

LEARNING ABOUT

COLORECTAL CANCER



Treatment Options for Colorectal Cancer: A Guide for Patients

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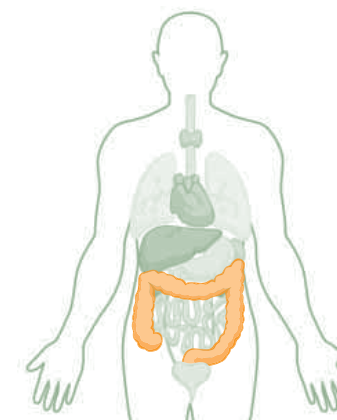
The goal of this guide is to help you learn about colorectal cancer, treatment options available to you, and strategies to help you manage the disease while maintaining your well-being. It also discusses current research and looks at future therapies in colorectal cancer. For your convenience, you can find a glossary at the end of this booklet, to help you better understand the terminology used in colorectal cancer.

The contents of this guide have been independently reviewed and approved by the appropriate medically qualified experts.

Colorectal cancer grows slowly, usually in a predictable way, and when diagnosed at an early stage, it is often curable.

What is Colorectal Cancer?

Cancers that start in the cells that line the inside of the colon (the longest part of the large intestine) and rectum (the last few inches of the large intestine before the anus) are called colorectal cancers. The colon and rectum form the large intestine (large bowel), which is the last portion of the digestive system. The digestive system, which is made up of the esophagus, stomach, and small and large intestines, extracts and processes nutrients (vitamins, minerals, carbohydrates, fats and proteins) from food and helps pass waste material out of the body.



The important news about colorectal cancer is that it usually starts from a pre-cancerous growth called a polyp and grows slowly, usually in a predictable way. It therefore can be preventable with screening, and when diagnosed at an early stage, it is often curable.



Stages of Colorectal Cancer

Once a cancer diagnosis is made, the cancer will be described by a stage and grade. Colorectal cancer staging describes the size of the tumour, how far it has grown into the colon or rectum wall, and whether the cancer has spread to lymph nodes or other places in the body past the place where it began to grow. Colorectal cancer has five stages:

Treatment for colorectal cancer will depend on its stage and grade. Knowing the stage and grade of the cancer can help you and your healthcare team decide which treatment is best for you.

Stage 0 – Cancer cells are located only in the inner lining of the colon or rectum. Typically, this is confined to the surface of a *polyp* (a growth that protrudes from a mucous membrane). It is also known as *carcinoma in situ*.

Stage 1 – Cancer cells have spread from the inner lining into the middle layers of the muscular wall of the colon or rectum.

Stage 2 – Cancer has spread to the outside surface of the colon or rectum, and may involve nearby tissues but not the *lymph nodes*.

Stage 3 – Cancer involves the nearby *lymph nodes*.

Stage 4 – Cancer has spread to other distant parts of the body, such as the liver or lungs.

In addition to the cancer stage, it is also useful to determine the grade of the cancer. To determine the grade of a tumour, a *biopsy* sample is examined under a microscope. Comparing the cancer cells look and behaviour to normal cells will enable a determination of the grade and help enable your doctor to estimate how quickly the cancer may be growing. Colorectal cancer has three grades:

Grade 1 or Low grade – typically means that cancer is slow growing, also known as well differentiated.

Grade 2 or Moderate grade – also known as intermediate differentiation.

Grade 3 or High grade – means that cancer is faster growing, also known as poorly differentiated.

Note: Items in italics are further defined in the Colorectal Cancer Terminology section.

What are the Treatment Options?

Your treatment will depend on your general health as well as the type, stage and grade of the cancer. For colorectal cancer, your treatment may include a combination of surgery, *radiation therapy*, *chemotherapy* and *biological therapy*. Working together with your healthcare team, you will decide what treatments will be best for you. You may be invited to take part in a *clinical trial* to test newer treatment options or combinations.

Treatment for colorectal cancer includes one or more of the following:

Surgery

Surgery is the main treatment for colorectal cancer. Surgery is used to cure the cancer in the early stages by completely removing the tumour and tissues affected by it. It's occasionally possible that surgery may also be offered to people whose tumours have returned in the pelvis or spread to the liver or the lungs. For people with disease that cannot be removed in total, surgery may be offered to help relieve the symptoms of cancer.

The size of the tumour and its location (where it is in the intestine) will determine which surgery is right for you.

Different surgical procedures are used to remove tumours depending on their size, location, how far they have grown into the wall of the colon or rectum, and the amount of colon or rectum that needs to be removed. For removal of small early cancers such as cancerous polyps, a tube (or scope) is inserted through the rectum, while for larger tumours removal of the part of the intestine containing the cancer is usually necessary. If a part of the intestine is removed, the remaining healthy parts of the intestine are sewn together. If this can't be done immediately, a temporary colostomy may be performed where an opening will be made in the abdomen and the colon will be pulled through this opening to the outside of the body. This will help the body pass the waste directly from the colon through the opening in the skin and into a bag, which can be emptied regularly. Because every patient is different,



for some a colostomy may be permanent while for others it may only be needed until the operation site heals and after about 2-3 months the colostomy can be removed (or reversed). Your healthcare professional team will teach you how to manage a colostomy and allow you to continue to participate in everyday activities.

For some patients with colorectal cancer that has spread only to the liver, specialized surgery may be an option to remove liver metastases if they are small or few in number.

Radiation therapy for rectal cancer (also called *radiotherapy*)

During radiation therapy, high doses of a special type of energy (radiation) are aimed at the area where the cancer is growing and destroys cells, making it impossible for them to grow and divide. Radiation therapy destroys cancer cells, which grow uncontrollably, but it also can damage healthy cells nearby. The good news is that healthy cells are able to repair themselves after the therapy is complete.

There are two types of radiation therapy that can be used: *external beam radiation therapy* and occasionally *brachytherapy*. In external beam radiation, the beam of radiation is directed at the tumour. In *brachytherapy*, radioactive material is placed inside the tumour, making it possible to treat the cancer in a very focused manner.

Radiation therapy is more commonly used to treat rectal cancer. It is rarely used for colon cancer because the colon is quite mobile and cancers, even when on the surface, tend to push away from nearby structures and the local risk of contamination by the cancer is low. The small intestine is also nearby and it further limits the sorts of radiation dosage that might be necessary.

The opposite is however true for the rectum, where local spread can readily contaminate the side-wall of the pelvis and in addition the small intestine is at a safe distance. This means the radiation oncologist can deliver high doses of the cancer-killing radiation more safely for rectal cancers either before or after surgery. It is following the detailed pathology analysis of rectal cancers that a decision about the need for radiation is usually reached.

Side effects that may be experienced after radiation are a feeling of being more tired than usual, occasionally diarrhea, and perhaps changes to the skin such as redness

or tenderness in the area of the body where the treatment was applied. These side effects are temporary and will usually go away when the treatment period is over and the normal cells have had the chance to repair themselves, usually within one to two weeks.

Chemotherapy

Commonly drugs are used to treat the different stages of colorectal cancer. *Chemotherapy* is the use of anti-cancer medicines (chemotherapy drugs) that are typically given by injection, or sometimes as pills, to destroy cancer cells.

First, a word about how these drugs are named. When a drug's name is shown beginning with an upper case letter (such as **E**loxatin®) this is the name chosen by the manufacturer. Eloxatin is also known as oxaliplatin, spelled in lower case. This is known as the drug's generic name, which is the version of the drug's name that is, for example, more often used by doctors. We have tended to use both formats in this guide thus:

Eloxatin (oxaliplatin) is an important drug used in the management of colorectal cancer....

While chemotherapy drugs work to destroy cancer cells and prevent cancer cells from growing and spreading, they also damage healthy cells just like radiation, and may cause side effects. Damage to healthy cells is temporary and they will repair themselves after the treatment stops.

Some of the side effects you may experience include nausea, vomiting, soreness in the mouth, loss of appetite, tiredness, hair loss, diarrhea, neurotoxicity, an increased risk of infection, and bleeding. Your health team will carefully monitor any side effects and provide medications that are effective in reducing the symptoms.



Chemotherapy treatment may be given before or after surgery. It may be used:

- 1) Before surgery (*neoadjuvant therapy*) and sometimes combined with radiation therapy to shrink a rectal tumour;
- 2) After surgery to destroy any microscopic cancer cells left behind and therefore to reduce the risk of the cancer coming back (*adjuvant therapy*); or
- 3) To help slow down and control the cancer when the cancer has spread to distant organs. This is also called “palliative chemotherapy” where the goal is to control symptoms and extend life but, ultimately, the cancer is not curable.

In many cases, a combination of chemotherapy drugs is used. For example 5-FU with Leucovorin (usually referred to as 5-FU/FA or 5-FU/LV) PLUS, Eloxatin (FOLFOX).

The types of chemotherapy drugs, and certainly the doses and schedules, vary for each patient and the treatment plan will depend on your unique situation. The most commonly used chemotherapy drugs utilized to treat colorectal cancer are fluorouracil (5-FU, Adrucil®) and folinic acid (Leucovorin®, which is added to increase the effectiveness of 5-FU). 5-FU has been used for many years and its effectiveness proven. Newer drugs include oxaliplatin (Eloxatin), irinotecan (Camptosar®, CPT-11), capecitabine (Xeloda®) (this is an 5-FU in pill form), and raltitrexed (Tomudex®) (may be used instead of 5-FU for patients with advanced colorectal cancer who are unable to tolerate 5-FU).

Chemotherapy for Primary Colon Cancer

For people with *primary colorectal cancer* that is at high risk for recurrence (stage 3 and high-risk stage 2 colon cancer), the most common chemotherapy combination used as *adjuvant therapy* is **FOLFOX**: folinic acid (Leucovorin), fluorouracil (5-FU, Adrucil), oxaliplatin (Eloxatin) given intravenously every two weeks for a planned total of 12 treatments. For people who are not able to tolerate the FOLFOX treatment regimen, oral capecitabine (Xeloda) may be used instead.

Chemotherapy for Advanced or Metastatic Colorectal Cancer

There are several choices of chemotherapy for advanced or metastatic colorectal cancer, which are decided upon in discussion with your medical oncologist, and tailored specifically to your situation. In general terms, the most common

chemotherapy combinations used to treat advanced or metastatic colorectal cancer include:

- 1) **FOLFOX**: folinic acid (Leucovorin), fluorouracil (5-FU, Adrucil), oxaliplatin (Eloxatin);
- 2) **FOLFIRI**: folinic acid (Leucovorin), fluorouracil (5-FU, Adrucil), irinotecan (Camptosar, CPT-11);
- 3) FOLFOX together with bevacizumab (Avastin®) (a *targeted biological therapy*) as first or second choice therapy;
- 4) FOLFIRI taken together with bevacizumab;
- 5) Capecitabine (Xeloda) taken instead of 5-FU combination treatments. In exceptional circumstances, raltitrexed (Tomudex) may be taken instead of 5-FU for people who can't tolerate 5-FU. Cetuximab (Erbix®) is another type of targeted biological therapy, which may be taken alone, or in combination with irinotecan after previous chemotherapy treatments have failed.

Biological therapy

Biological therapy is also a newer approach that may be used to treat some stages of colorectal cancer. This form of therapy uses the immune system to fight cancer or to help lessen the side effects of other cancer treatments by using natural body substances or drugs to strengthen the body's immune system and boost its own defences. Some biological drugs can target certain cells without damaging healthy cells (*targeted therapy*). Combining biological therapy with the now standard treatments such as 5-FU, Leucovorin and Eloxatin (**FOLFOX**), offer the hope of even better outcomes in the future.

As with all chemotherapy treatments you may experience side effects. Because everyone responds to treatment differently, your side effects may be different as well. Talk to your healthcare team to learn ways to manage these.



The most common biological (targeted) therapy drugs used are bevacizumab (Avastin) and cetuximab (Erbix). Both bevacizumab and cetuximab are *monoclonal antibodies*.

Avastin is currently available in Canada for the treatment of metastatic cancer of the colon and rectum. Avastin targets the vascular endothelial growth factor (VEGF), which is one of the main proteins (substances) made by cells used to help build blood vessels that make small tumours grow larger. Avastin works by sticking to VEGF and stopping blood vessels from reaching a tumour. Without blood supply, the tumour dies. Avastin also improves how chemotherapy drugs work by helping carry these drugs directly to the tumour. In recent studies, it was shown that when Avastin was taken together with 5-FU based chemotherapy regimens it improved their effectiveness in treating advanced colorectal cancer.

Talk to your healthcare professionals if you have any questions or concerns about your treatments.

Erbix works by targeting the epidermal growth factor receptor (EGFR) on the cancer cell. EGF receptors help cancer cells grow and survive by transmitting signals to these cells. Erbix sticks to these receptors, which cuts off this signal transmission to cancer cells and causes these cells to die. There are several situations where Erbix may benefit some people more than others. For example, Erbix will only work in people who have EGF receptor molecules on the outside of their cancer cells (EGFR-positive) (note: sometimes given with EGFR-negative).

Also, people who had been treated with irinotecan chemotherapy and whose cancer stopped responding to this drug can benefit from Erbix when taken together with irinotecan or by itself.

Because drugs, doses and schedules may vary from person to person, your doctor will decide on the treatment plan that is best suited for you. The side effects will be different depending on the type of therapy.

Eloxatin and the Treatment of Colorectal Cancer

What is Eloxatin?

Eloxatin, also referred to as oxaliplatin, is a chemotherapy drug used to treat people with both localized and *metastatic* colorectal cancer. Eloxatin is typically used together with 5-fluorouracil (5-FU) and leucovorin to treat people with Stage 3 (lymph-node positive) colon cancers after surgery to remove the tumour.

How does Eloxatin work?

Eloxatin is a derivative of platinum that can prevent cancer cells from dividing.

Who should not take Eloxatin?

Eloxatin should not be given to people who are allergic to oxaliplatin or other platinum-containing ingredients or to other ingredients in the product. People with severe kidney disease, and women who are pregnant or breast-feeding should not use Eloxatin.

How well does Eloxatin work in treating colorectal cancer?

Clinical trials have demonstrated that Eloxatin is a very effective drug in the treatment of colorectal cancer.

In a large recent *clinical trial* of 795 people with metastatic colorectal cancer, those who received Eloxatin together with 5-FU/LV (*FOLFOX*) showed a significant improvement compared to patients receiving other conventional treatments. In patients on Eloxatin and 5-FU/LV, their cancer growth slowed down resulting in a longer life than patients who received other drug combinations.

In another large, international clinical trial, 2246 people with stage 2 or 3 colon cancer who had surgery to completely remove the primary tumour received Eloxatin with 5-FU/LV (*FOLFOX*) or 5-FU/LV alone. The results of this study showed that people with stage 3 cancer who received *FOLFOX* had a longer, cancer-free life than people who received only 5-FU/LV.



What are the side effects of Eloxatin?

Like many chemotherapy medicines, you may experience side effects with Eloxatin. Most side effects are manageable, but occasionally it may be necessary to stop the treatment.

Side effects include nausea, diarrhea, vomiting, fatigue (tiredness), stomatitis (sores in the mouth), low blood counts, pain at the injection site, respiratory (breathing) problems, and neuropathy (nerve changes that can be felt as tingling or numbness in hands and feet, muscle weakness and other changes in sensations).

Ways to help prevent and manage neuropathy

One of the most common triggers of Eloxatin neuropathy is exposure to cold. To help prevent unpleasant nerve sensations, try not to touch cold or frozen objects, consume cold foods or drinks, and breathe cold air.

Pharyngeal dysphasia (a feeling of tightness or discomfort in the throat which makes it difficult to breathe or swallow) is an occasional symptom of neuropathy. This symptom may be frightening, but it is only a sensation and does not actually interfere with breathing. It usually takes a few minutes for this sensation to go away on its own.

Some other symptoms of neuropathy may interfere with everyday activities such as writing, buttoning clothes, swallowing, difficulty walking and picking up things.

While many symptoms of neuropathy are temporary, they may continue for a long time. Again your healthcare team will support and guide you.

Like most other chemotherapy drugs, Eloxatin can also lower the number of white blood cells (neutropenia), red blood cells (anemia) and platelets (thrombocytopenia). White blood cells help your body fight infection, and if their number is lower than normal, you are at higher risk of having an infection. Most people receiving Eloxatin who have neutropenia do not develop infections.

When you have a lower than normal number of platelets (cells that help blood clot and control the bleeding), you may be prone to bleeding. Anemia (a lower than normal number of red blood cells) can make you feel tired.

To make sure that your blood cell numbers are under control, your doctor will check your blood count regularly.

There are effective medications to help control a low white or red blood cell count. Sometimes blood transfusion is used to remedy the situation and often, with the passage of a bit of time, your body will replenish the blood levels on their own.

Other possible side effects include constipation, stomach pain, loss of appetite and hair loss.

Talk to your doctor immediately if you are experiencing persistent vomiting, diarrhea or cough, fever or signs of infection (redness or swelling at the injection site, cough that brings up mucus or sore throat), allergic reactions (trouble breathing, tightness in the throat, rash, hives or swelling of the lips or tongue), and neuropathy symptoms that interfere with daily activities.

Talk to your doctor if you are experiencing side effects.

Ongoing Research and the Future of Treatment

Ongoing research in colorectal cancer has led to advances in treatment and new ways to manage side effects related to treatment, which has helped improve the outlook and quality of life for many people living with this disease.

Always in search of more effective treatments, many *clinical trials* are done to test different combinations of drugs that are already used separately to treat colorectal cancer. More clinical trials are studying the addition of *targeted therapy* such as bevacizumab or cetuximab to chemotherapy as first, second and third-choice therapies.



Clinical trials that are currently underway include:

- 1) Cetuximab (Erbix) and/or bevacizumab (Avastin) together with combination chemotherapy in treating metastatic colorectal cancer;
- 2) Oxaliplatin (Eloxatin), leucovorin and fluorouracil with or without bevacizumab in treating people who had surgery for stage 2 colon cancer;
- 3) Chemotherapy with or without bevacizumab in treating patients with stage 2 or stage 3 rectal cancer; and
- 4) Combination chemotherapy with or without bevacizumab in metastatic or *locally advanced* colorectal cancer that cannot be removed with surgery.

In addition to the existing targeted therapies, new drugs are being developed. New treatments such as panitumumab (Vectibix®) (a drug similar to cetuximab) are being investigated in clinical trials as a choice treatment in colorectal cancer.

Because of ongoing research, new discoveries help contribute to constant change in knowledge and understanding of cancer. This information helps researchers and healthcare professionals to develop practices in prevention, detection and treatment of colorectal cancer, as well as improving the quality of life of people with this disease.

Colorectal Cancer Terminology

5-fluorouracil (5-FU): A drug used as a treatment usually for colorectal cancer. It is a type of anti-metabolite (a drug that is very similar to natural chemicals in normal cellular reactions but different enough to interfere with cell division and function).

5-FU/FA: See 5-FU/LV.

5-FU/LV: Chemotherapy regimen drugs commonly used together — fluorouracil (5-FU, Adrucil) and folinic acid (Leucovorin). Also referred to as 5-FU/FA.

Adjuvant therapy: Treatment given after the primary (main) treatment is received, and all visible signs of the cancer removed, to help increase the chances of a cure. Adjuvant therapy may include chemotherapy, radiation therapy, biological therapy or other therapy. (See also Neoadjuvant therapy.)

Biological therapy: Type of therapy that uses the immune system to fight cancer or to help lessen the side effects of other cancer treatments by using natural body substances or drugs to strengthen the body's immune system and boost its own defences. Some biological drugs can target certain cells without damaging healthy cells. (See also targeted therapy.)

Biopsy: A procedure in which a sample of cancerous tissue is removed for analysis under the microscope to help precisely diagnose the type of cancer and its grade.

Brachytherapy: A type of contact radiation therapy that uses a sealed radioactive source (an implant), which is placed in or near the tumour, and makes it possible to treat cancer with high radiation doses in a very focused manner.

Carcinoma in situ: A group of severely abnormal cells that are confined to the tissue in which they first formed, but they may become overtly cancerous and infiltrate into nearby normal tissue. In the bowel, in-situ carcinoma is typically seen on the surface of a polyp.



Chemotherapy: Drug treatments that help destroy cancer cells by interfering with the cancer cells ability to divide. These drug treatments are typically given every few weeks thereby allowing normal tissues and blood counts to recover in the interval.

Clinical Trial: A research study designed to answer a question about the effectiveness of new therapies or new ways of using already existing therapies, and determine whether they are safe and effective.

External beam radiation therapy: A machine located outside the body is used to direct radiation at the cancer and surrounding tissue. This type of radiation is used to treat most types of cancer and it is done on an outpatient basis. Patients typically receive one treatment every day from Monday through Friday and a course of treatment may continue for several weeks.

FOLFIRI: Chemotherapy regimen, which includes a combination of folinic acid (Leucovorin), fluorouracil (5-FU, Adrucil) and irinotecan (Camptosar, CPT-11).

FOLFOX: Chemotherapy regimen, which includes a combination of folinic acid (Leucovorin), fluorouracil (5-FU, Adrucil) and oxaliplatin (Eloxatin).

Immunotherapy: see Biological Therapy.

Leucovorin: Medicine (drug) used to increase the antitumour effects of fluorouracil and tegafur-uracil, a pill treatment alternative to fluorouracil that is injected into the vein. It is also used to help protect normal cells from high doses of the anticancer drug methotrexate.

Lymph node: Also called lymph gland, is a rounded mass of lymphatic tissue. Lymph nodes filter lymph (lymphatic fluid) and can trap for a while cancer cells that are leaving an organ. In the bowel, lymph nodes are present on the surface of the bowel and along the blood vessels going to the bowel. Removing them is an important aspect of the initial surgery. When the lymph nodes are involved in colorectal (bowel) cancers, the Stage automatically becomes 3 (or 4 if distant organs are also involved).

Locally advanced cancer: A descriptive term to describe cancer that has spread from where it started on the inner surface of the bowel, through the bowel wall to involve nearby tissues or lymph nodes.

Metastatic: A cancer that has spread from where it started (primary tumour) to other (distant) parts of the body such as the liver and lungs.

Monoclonal antibody: A substance such as protein, which is made in the laboratory. These antibodies are designed to have an exact attraction for certain molecules found on the surface of cells and those that are part of cancer. Monoclonal antibodies are designed to target the malignant cells that form the tumour. (See also Targeted therapy and Biological therapy.)

Neoadjuvant therapy: Treatment given before the primary surgical treatment. Examples of neoadjuvant therapy include chemotherapy and radiation therapy. Neoadjuvant therapy is usually given to make the surgery easier and more effective. (See also Adjuvant therapy.)

Polyp: A growth that protrudes from a mucous membrane, which is the moist inner lining of cavities such as the nose, mouth, stomach and bowel.

Primary colorectal cancer: Here the word "primary" describes where the cancer originated. In this case a cancer starting in the bowel (specifically the colon or rectum).

Radiation therapy (also called radiotherapy): The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors. (See also External beam radiation therapy and brachytherapy.)

Targeted therapy: Type of biological therapy that works by targeting or aiming at specific molecules or proteins that play a role in cancer cell growth and spread. People with metastatic colorectal cancer can receive targeted therapy, but more studies need to be completed before biological therapies are used for treating early stages of colorectal cancer. (See also Biological Therapy.)



Where to Find Support...

Colorectal cancer is the second leading cause of death from cancer in Canada. One in 14 men is expected to develop colorectal cancer during their lifetime and one in 28 will die of it. In women, one in 16 is expected to develop colorectal cancer during their lifetime and one in 31 will die of it. Death from colorectal cancer continues to decline in both men and women due to improvements in treatments, especially chemotherapy. Screening for colorectal cancer can lower the risk of getting it and dying from it.

If you or someone close to you has been newly diagnosed with colorectal cancer or is in active treatment, you don't have to go through this alone.

Colorectal cancer support groups exist in several communities across Canada that offer meetings where patients, caregivers and families can share their experiences, offer help and provide information. Because everyone's cancer experience is different, connecting with others who are going through similar experience can help you learn how to deal with many everyday issues, make tough decisions and cope with a range of emotions.

For more information or to find a support group in your area, call our toll-free number 1-877-50COLON (26566) or visit our website at www.colorectal-cancer.ca.

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WHILE EVERY EFFORT HAS BEEN MADE TO ENSURE ACCURACY IN THIS BOOKLET AS TO CURRENT MEDICAL PRACTICE IN CANADA, IT CANNOT BE FULLY COMPREHENSIVE. INDIVIDUAL NEEDS VARY AND THE BOOKLET SHOULD NOT BE USED AS A SUBSTITUTE FOR PROPER MEDICAL CARE.

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Colorectal Cancer
Association of Canada

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