



Patient and Caregiver Immunotherapy Guide



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PATIENT GUIDE

IMMUNOTHERAPY BASICS FOR COLORECTAL CANCER



*What is the right care
for me?*

Treating colorectal cancer today is different than it was a few decades ago. In the past if you had colorectal cancer, you might have received the standard therapy used for all people with colorectal cancer. This might include surgical interventions, radiation, or chemotherapy. With the advancements in research, we now understand colorectal cancer better. We now know that two people may have very different kinds of tumours at the cellular (molecular or genetic) level. This requires a personalized treatment approach, a management strategy that targets the tumour specific to the individual type.

Since every individual has different tumor specifications, the question arises: how do we identify tumour types?

We identify tumour specifications with a diagnostic procedure called biomarker testing. Biomarker testing allows health care providers to uncover specific genetic and molecular characteristics which can help them refine and provide a specific care plan for you.

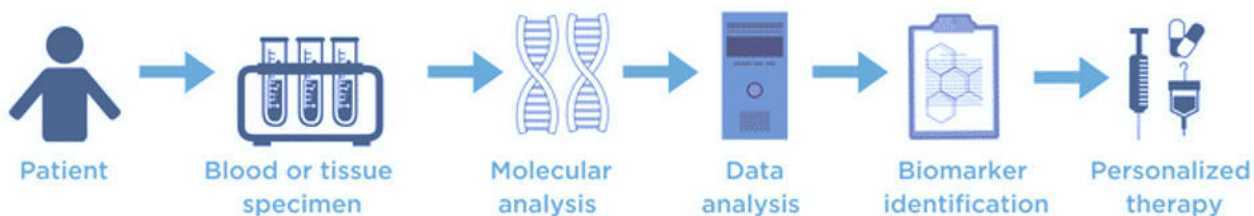


What is the role of biomarkers in personalized medicine?

Biomarkers or biological markers are molecules found in body tissues and fluid, including tumour tissue and blood. They are sometimes referred to as tumour markers or molecular markers. When specific biomarkers are present, it tells your doctors valuable information about your colorectal cancer type and can also help to determine whether a particular treatment, specifically immunotherapy treatment will be effective for you.

With biomarker testing we can evaluate whether colorectal cancer of your tumour specifications would be eligible for immunotherapy or not.

Role of a Biomarker





What is Immunotherapy?

Although a relatively newer treatment strategy, immunotherapy is being actively researched for the past few decades. Currently, many immunotherapy agents have become standardized therapeutic options for many different cancer types. Immunotherapy now plays a critical role in improving prognoses of patients with cancers that were previously incurable.

Immunotherapy is a type of treatment that uses a person's own immune system to fight cancer. Originally, the immune system is responsible for attacking foreign/harmful substances like bacteria, viruses, and cancer cells. But cancer cells can hide from the immune system preventing any attacks thereby causing growth of the tumor. With immunotherapy, the cancer cells are no longer hidden. The immune system can identify them as harmful and initiate attack.

Immunotherapy is designed to stimulate an immune reaction against cancer cells, enabling the body to fight the disease more effectively. Immunotherapy strengthens the immune system's ability to fight cancer.

How does immunotherapy work?

Immunotherapy essentially involves priming your natural immune defenses to recognize, target, and destroy cancer cells effectively.

Immunotherapy acts on the body's immune system, intervening in the communication between a specialized type of immune cell, the T cell, and the target tumour cells. PD-1 is one protein that is expressed on the surface of cells. It plays a role in controlling the immune system's response so that it does not attack our own cells. PD-1 is involved in preventing autoimmune diseases, but it can also prevent the immune system from effectively attacking cancer cells.

An important approach in immunotherapy has been to target PD-1. PD-1 is a receptor that acts as a "lock" that can only be opened or activated when it comes in contact with the right "key", or ligand, known as PD-L1. PD-1/PD-L1 activation causes a decrease in immune activity. By blocking this interaction with PD-1/PD-L1 inhibitors, the brake on the immune system is lifted and the T cells are able to attack cancer cells more effectively.



Immunotherapy in Colorectal Cancer

The treatments that have found to be effective in treating colorectal cancer are:

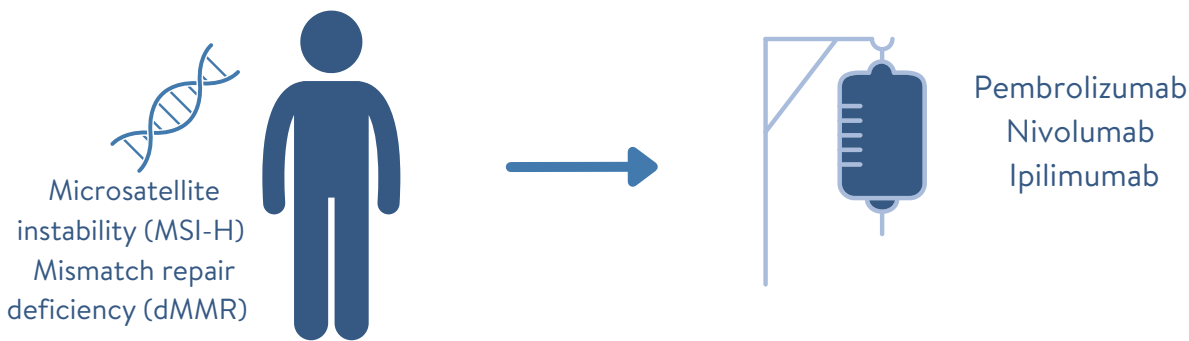
- Pembrolizumab (Keytruda ®), given through intravenous infusion
- Nivolumab (Opdivo®), given through intravenous infusion
- Ipilimumab (Yervoy®), given through intravenous infusion

*Ipilimumab is typically used in combination with nivolumab.



How do I know if immunotherapy is for me?

In the treatment of colorectal cancer, immunotherapy has so far been shown to be effective in a small subset of patients. 15% of advanced colorectal cancer cases are known to have genetic mutations that do not respond well to standard therapy and could be potential candidates for immunotherapy. Those include colorectal cancer tumours expressing the following genetic mutations:



Recent advances in clinical research have found that immunotherapeutic drugs are an effective and viable treatment option for this subset of patients with the aforementioned mutations.

When diagnosed with colorectal cancer, the primary requisite is to have active discussions with your healthcare provider regarding your medical decisions and goals.

If your doctor does not include biomarker testing as part of standard of care, make sure to ask them for one to know if immunotherapy is for you.

It's important that biomarker testing required for your personal situation occurs as early as possible to guide your care and treatment plan. If you are diagnosed with stage IV metastatic colorectal cancer, you should be tested for at least three predictive biomarkers: RAS, BRAF, and MSI/dMMR. Specifically, testing for MSI/dMMR can help match you to immunotherapy. Information about these specific biomarkers will guide treatment decisions and offer insight into how effective treatments will be for you. Testing for other biomarkers may also inform treatment options. As research advances- the number of biomarkers discovered will increase.

More information on biomarker testing can be found on our website: [What Patients Need to Know](#)

ACCESSING IMMUNOTHERAPY

 *Is immunotherapy covered by the health insurance plan?*

In 2021, the CADTH pCODR Expert Review Committee (pERC) recommended that pembrolizumab should be reimbursed as monotherapy for the first-line treatment of metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (cite).

This means that patients starting first-line treatment will be able to have reimbursed access to pembrolizumab (Keytruda) in all institutions across Canada.

Colorectal cancer patients do not have reimbursed access to nivolumab and ipilimumab, just as yet.



The cost of biomarker testing may vary depending on your institution and immunotherapy can vary depending on your source of access (if applicable). But testing is rapidly becoming standard practice across Canada.

For instance, if participating in a clinical trial, there should be no costs incurred on the medical consumption, but you might have to pay for your travel and other miscellaneous costs. When participating in the trial, make sure to confirm with the investigators as to compensation offered, if any.



What are clinical trials?

Clinical trials are research studies performed in people that evaluate new ways of preventing, detecting, treating or managing cancer or other diseases. Immunotherapy being a novel approach to cancer treatments is the focus of many clinical trials in Canada. Participating in a clinical trial that has evidence of improving prognosis for your specific tumor can primarily be life saving for you and secondarily advance research for future patients.



How to join a clinical trial?

You can do the following to join a clinical trial:

- Speak with your healthcare team and inquire for eligible clinical trials
- Contact one of our Patient Support Specialists at CCC
- Access these Canadian Clinical Trials Resources (see below)

It Starts With Me

www.itstartswithme.ca is the central resource created by N2 Canada to help potential participants, families, caregivers, and the general public to understand basics about clinical trials and clinical research.

Canadian Cancer Clinical Trials Network (3CTN) Clinical Trials Navigator

3CTN's Clinical Trials Navigator can help patients with cancer search and connect to clinical trials they may be eligible for. The patient begins by filling out a Consent Form, or their physician may fill out a Referral Form. The patient is connected with the Clinical Trials Navigator, which will help them search for all eligible trials. Contact the Clinical Trials Navigator at clinicaltrialsnavigator@wrh.on.ca; P: (519) 253- 3191 ext. 58583 F: (519) 253- 8102

Canadian Cancer Trials Database

This Canadian database enables you to filter your clinical trial search by cancer type, province, city/town, as well as by drug, age, and other specifics of your disease. The site also provides an option to sign up for trial alerts, which will notify you by e-mail when a new trial for a selected type of cancer or locations becomes available.

Health Canada's Clinical Trials Database

Provides a listing of specific information relating to phase I, II and III clinical trials in patients. You can contact Health Canada support staff directly by email or telephone for assistance.

You can visit the CCC website for more information on national and provincial [clinical trial resources](#).

The [MERCK Access program](#) is an initiative to ease accessing Pembrolizumab for colorectal cancer.

UNDERSTANDING THE DIFFERENT THERAPIES

Pembrolizumab (Keytruda®)

The KEYNOTE-177 trial showed that pembrolizumab significantly extended progression-free survival (the amount of time from the beginning of treatment to when the cancer progresses or worsens) when it was used as initial treatment for patients with MSI-H or dMMR advanced colorectal cancer compared to standard of care chemotherapy. Pembrolizumab also caused far fewer side effects.


Pembrolizumab is currently approved by Health Canada, and is reimbursed by provincial health care plans for colorectal cancer. Some drugs may be accessible through compassionate access or expanded access programs.

Nivolumab (Opdivo®) and Ipilimumab (Yervoy®)

Nivolumab and ipilimumab are immunotherapy drugs given in combination for the treatment of MSI-H/dMMR advanced colorectal cancer that did not respond to previous chemotherapy. The CheckMate 142 trial found that the combination of nivolumab plus low-dose ipilimumab in the first-line treatment of patients with metastatic colorectal tumours that are MSI-H/dMMR produced very positive outcomes in patients, and caused far fewer side effects compared to chemotherapy. The confirmatory phase III trial, CheckMate-8HW is currently in progress.

Nivolumab and ipilimumab are currently approved by Health Canada for the treatment of advanced colorectal cancer, though it is still not covered by provincial health care plans. However, if immunotherapy could be right for you, talk to your medical team as some drugs may be accessible through compassionate access or expanded access programs.

MANAGING IMMUNOTHERAPY

 *What types of questions should I be asking my healthcare provider about immunotherapy?*

- What are the treatment options for my tumour type? What is their reimbursement program like?
- Are there any financial bursary programs with immunotherapy?
- What clinical trials are applicable for me and how do I access them?
- If there is no immunotherapy program approved for me, is there any other treatment or clinical trial I should look out for?
- Will I be receiving only immunotherapy or other treatments as well?

- What short-term and long-term side effects are expected with immunotherapy?
- How are the side effects different from traditional chemotherapy?
- Will I be immunocompromised with immunotherapy?
- How long does the treatment last?
- What will the treatment experience be like? How do I better prepare myself?
- How will the therapy affect my day-to-day activities?
- Will the therapy have an impact on my fertility?
- Is there another patient I can talk to about their experience with immunotherapy?
- Are there any dietary or lifestyle restrictions or precautions with this therapy that I should be mindful of?
- Are there any restrictions on smoking, alcohol, and substance habits with this therapy?

 *How frequently will I receive immunotherapy? And how long is the course of treatment?*

The frequency and duration of your treatment will be tailored according to the specifics of your cancer. Your healthcare provider will draw out a care pathway for you with a detailed plan of management. Generally, immunotherapy is given intravenously between every 2 weeks to every 6 weeks.

 *What side effects should I watch out for or report?*

Remember that not all patients will experience all of the side effects mentioned above. If you do experience any side effects, be sure to talk to your medical team immediately to learn about options to help manage and prevent the worsening of side effects. Most side effects will go away entirely once treatment has ended; however, some side effects can be cumulative and may become more severe with time or when given in combination with other drugs.



Common side effects of Immunotherapy for CRC

Common side effects of Pembrolizumab

Feeling tired
Itching
Rash
Constipation
Pain in muscles, bones/joints and abdomen
Diarrhea
Nausea
Shortness of breath
Cough
Fever
Decreased appetite

Common side effects of Nivolumab

Feeling tired
Decreased appetite
Cough
Diarrhea
Itching
Rash
Nausea/vomiting

Common side effects of Ipilimumab

Feeling tired
Diarrhea
Nausea
Itching
Rash
Vomiting
Headache
Weight loss
Fever
Decreased appetite
Difficulty falling or staying asleep

Your oncologist will discuss all side effects more thoroughly, including the rare ones. Make sure to enquire how to best manage your side effects.



How do I manage the side effects?

Side effects of immunotherapy depend on the type of treatment and the individual's baseline health. Talk to your health care provider about the possible side effects and management strategies.

Supportive care is provided by the healthcare team to prevent or treat side effects. Always keep the team posted of your experience with the therapy irrespective of how serious it is.

Depending on the severity of your side effects, the health care team will alter your treatment and continue monitoring accordingly.

Being proactive in the decision making of your cancer care is key. Having a clear conversation about the expected side effects and management essentials with the treatment is important before you start your journey with immunotherapy. <https://redefining-cancer-treatment.ca/> is a great resource for gathering more patient centered experiences and information regarding immunotherapy and coping mechanisms.

What resources can I use for more support and information?

Colorectal Cancer Canada is here for you every step of the way. If you can't find what you are looking for, please do not hesitate to contact us at info@colorectalcancercanada.com.

Support Groups

Colorectal Cancer Canada offers a variety of different support groups with trained staff and social workers. These support groups are offered monthly and allow you to meet with colorectal cancer patients and caregivers and ask questions that you may have about immunotherapy.

Website & Social Media

Colorectal Cancer Canada's social media pages and website will keep you informed on all updates regarding immunotherapy for colorectal cancer and patient experiences. Find our social media by searching for Colorectal Cancer Canada on Facebook, or following @ColonCanada on Twitter and Instagram. Our website: www.colorectalcancercanada.com



CAREGIVER GUIDE




GIVING CARE TO YOUR CARE PARTNER

How can I better accommodate my loved one's needs during their course of immunotherapy?

Cancer is as much of a journey for the caregiver as it is for the patient. To accommodate your loved one's needs during their course of immunotherapy, you can help in the following ways:

- Be involved in medical discussions and decisions with the health care team.
- Provide care and be present with your loved one during the treatment and consultations with the health care team.
- Provide emotional support, positivity, and strength throughout their journey.
- Prepare a financial plan for the cancer management.
- Gather information and resources for the therapy.
- Keep all records of your loved one and ensure their compliance to the visits.
- Self-care is essential to be there for your loved one



What questions should I be asking the healthcare team about my loved one's treatment?

- Is immunotherapy the best choice of management for my care partner?
- What would the care pathway and timeline look like?
- What is the expected frequency and duration of this therapy?
- What has the experience of other patients been like with immunotherapy?
- How should we access the treatment?
- How can we better prepare for the treatment?
- Are there any dietary or lifestyle restrictions or precautions with this therapy that we need to be mindful of?
- Are there any restrictions on smoking, alcohol, and substance habits with this therapy?
- How do we inform the health care team in case of an emergency?
- What are the expected outcomes with the therapy and till when can we expect to see results or measure progress?
- What side effects are expected with the immunotherapy?
- How would we manage the side effects?

How do I help manage the side effects?

To help manage the side effects:

Primarily, discuss expected side effects, their duration, frequency, and monitoring guidelines with the health care provider. Note down the management tips mentioned by the provider and act accordingly.

Few side effects may be experienced as soon as the therapy is provided and others may accumulate over time. It is best to monitor your loved one's health, inform the team, and follow their advice.

Conclusion

Immunotherapy is a product of the advances in science over decades. It provides an opportunity for patients when alternate methods of treatment do not seem to work. If you are diagnosed with colorectal cancer, and if you are eligible for immunotherapy, be proactive about the discussions involving access, treatment specifics, cost, duration, expected outcomes, and logistics.

Do not hesitate to reach out to Colorectal Cancer Canada. Our team of trained staff and social workers are ready to answer all your questions and support you as needed throughout your journey.





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