Influenza vaccine recommendations for adults with cancer

We recommend that providers should offer an age-appropriate inactivated influenza vaccine to all patients without contraindications to the vaccine.[1-4] The high dose inactivated influenza vaccine is Health Canada approved for adults age 65 and older and is publically funded in BC for adults age 65 and older who live in long term care facilities or assisted living facilities.[5]

Currently, there is not enough information to recommend the high dose over the standard dose inactivated influenza vaccine in the general oncology population.

Influenza vaccine type	Population	When should patients receive the influenza vaccine?
Inactivated influenza vaccine: recommended if not medically contraindicated **LIVE attenuated influenza vaccine** (e.g. intranasal FluMist®): **NOT** recommended	Patients before starting active chemotherapy	Ideal: 2 weeks or longer before first round of chemotherapy Minimum: 2 days prior to starting chemotherapy
	Patients on active chemotherapy, including treatment with rituximab	Within 2 to 3 days prior to the next chemotherapy cycle
	Patients on maintenance rituximab therapy (e.g. given every 3 months)	At any time during maintenance therapy
	Patients on targeted therapy	At any time during treatment
	Patients on radiation therapy	At any time during treatment while blood counts are near normal range* *Injection should be given on the opposite side if unilateral treatment is given

	Patients on checkpoint inhibitor immunotherapy	Depends on the immunotherapy regimen:
		• PD-1 inhibitor (e.g. pembrolizumab, nivolumab) or PD-L1 inhibitor (e.g. atezolizumab, durvalumab) monotherapy:
		  ○ at any time during therapy
		• CTLA-4 inhibitor, alone (e.g. ipilimumab, tremelimumab) or in combination (e.g. ipilimumab + nivolumab):
		  ○ should **NOT** receive any vaccine within 4 to 6 weeks of starting treatment or within 4 to 6 weeks of last dose

Family, care providers and close contacts of patients with cancer should be encouraged to consider receiving either inactivated or live attenuated influenza vaccine if not contraindicated.[2,6]		

These recommendations do not apply to Hematopoietic Stem Cell Transplant (HSCT) patients. For more information, discuss with physician or see here for HSCT recommendations.

When should patients receive the influenza vaccine? Details on timing.

Patients should ideally receive the influenza vaccine 2 weeks before starting active chemotherapy to allow for adequate antibody production, although some protection may be afforded before that time.[3] We still recommend that patients receive the influenza vaccine within 2 weeks, but minimum 2 days before starting, over not receiving the vaccine at all. This timing may result in reduced efficacy but is still safe.

Similarly if active chemotherapy is started, we recommend that patients receive the influenza vaccine 2-3 days before their next chemotherapy cycle when blood counts are likely near normal range. Although the optimal timing for efficacy when administering the influenza vaccine in patients on active chemotherapy is not clear,[7-9] this timing is recommended to avoid the confusion around the cause of mild flu-like symptoms, infusion-related or other injection-related reactions if the patient were to receive the vaccine around the day of or soon after receiving chemotherapy. Such reactions may affect a patient's current or subsequent chemotherapy cycle if the reaction is thought to be infection- or chemotherapy-related.

Patients on maintenance rituximab therapy can receive the influenza vaccine anytime during maintenance therapy. While it is safe for these patients to receive the influenza vaccine, several small studies suggested that patients receiving rituximab have a reduced immune response to the influenza vaccine.[10-12] However, patients can still be offered the influenza vaccine for the chance of generating some immune response, rather than none at all.

Although the optimal window to receive the influenza vaccine for patients on CTLA-4 inhibitors (monotherapy or combination therapy) is unknown, we recommend these patients should not receive the influenza vaccine within 4 to 6 weeks of starting treatment or within 4 to 6 weeks of last dose.[13] Anecdotal reports found cases of severe immune related adverse events in patients on combination ipilimumab and nivolumab after receiving the influenza vaccine.[14] This adverse reaction is suspected to be more related to ipilimumab than nivolumab.

The influenza vaccine appears to be safe for patients on other immune checkpoint inhibitors such as anti-PD-1 inhibitors, PD-L1 inhibitors. While early studies suggested a risk of severe immune related adverse events associated with the influenza vaccine in patients receiving immune checkpoint inhibitors, a recent large observational study suggested that there is not an increase in the incidence or severity of new onset immune related adverse events in patients on immune checkpoint inhibitors who receive the influenza vaccine.[15]

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