BC Cancer Influenza vaccine recommendations for adults with cancer

All adults with cancer should receive an age-appropriate **inactivated influenza vaccine**, if there are no contraindications to the vaccine.[1-4]

Table 1: Inactivated influenza vaccines for adults

Age Category / Living Situation	Funded influenza vaccines in British Columbia
All adults under 65 years	Quadrivalent inactivated influenza vaccine (FLUZONE® QUADRIVALENT, FLULAVAL® TETRA)[5]
Adults 65 years and up • Residing in the community	Adjuvanted trivalent inactivated influenza vaccine (FLUAD®)[6]
Adults 65 years and up • Residing in long-term care, assisted living, or First Nations Community	High-dose quadrivalent inactivated influenza vaccine (FLUZONE® HIGH DOSE QUADRIVALENT)[6]

Live attenuated influenza vaccine (intranasal FLUMIST®) is NOT recommended for adults actively receiving cancer treatment, however it may be considered for patients if their cancer is in remission and it has been at least 3 months since their last chemotherapy and/or radiation treatment, or at least 6 months after anti B-cell antibody (i.e. rituximab), and their T cell function is normal.[3,4]

Family, care providers, and close contacts of people with cancer should receive either the inactivated or live attenuated influenza vaccine if not contraindicated, however those receiving the live attenuated influenza vaccine should avoid close contact with patients who are severely immunocompromised for at least 2 weeks following vaccination due to the theoretical risk for transmitting the vaccine virus.[2-4]

Table 2: Influenza vaccine – Timing in adults with cancer

Patient population	When should patients ideally receive the influenza vaccine?	
Before starting chemotherapy	At least 2 weeks before starting first round of chemotherapy to maximize immunogenicity (if feasible depending on the urgency of chemotherapy), or the live influenza vaccine at least 4 weeks before.	
On chemotherapy *(may include treatment with rituximab)*	Within 2 to 3 days before the next chemotherapy cycle (preferred if feasible)	
On maintenance rituximab *(e.g., given every 3 months)*	At any time during maintenance therapy	
On targeted therapy	At any time during treatment	
On radiation therapy	At any time during treatment while blood counts are near normal range *(vaccine should be given on the opposite side if unilateral treatment is given)*	
On checkpoint inhibitor immunotherapy	At any time during therapy *(see Additional timing considerations below)*	PD-1 inhibitors: cemiplimab, nivolumab, pembrolizumab PD-L1 inhibitors: atezolizumab, avelumab, durvalumab CTLA-4 inhibitors: ipilimumab, tremelimumab Combination CTLA-4/PD-1 inhibitors: ipilimumab + nivolumab
The recommendations in this table do not apply to Hematopoietic Stem Cell Transplant (HSCT) patients. For more information, discuss with physician or see HSCT recommendations.		

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Influenza vaccine – Additional timing considerations:

The influenza vaccine may administered at the same time, or at any time before or after the administration of other vaccines, including the COVID-19 vaccine.[3,7]

General timing with chemotherapy:
While administration of the inactivated vaccine at any time before, during, or after immune-suppressing cancer treatment is safe, its efficacy may be reduced.[4,11]

Patients should ideally receive the influenza vaccine at least 2 weeks before starting chemotherapy to allow time for adequate antibody production, if feasible depending on the urgency of chemotherapy.[1,2,4]

If a patient has already started receiving chemotherapy, they can safely receive the influenza vaccine at any time during chemo treatment, however consensus is to give the vaccine within 2 to 3 days before the next chemotherapy cycle when blood counts are most likely near the normal range and patients have recovered from their last cycle. Although the optimal timing for efficacy when administering the influenza vaccine in patients on chemotherapy is not clear, this timing is recommended to avoid the confusion around the cause of mild flu-like symptoms, or infusion-related or other injection-related reactions, if the patient were to receive the vaccine on the day of or soon after receiving chemotherapy.[8-10] Such reactions may affect a patient's current or subsequent chemotherapy cycle if the reaction is thought to be infection- or chemotherapy-related.

Timing with rituximab therapy:
Patients receiving maintenance rituximab therapy can receive the influenza vaccine at any time during maintenance therapy. While it is safe for these patients to receive the influenza vaccine, several small studies suggest that patients receiving rituximab have a reduced immune response to the influenza vaccine.[12-13] Although response to the influenza vaccine may be inadequate in these patients, consensus is that patients on maintenance rituximab may receive the vaccine at anytime even if there is a reduced response.

Timing with immune checkpoint inhibitors:
Patients receiving immune checkpoint inhibitors (PD-1, PD-L1, and CTLA-4 inhibitors alone or in combination) can receive the influenza vaccine at any time during therapy. Early anecdotal reports found cases of severe immune-related adverse events (irAEs) in patients on combination CTLA-4/PD-1 inhibitor therapy after receiving the influenza vaccine.[14] Additionally, an early study suggested a risk of severe irAEs associated with influenza vaccination in patients receiving a PD-1 inhibitor.[15] Two recent systematic reviews, however, found that in most subsequent and larger studies, the overall safety and efficacy of influenza vaccination in patients receiving immune checkpoint inhibitors was not substantially different from that observed in the general population, and that vaccination does not increase the risk of irAEs compared to unvaccinated patients.[16-17] Most patients in the systematic reviews received PD-1 inhibitors, but PD-L1 inhibitors and combination CTLA-4/PD-1 inhibitors were also represented in much smaller patient numbers.[16-18] Despite limited safety data in patients receiving combination CTLA-4/PD-1 inhibitors, no new data have emerged that suggest an increased risk of severe irAEs with influenza vaccination. Where feasible, patients receiving combination CTLA-4/PD-1 inhibitor therapy should receive the influenza vaccine prior to starting treatment. For patients experiencing a severe irAE with combination CTLA-4/PD-1 inhibitor therapy, consideration should be given to deferring influenza vaccination, especially given that combination therapy is of limited duration.

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