, and is based on known evidence as of January 22, 2021

*However, life-saving or prolonging therapy should not be delayed solely for the purposes of completing immunization.*

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

a. Risk of morbidity related to COVID-19 infection (including local prevalence of the pandemic, cancer type, comorbidities that confer higher risk categories in 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 adult patients with cancer commencing, or already receiving, treatment for their cancers outside the setting of hematopoietic stem cell transplant (HSCT) are listed in Table 2 below.

Special considerations for immunotherapy:

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 to up to 6 months following treatment completion.

b. **Checkpoint inhibitors**
   Previous studies have not signaled an increased risk of complications of COVID-19 for patients on checkpoint inhibitors such as CTLA-4 inhibitors (e.g., ipilimumab), PD-1 inhibitors (e.g., nivolumab, pembrolizumab) and PD-L1 inhibitors (e.g., atezolizumab, durvalumab). There have been theoretical concerns of an enhanced immune reaction particularly with CTLA-4 inhibitors. However, given the seriousness of COVID-19 infection, immunization is still recommended in this group even if a four-week window cannot be confirmed.

**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><strong>Pfizer-BioNTech vaccine:</strong></td>
</tr>
<tr>
<td>- <em>Before starting active treatment</em></td>
<td>- Two injections usually given with 21-42 days apart(^{10})</td>
</tr>
<tr>
<td></td>
<td>- Second injection at least two weeks before treatment*</td>
</tr>
<tr>
<td></td>
<td>- First injection at least five weeks before treatment</td>
</tr>
</tbody>
</table>

Released:

Next Review:

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Population | When should patients receive COVID-19 vaccine?
---|---
Modern mRNA vaccine:
- Two injections usually given with 28-42 days apart\textsuperscript{11}
- Second injection at least two weeks before treatment\textsuperscript{*}
- First injection at least six weeks before 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 for the purposes of completing immunization.

- **During cyclical treatment**
  First injection about one week before next treatment (i.e., one week after nadir of myelosuppression)

- **During maintenance or non-cyclical treatment (e.g., rituximab given every 3 months)**
  At any time during treatment

Endocrine therapy, targeted therapy (including PARP inhibitors)
At any time during treatment

Systemic corticosteroids\textsuperscript{†}
Ideally systemic corticosteroids (at daily doses $\geq 20$ mg prednisone or equivalent) should be avoided, or completed at least 28 days before commencing first vaccine dose when possible.\textsuperscript{8} If it is not possible, immunization should proceed.

Patients due to start radiation therapy
If immunization is pending, and it is possible to delay start of radiation therapy without compromising outcomes, start of radiation therapy should be delayed until anticipated immunity is achieved before commencing radiation therapy. Life-saving or prolonging therapy should not be delayed solely for the purposes of completing immunization.
Population | When should patients receive COVID-19 vaccine?  
--- | ---  
Patients on radiation therapy‡ | At any time during treatment while blood counts are near normal range, ideally as early in the course of radiation therapy as possible.  
Patients who have completed a course of radiation therapy or during a regimen of cyclical radioisotope therapy‡ | 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.

* 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

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